

Lichen planus and its association with diabetes mellitus



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ABSTRACT

Background: Lichen planus(LP) is a unique common inflammatory disorder that is clinically characterized by violaceous pruritic flat polygonal papules or plaques. Recently, an association between LP and diabetes mellitus has been viewed with greater interest. Several studies done in assessing the association between these show conflicting results.

Aims and Objectives: The aim of this study was to find an association between LP and diabetes mellitus. **Materials and Methods:** A cross-sectional comparative study was conducted in the Outpatient Department (OPD) of Dermatology, Bir Hospital. Any patient presenting at dermatology OPD above 16 years of age with LP were taken as cases. Age- and gender-matched patients with skin disease other than LP were taken as controls. The test was done by collecting 2ml of blood and serum HbA1c level was assessed allowing the blood to stand in a cuvette for 5 min inside the Erba Mannheim XL-300 analyzer to interact with DS5 reagent. The result was interpreted as per the calibration in the printed chromatogram.

Results: Male preponderance with a male: female ratio of 1.08:1 was found in this study. The mean age of onset of LP was earlier in male 40.11 years than in female 44.66 years. Likewise, hypertrophic(30%) followed by eruptive(27.5%) was the most common variants of LP found in this study. Diabetes was more common in males(75%) with LP than in females(25%) with LP. Patients having longer duration of LP were more commonly associated with diabetes mellitus. Among clinical variants of LP, diabetes was associated more with eruptive variant followed by classic and hypertrophic variants. The prevalence of diabetes was higher in case(16%) than in control(4%), $P=0.046$. **Conclusion:** This study showed an association of LP with diabetes mellitus, the association being statistically significant($P=0.046$). It, therefore, is desirable to do HbA1c level screening in patients with LP for timely detection of diabetes mellitus.

Key words: Lichen planus; HbA1c; Diabetes mellitus

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INTRODUCTION

Lichen planus(LP) is a unique common inflammatory disorder that affects the skin, mucous membranes, nails, and hair. It is the most typical and best characterized lichenoid dermatosis often with a chronic course with relapses and remissions. It primarily affects the flexure surface of the wrists, thighs, and distal one-third of lower extremities.¹

The exact incidence and prevalence of LP are not known, but the overall prevalence is believed to be somewhat less than 1% of the general population. At least two-third of cases occur between the ages of 30 and 60 years of age.²

According to the outpatient department (OPD) register of the Department of Dermatology, Bir Hospital, a total of 32,395 new patients attended the OPD in 2018–2019AD (2075 BS), out of which 459(1.41%) were diagnosed as having LP of which males were 213(46.40%) and females were 246(53.59%).

It has been proposed that immunologic defect implicated in the pathogenesis of LP may be related to the endocrine dysfunction in diabetes mellitus. The inflammatory cytokines involved in LP have been demonstrated to influence insulin signaling, lipid/carbohydrate metabolism, as well as adipogenesis.³

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The previous researchers have found the prevalence of diabetes mellitus and abnormal glucose tolerance among LP patients to be between 14% and 85%.⁴

There are no published studies in our country till date to assess an association between LP and diabetes mellitus. This study was conducted to find out the prevalence of diabetes mellitus in patients with LP and to see if there is any association between them. If a significant association between LP and diabetes mellitus is found, routine screening for diabetes can be advised to every LP patient in the future.

Aims and objectives

This study aims to find out an association between LP and diabetes mellitus.

MATERIALS AND METHODS

Following the ethical clearance from the Institutional Review Board of National Academy of Medical Sciences, a comparative cross-sectional study was conducted at Bir Hospital, Kathmandu, Nepal. The patients presenting to the dermatology OPD and diagnosed as LP and fulfilling the inclusion criteria were enrolled in the study as a case. On the basis of history and clinical examination, LP was diagnosed by the dermatologist. Age- and sex-matched patients with skin disease other than LP were enrolled as controls. Patients suffering from other dermatological disease which has an association with diabetes mellitus such as psoriasis and vitiligo, those who were under medications causing hyperglycemia such as steroids and beta-blockers, and those under medications causing lichenoid reactions such as ACE inhibitors, thiazide diuretics, and anti-malarials were excluded from the study.

Informed written consent was taken in either Nepali or English language whichever they felt comfortable assuring full confidentiality.

A detailed proforma of the participants including name, age, gender, occupation, educational status, marital status, age of onset, site of involvement of lesion, duration of lesion, severity of pruritus, variant of LP, presence of koebnerization, family history, presence of any systemic illness, and history of chronic use of medications such as ACEIs, thiazides, and antimalarials was filled by the researcher. All the participants underwent detailed physical and clinical examination.

