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Comorbid diseases in patients with lichen planus in Jordan: A comparative case control Study

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ABSTRACT

Lichen Planus (LP) is an immune mediated inflammatory skin condition characterized by the presence of pruritic purplish papular rash. We aimed to assess comorbid conditions such as diabetes mellitus, dyslipidemias, metabolic syndrome, vitamin D deficiency, hypothyroidism, hepatitis C virus, and autoimmune disease in lichen planus patients in Jordan. A case-control study was conducted among 102 cases with age and gender-matched 102 controls. A thorough clinical exam and blood testing of fasting blood glucose, lipid profile, Vitamin D and B12, thyroid function, uric acid, and hepatitis C status were done. The mean age of patients was 43.7± 16 years, and females predominated 58 (57%). The cases had higher levels of blood glucose (p-value 0.03), LDL (0.001), TG (p-value 0.001), total cholesterol (p-value 0.001), uric acid (p-value 0.001) and systolic blood pressure (p-value 0.001), and lower levels of HDL (p-value 0.001), vitamin D (p-value 0.001), and T4 (p-value 0.001) compared to controls. However, there was no significant difference regarding TSH, B12, and hepatitis C status. After adjustment of age and gender, linear regression revealed that all findings were similar. The study revealed that LP patients had significant alternations with comorbid conditions such as high blood glucose, dyslipidemias, low thyroid hormone, low vitamin D levels, low uric acid levels, and high blood pressure.

Keywords: *Lichen planus comorbidities, Diabetes, Dyslipidemia, Jordan, thyroid disease.*

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INTRODUCTION

Lichen Planus (LP) is an idiopathic T cell-mediated inflammatory disorder of the skin and the mucus membrane. The wrists, lower back, and ankles are the most typical locations for its pruritic, violaceous papules and plaques to form. Overlying the lesions is a lattice-like network of white lines known as Wickham striae, best seen on the buccal mucosa, where erosions can also be present [1–5].

According to the prevailing theory behind the pathogenesis of LP, contact allergens, drugs, and viruses can all modify epidermal self-antigens and activate cytotoxic CD8+ T cells. T-cell targeting and death come from the changed self-antigens cross-reaction with the usual self-antigens on basal keratinocytes [6–10].

Numerous agents have been linked to the development of LP, but the link with viruses, particularly the hepatitis C virus, has received considerable attention (HCV). Patients with LP are five times more likely than the general population to test positive for HCV, and those who are already HCV-positive are 2.5 to 4.5 times more likely to develop LP [11–13].

There are many differences in the natural history of LP. Most cutaneous lesions in individuals spontaneously disappear within 1 to 2 years after initial manifestation. However, recurrences are frequent, and persistent skin darkening frequently follows [14]. Oral LP, in contrast, is a persistent condition that may or may not resolve away [15]. Drug-induced LP progressively fades away after stopping the offending drug [16].

In adults worldwide, cutaneous LP affects 0.2% to 1% of them (1). More frequently reported in 1% to 4% of the population is oral LP. Overall, women are affected 1.5 times more commonly than males, and most cases appear between 30 and 60 [17]. Children make up fewer than 5% of all LP cases; thus, it is uncommon in them [18]. Recent studies found that African Americans and people of Indian and Arabian heritage have a greater incidence of LP. Given that up to 10% of first-degree relatives of patients may also contract the illness, there does seem to be a familial component [19].

Many reports have found discrepancies in blood parameters in LP patients compared to healthy subjects; Diabetes mellitus, Dyslipidemias, metabolic syndrome, vitamin D deficiency, hypothyroidism, Hepatitis C virus, and autoimmune disease were found to be associated with LP [20–25]. Nevertheless, the evidence regarding LP comorbidities is growing; hence, this study was conducted to evaluate the blood profile and comorbidities of LP patients in Jordan.

MATERIALS AND METHODS

The study utilized a case-control design; the study was conducted among LP patients who attended the outpatient clinic of Jerash teaching hospital from October 2019 to November 2021. All patients diagnosed with LP for longer than two months were included. Controls were patients who attended the clinic for other reasons. Those who have been diagnosed with psoriasis, vitiligo, alopecia areata, eczema, pregnant and lactating women, patients who are known to have diabetes, hypertension, gout, pernicious anemia, or received B12 injection over the last six months, received blood transfusion over the last six months, received vitamin D over the last six months thyroid dysfunction or on thyroxin, patients using lipid-lowering drugs and patients who had received any systemic treatment for LP including oral corticosteroids, retinoids, metronidazole, cyclosporine, allopurinol or colchicine, and methotrexate, in the past six were all excluded to eliminate confounding.

Data collection was done using a structured data collection sheet, including socio-demographic information, lichen planus type, duration of disease, and family history. Blood pressure was measured using a sphygmomanometer.

Venous samples were taken from all patients and controls after an overnight fast of at least an eighth for measuring:

Plasma fasting glucose using glucose oxidase method.