All the patients were sent to biochemistry laboratory for an analysis of HbA1C level. Determination of HbA1c level was done by fully automated clinical chemistry analyzer Erba Mannheim XL-300 through principle of

chromatography. For this, 2 ml of venous blood was drawn from antecubital vein of the patient, 20 μ l of which was drawn through micropipette and was allowed to stand in a cuvette for 5 min inside the analyzer to interact with DS5 reagent. The result was interpreted as per the calibration in the printed chromatogram. The diagnosis of diabetes mellitus was made with serum HbA1C level >6.5% according to the diagnostic criteria developed by the American Diabetes Association, 2018.

In case of a known case of diabetes mellitus, the period of onset of LP in relation to diagnosis of diabetes mellitus was noted. In case of an abnormal HbA1c level, the patients were referred to endocrinology OPD of Bir Hospital for the management. All patients with LP were managed in the department of dermatology with regular follow-up. The entire cost for this study was borne by researcher. The diagnosis of diabetes mellitus was made according to the diagnostic criteria developed by the American Diabetes Association, 2018. The collected data were stored in an electronic database (MS Excel Sheet). Statistical analyses were performed with statistical software (SPSS 22.0 for Windows). Results were analyzed using appropriate statistical methods. All the meaningful statistics were worked out. Chi-square test was used when appropriate. P-value was calculated under the pre-determined level of significance (0.05) and confidence interval (CI) of 95% was constructed. Results were expressed as percentages, mean \pm standard deviation, and median for variables.

RESULTS

Fifty patients diagnosed with LP were included as cases and a same number of age- and sex-matched patients with skin diseases other than LP were selected as controls. Out of 50 cases, 26 (52%) were male and 24 (42%) were female. Male: female ratio was 1.08:1. Age of patients ranged from 17 to 75 years. Maximum number of cases was found in the age group of 36–45 years. Minimum number of cases was found in greater than 65 years of age, as shown in Table 1.

The mean age of onset of the disease was earlier in male 40.11 years than in female 44.66 years. Likewise, hypertrophic (30%) followed by eruptive (27.5%) LP was the most common variant found in this study. Diabetes was more common in males (75%) with LP than in females (25%) with LP. The prevalence of diabetes was higher in case (16%) than in control (4%) $P=0.046$, as shown in Figure 1.

Patients having duration of LP for more than 2 years were more commonly associated with diabetes mellitus, as shown in Figure 2.

Among clinical variants of LP, diabetes was common among eruptive variant followed by classic and hypertrophic variants; however, the association was statistically insignificant ($P=0.62$), as shown in Figure 3.

DISCUSSION

LP is a chronic inflammatory disease, with an unknown cause that affects the skin, genitalia, mucous membranes, or appendages. Many studies have been done in the past that have suggested a positive association between LP and metabolic disorders such as diabetes mellitus and dyslipidemia. The previous researchers have found the prevalence of diabetes and abnormal glucose tolerance among LP patients to be between 14% and 85%.⁴⁻⁹ Although the etiopathogenesis of LP is not fully understood, it is believed that LP represents a T-cell-mediated inflammatory disorder. It has been proposed that immunological defect implicated in the pathogenesis

of LP has been implicated to be related to the endocrine dysfunction in diabetes mellitus. The inflammatory cytokines involved in LP have been demonstrated to influence insulin signaling, lipid/carbohydrate metabolism, as well as adipogenesis.³ Knowledge of an association between LP and diabetes mellitus would allow appropriate primary and secondary preventive measures to be applied. HbA1C level screening routinely in LP patients may be useful in timely detection of diabetes mellitus which when timely addressed can prevent complications of DM and also prevent the progression of development of cardiovascular diseases.¹⁰

The main aim of our study was to establish an association between LP and DM for which 50 clinically diagnosed cases of LP and same number of age- and sex-matched controls with dermatoses other than LP were enrolled.

Although it is said that there is no sexual predilection in LP,¹¹ in our study, 26(52%) of the cases were male and 24(48%) were female with a slight male preponderance with a male: female ratio of 1.08:1 similar to a study done by Mushtaq et al.¹² This was however in contrast to the finding by Dreiherr et al.,¹³ and Abdallat and Maaita¹⁴ that showed higher female preponderance.

All the age groups from 16 years and above were included in our study. About 58% of the study cases belonged to the age group of 30–65 years which was similar to a study done by Budimir V et al., where 66.7% of cases belonged to this age group.¹⁵

The mean age of onset of LP in our study was 42.3 years (SD 14.52) which is in contrast to the later age of onset of 57.8 years in a study by Laurantano et al.,¹⁶ and 59.2 years in a study by Nancy et al.¹⁷ Our finding was, however, similar with earlier mean age of onset of 39.7 years as observed in a study by Abdallat and Maaita.¹⁴

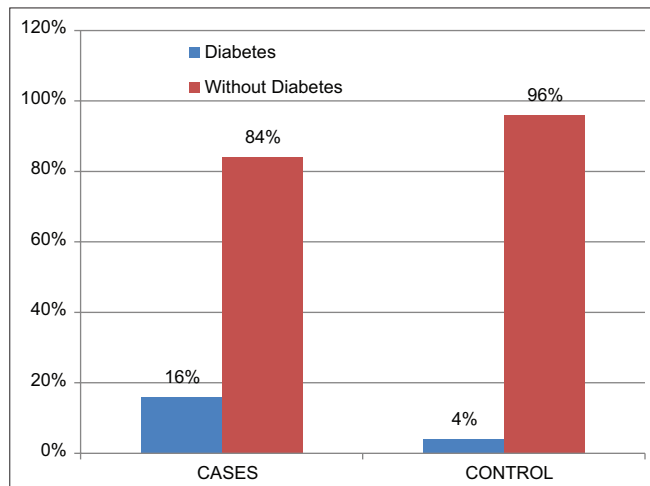


Figure 1: Bar diagram comparing prevalence of diabetes among cases and controls

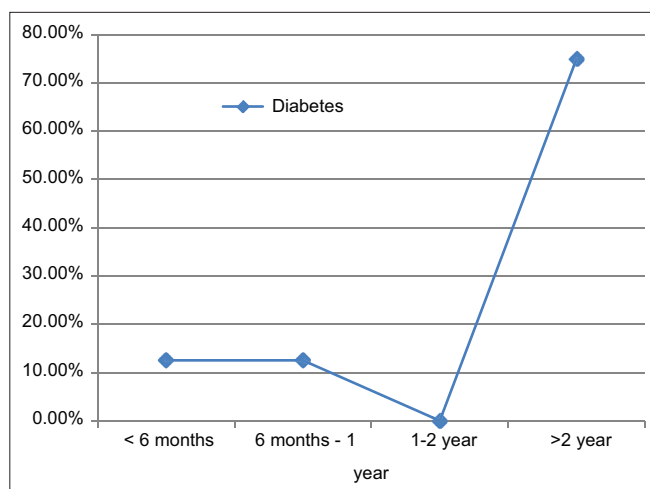


Figure 2: Line chart showing duration of lichen planus in patients with diabetes

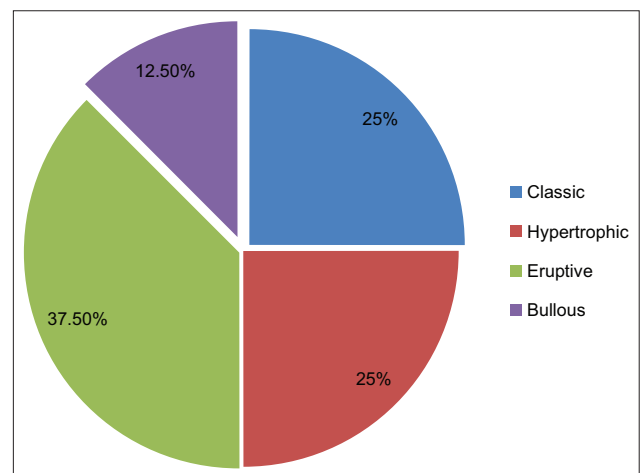


Figure 3: Pie chart showing variants of lichen planus in cases with diabetes

Mean age of onset in our study among females with LP was 46.66 years (SD 12.88) which was higher than 40.11 years (SD 15.33) in males ($P=0.636$). This finding was consistent with findings in studies by Arias-Santiago et al.,¹⁸ and Seyhan et al.⁴

Among 50 cases studied, the most common variant observed was hypertrophic type 15(30%), followed by eruptive 13(26%), classic 11(22%), mucosal 7(14%), LPP 2(4%), actinic 1(2%), and bullous 1(2%).

This relatively higher representation of hypertrophic LP in our study compared to most other studies showing classic LP to be a consistently common variant could be due to persistent and treatment refractory nature of hypertrophic variant compared to the short-lived and treatment responsive nature of classic type.

While observing sites affected by LP in this study, lower limb was found to be the most common site involved 38%, followed by oral mucosa 24%, trunk and extremities 20%, upper limb 20%, face 8%, and genital mucosa 2%. Like in our study, lower limb was the most common site involved in studies done by Bhattacharya et al.¹⁹(55.6%), Parihar et al.²⁰(77.2%), and Yusuf et al. (58%).²¹

The mean duration of LP in our study was 11.34 months (SD 2.88) which is consistent with a mean duration of LP of 8.2 months and 2.77 months in studies done by Yusuf et al.,²¹ and Pandhi et al.,²² respectively. This was in contrast with the longer average duration of illness of 21.13 months (SD 24.07) as observed by Seyhan et al.,⁴ in his study.