Serum lipid levels (LDL, HDL, TG) using enzymatic procedures.

Vitamin B12 level was measured using a competitive-binding immunoenzymatic assay.

Vitamin D level using the Elecsys Vitamin D total II Cobas test described by Roche.

Uric acid level using uric acid Enzymatic colorimetric method

TSH and T4 were assayed by radioimmunoassay

Hepatitis C antibody using enzyme-linked immunosorbent assay method

Data were cleaned and entered into a Microsoft Excel datasheet, then imported and analyzed using SPSS version 28 software. Categorical data was represented in the form of frequencies and proportions, and continuous data in the form of mean and standard deviation. Comparison between cases and controls was made using analysis of variance, and multivariate analysis was conducted through linear regression test. MS Excel and MS word were used to obtain graphs such as bar diagrams. Data was represented after analysis in the form of uni-variable tables, bi-variable tables, figures, and narrative illustrations. The research protocol was approved by the IRB at Yarmouk University number (Rd/119/11).

RESULTS

The study was conducted in 102 patients with Lichen planus and age and gender-matched 102 controls. The mean age of patients was 43.7± 16 years, while the mean age of controls was 44± 14 years with no significant difference (p-value 0.07). Among cases, males were 44 (43%), and females were 58 (57%), while among controls, males were 40 (39%), and females were 62 (61%) (p-value 0.6) (Table 1).

TABLE 1: Demographic characteristics

	Control	Case	Total	p-value
Age	43.7± 16	44± 14	44± 15	0.7
Gender				0.6
Male	44 (43%)	40 (39%)	84 (41%)	
Female	58 (57%)	62 (61%)	120 (59%)	

Regarding lichen planus patients, a family history of lichen planus was found in 4 (4%), the mean duration of the disease was 15± 8.7 months (Table 2), and the commonest type was the classical subtype 58 (56.9%) (Figure 1).

TABLE 2: Clinical characteristics

	Frequency (%)
Family history	4 (4%)
Duration	15± 8.7

Comparison of blood profile between cases and controls revealed that there was a statistical difference between cases and controls in all parameters except TSH, B12, and hepatitis C status. Compared to controls, lichen planus patients had significantly higher bold glucose levels (116.3± 35 mg/dL Vs. 105.2± 38 mg/dL, p-value 0.03), lower HDL level (42.4± 4 mg/dL Vs. 47± 5mg/dL, p-value 0.001), higher LDL level (145± 16 mg/dL Vs. 130.8± 10 mg/dL, p-value 0.001), higher triglycerides level (156.5 ± 16 mg/dL Vs. 139± 12 mg/dL, p-value 0.001), lower total cholesterol level (176± 27 mg/dL Vs. 188.9± 42 mg/dL, p-value 0.01), lower vitamin D level (8± 3 ng/L Vs. 14± 5 ng/L, p-value 0.001), lower T4 level (13.9± 2 ng/mL Vs. 15.6± 2 ng/mL, p-value 0.001), lower uric acid level (3.6± 1 mg/dL Vs. 5.3± 2 mg/dL, p-value 0.001), and higher blood pressure level; systolic (133± 7 mmHg Vs. 130.9± 7 mmHg, p-value 0.04), and diastolic (82.3± 5 mmHg Vs. 80± 5 mmHg, p-value 0.007) (Table 3). After adjustment of age and gender, linear regression revealed that all findings were similar (Table 4).

TABLE 3: Comparison of blood tests

	Control	Case	Total	P-value
Glucose	105.2± 38	116.3± 35	110.7± 37	0.03
HDL	47± 5	42.4± 4	44.8± 5	0.001
LDL	130.8± 10	145± 16	137± 15	0.001
TG	139± 12	156.5± 16	147.9± 17	0.001
Total cholesterol	176± 27	200± 48	188± 37	0.001
Vitamin D	14± 5	8± 3	11.4± 6.8	0.001
TSH	3.7± 3	4.2± 2	4± 2.8	0.2
T4	15.6± 2	13.9± 2	14.7± 2.5	0.001
Uric acid	5.3± 2	3.6± 1	4.4± 1.8	0.001
B12	258± 68	240± 70	249± 70	0.07
Systolic BP	130.9± 7	133± 7	132± 7	0.04
Diastolic BP	80± 5	82.3± 5	81± 5	0.007
Hepatitis C+	1 (1%)	2 (2%)	3 (1.5%)	0.5
Hepatitis C-	101 (99%)	100 (98%)	201 (98.5%)	