LP is known to be the second most common dermatosis after psoriasis where true koebnerization is known to occur. This phenomenon was seen in 5(10%) of study population in our study which is less as compared to 37.5% and 38.5% of cases presenting with koebnerization as observed by Khondekar et al.,²³ and Nnoruka et al.,²⁴ respectively.

After the prototype study done by Grinspan et al.,²⁵ on an association between LP and DM that showed the prevalence of DM to be 38%, many studies are being carried out to establish an association between the same. In our study, DM was found to be present in 16% of cases compared to 4% among controls ($P=0.046$) which was consistent with a finding by Seyhan et al.,⁴ in his study where DM was present in 26.7% among cases compared to 3.3% among controls ($P=0.007$). The difference between the mean HbA1C level among cases and controls was significant in this study ($P=0.001$) unlike in our study where the statistical significance could not be established between the difference of mean HbA1C among cases and controls ($P=0.214$). Statistical association between LP and

diabetes seen in our study was consistent with the findings by Kumar et al.²⁶($P=0.021$), Eshkevari et al.²⁷($P=0.008$), and Denli et al.⁶($P=0.008$). This was in contrast with the studies by Dreiherr et al.¹³($P=0.52$), and Arias-Santiago et al.¹⁸(0.14), where the statistical association could not be established.

Among the LP patients who had DM in our study, 6(75%) were male and 2(25%) were female. There was no statistical significance established between gender and prevalence of DM ($P=0.47$) similar to the findings by Atefi et al.²⁸($P=0.78$), and Arias-Santiago et al.¹⁸($P=0.63$).

In a study by Kumar et al.,²⁶ classic variant of LP was the most common variant found among diabetic patients as seen in yet another study conducted by Zakaria et al.²⁹ In contrast, in another study done by Baykal et al.,³⁰ mucosal variant was more prevalent in LP patients with diabetes. In our study, however, eruptive variant was the most common variant 3(37.5%) followed by classic 2(25%) and hypertrophic variant 2(25%) but no statistical significance could be established between the type of LP and diabetes mellitus ($P=0.62$).

The mean age of onset of DM in this study was 49.25 years (SD 16.18) compared to 69 years (SD 5.65) among control group ($P=0.458$) which is similar to a study done by Margot et al.,³¹ where mean age of onset of DM was 48.4 years in cases compared to 50.8 years in controls ($P=0.34$). In contrary, in a study done by Atefi et al.,²⁸ mean age of onset of DM was 56.02 years which was higher compared to 48.05 years among the controls ($P=0.039$).⁹

There was no statistical significance found regarding the duration of LP and DM while comparing among those having LP for less than 2 years and more than 2 years in a study done by Kumar et al. ($P=0.221$).²⁶ This finding is in contrast to our finding of DM being more prevalent among those with LP of more than 2 years ($P=0.011$).

Baykal et al.,³⁰ in a case-control study reported mean duration of LP to be significantly higher 54.29 months (SD 68) among diabetic patients compared to 23.17 months (SD 35.8) among non-diabetic group ($P=0.034$) similar

Table 1: Age and gender distribution among cases and controls

Age (years)	Cases (n)		Controls (n)		Total
	Males	Females	Males	Females	
16-25	5	2	5	2	14
26-35	5	5	5	5	20
36-45	8	5	8	5	26
46-55	1	6	1	6	14
56-65	5	4	5	4	18
>65	2	2	2	2	8
Total	26	24	26	24	100

to our finding. Yet, another study by Atefi et al.,²⁸ showed the duration of LP to be significantly higher among the diabetic group ($P=0.0024$).

Limitations of the study

The data were sampled from only one hospital in a defined period of time and during the first visit of the patients. Furthermore, the sample size is limited so it may have limitation in generalization of results. Case-control studies also do not allow the proper understanding of the directionality of the association to be ascertained. Hence, more studies with larger numbers of patients are required to confirm these findings and to analyze the pathogenic mechanisms underlying increase in risk of diabetes mellitus in these patients.

CONCLUSION

This study showed a significant association between LP and diabetes mellitus ($P=0.046$). Patients having longer duration of LP were commonly associated with LP. While hypertrophic and eruptive variants of LP were the most common variants of LP seen in this study, eruptive variant the most common variants of LP seen in association with diabetes mellitus. Diabetes mellitus was found to be more in males than females with LP. It is, therefore, appropriate to do regular HbA1C screening in all patients who present with LP for timely detection of diabetes mellitus which can prevent the complications related to it by timely interventions and also can reduce the cardiovascular morbidity in these patients in a long run.

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SA-Concept and design of the study, prepared first draft of manuscript, statistical analysis, and interpreted the results. **AK**- Concept and coordination, reviewed the literature, and manuscript.

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