TABLE 4: Factors affecting blood tests

	Disease (Case/Control)	Age (getting older)	Gender (female/male)
Glucose	10.2 (0.01*)	1.4 (0.001)	1.1 (0.7)
HDL	-4.8 (0.001*)	0.1 (0.001)	-0.3 (0.5)
LDL	14 (0.001*)	0.4 (0.001)	-1.5 (0.3)
TG	17 (0.001*)	0.01 (0.8)	-0.6 (0.7)
Total cholesterol	24.8 (0.001*)	-0.1 (0.5)	2.4 (0.6)
Vitamin D	3.2 (0.001*)	-0.02 (0.3)	-0.5 (0.4)
TSH	0.4 (0.2)	0.01 (0.2)	-0.09 (0.8)
T4	-1.7 (0.001*)	-0.002 (0.8)	0.2 (0.5)
Uric acid	-1.7 (0.001*)	-0.005 (0.5)	-0.08 (0.7)
B12	-17 (0.07)	0.05 (0.8)	10 (0.3)
Systolic BP	2 (0.03*)	-0.004 (0.9)	-1.9 (0.06)
Diastolic BP	2 (0.005*)	-0.3 (0.2)	-1.6 (0.02)
Hepatitis C+	1 (0.2)	0.3 (0.3)	0.003 (0.08)

Odds ratio (p-value)

DISCUSSION

Lichen Planus (LP) is an idiopathic inflammatory disorder of the skin and the mucus membrane that affects 1% of the general adult population. LP is thought to be associated with numerous comorbidities; hence this study was conducted to evaluate blood profile and comorbidities associated with LP in the Jordanian population.

Through a case-control design, the study included 102 LP patients and their age and gender-matched controls, with a mean age of cases being 43.7± 16 years and a female predominance of 57%, consistent with recent reports that women are affected 1.5 times more commonly than males. Most cases appear between the ages of 30 and 60 [17].

Regarding the metabolic profile of LP patients in this study, significantly, they had higher Low-density lipoprotein, total cholesterol, Triglycerides, and blood glucose while having lower levels of High-density lipoproteins when compared to healthy controls. The same pattern was reported by Kumar et al. in India, as a statistically significant increased prevalence of increased low-density lipoprotein levels, low high-density lipoprotein levels, and diabetes mellitus was also observed in LP patients in their study [23]. Aryanian et al. emphasized these findings, specifying the male gender as a significant contributor along the side of LP [24]. Ilves et al. supported the association between these dyslipidemias and LP and their association with cardiovascular disease risk [22]. Furthermore, Ying et al., in their meta-analysis, patients with lichen planus are more likely to develop metabolic syndrome than the general population [21].

T 4 levels were significantly lower in LP patients compared to controls in this study, although TSH was higher in cases but statistically not significant. Similarly, Rahmani reported that T3 and T4 levels were significantly lower in LP patients with a significantly high TSH level [20]; consistently, Kumar et al. reported that hypothyroidism was commoner in LP patients compared to controls although statistically not evident [23].

The level of Vitamin D was lower in cases compared to controls; however, both groups had a mean Vitamin D level below the average recommended level. Evidence regarding the relationship between LP and vitamin D levels is still growing; Bahramian et al. found that LP patients had lower vitamin D levels compared to controls however, not reaching statistical significance, and Gupta et al. found that despite vitamin D deficiency was more prevalent in LP patients compared to controls, insufficiency was commoner in the control group compared to cases suggesting a population-wide defect in Vitamin D [26].

In the present study, the uric acid levels were significantly lower in LP patients compared to controls which were similar to what Chakraborti et al. reported [27]; hence uric acid is an important antioxidant. Low levels in LP patients may indicate high oxidative stress [28].

Interestingly, both systolic and diastolic blood pressures were elevated in LP patients compared to controls. Although a study by Christensen et al. reported that there is no significant difference in blood pressure between LP patients and the general population [29], Lynch suggested that the presence of 25 to 40% of hypertensive patients in LP patients indicated a piece of evidence that is difficult to explain in this proposed relationship [30].

In conclusion, the study revealed that LP patients had significant alternations with comorbid conditions such as high blood glucose, dyslipidemias, low thyroid hormone, low vitamin D levels, low uric acid levels, and high blood pressure. The study presented a part of a large body of evidence regarding the association of LP with the comorbidities mentioned above; however, further studies are needed to support these findings.

Limitations of the study

This is a case control study with a limited number of patients with lichen planus which may not be presenting the whole diseased individuals. This study is prone to recall and selection bias; in addition, it is difficult to establish a temporal relationship between lichen planus disease and possible associated comorbidities.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

The study's conception and design: Seetan, Zrekat, Elayan, and Al Omari , Mahdawi, Al-Sharadqa , Al-Rawabdeh, Batat, Albqowr , Abu tarboosh .Data acquisition: Seetan, Zrekat, Elayan, Al Omari, Mahdawi, Al-Sharadqa , Al-Rawabdeh, Batat, Albqowr and Abu tarboosh. Analysis and interpretation of data: Seetan, Zrekat, Al-Rawabdeh, Batat, Albqowr and Abu tarboosh. Writing and editing manuscript: Seetan, Zrekat, Elayan, and Al Omari , Mahdawi, Al-Sharadqa , Al-Rawabdeh, Batat, Albqowr , Abu tarboosh, all authors approved the final version of the manuscript.

Data Availability Statement

All data are available upon a reasonable request from the corresponding author

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