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ASSOCIATION OF LICEN PLANUS WITH HEPATITIS-C IN SOUTHERN PUNJAB POPULATION

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ABSTRACT

Introduction: Lichen planus (LP) is a chronic mucocutaneous disorder that has been increasingly associated with hepatitis C virus (HCV) infection. The relationship between these conditions is of particular clinical importance in Pakistan, where HCV prevalence is among the highest globally.

Objective: To evaluate the correlation of lichen planus with hepatitis C in patients reporting to a tertiary care dental institute in Southern Punjab.

Material and Method: This cross-sectional observational study took place at the Department of Oral Medicine, Nishtar Institute of Dentistry, Multan, under the guidance of Dr. Sahrish Liaqat between January 2025 and June 2025. One hundred and fifty LP patients clinically and histologically confirmed were recruited. Demographic and clinical characteristics were noted. Anti-HCV antibodies were detected in venous blood samples with ELISA, and PCR was done to demonstrate an active infection. Data were studied to determine the rate and connection between LP and HCV.

Results: Among 150 patients with LP, 54 (36%) were anti-HCV-positive, and PCR confirmed 47 (31.3%) with active infection. The most common was oral presentation (68%) with an increased incidence of HCV positivity (40.2%) as compared to cutaneous (23.8%). Patients in the middle age (31 to 50 years) had the highest HCV positivity (39.2%). Though females were more affected, the difference in gender was not statistically significant.

Conclusion: There is a close correlation between lichen planus and hepatitis C infection, especially in oral cases of lichen planus. Routine screening of HCV is advisable in patients with LP to help diagnose its presence early and adopt comprehensive measures in its management.

Keywords: Lichen planus, Hepatitis C virus, Oral lesions, Extrahepatic manifestation, Southern Punjab

INTRODUCTION

Lichen planus (LP) is a multifactorial, chronic, inflammatory mucocutaneous disease that has been extensively investigated in relation to viral infections, especially hepatitis C virus (HCV). The clinical manifestations of LP are inconsistent, although one of the most frequent and problematic manifestations is oral, which causes pain, burning, and has a severe effect on the quality of life. Past research has already pointed out a significant correlation between HCV and LP, whereby anti-HCV positivity was found to be elevated in patients who were diagnosed as having LP than in the rest of the population (1). The comorbidity of these conditions has become a topic of significant interest in dermatology and hepatology because of potential shared immunopathogenesis and clinical consequences. The presence of chronic HCV infection has also been linked with hematologic defects, which include thrombocytopenia, further complicating the disease burden and emphasising the criticality of thorough assessment of affected individuals (2). There is growing evidence that the relationship between LP and HCV is not unilateral, where HCV predisposes individuals to the development of LP and that people with LP have a higher chance of carrying HCV infection (3).

Systematic reviews and meta-analyses confirm the fact that this connection is not by chance but due to deeper immunopathological connections. The above-mentioned findings are also supported by case-control studies that show a significantly high prevalence of HCV in various populations in patients with LP, which further indicates that LP could be an extrahepatic manifestation of HCV (4). Cohort studies with large sample sizes have also shown a correlation between LP and other hepatic disorders such as cirrhosis, which highlights the significance of evaluating the liver functions of the LP patients (5). Clinical manifestations presage that LP manifests differently, perhaps in the context of HCV infection. As an illustration, patients with oral LP frequently exhibit more intensive symptoms and resistance to traditional treatment when they also possess HCV, which also highlights the importance of screening in persistent or atypical LP (6). The relationship is also evidenced by the report of clinical cases of various populations of varying sizes, with greater numbers of HCV-positive patients reporting mucosal and skin manifestations of LP (7). In addition, a comparison analysis of the prevalence rate of hepatitis B and C in the LP groups indicates that the latter has a better and patterned correlation than the former hepatitis B virus (8).

This exceptional pattern confirms the HCV hypothesis, HCV should have a direct role in the pathogenesis of LP, instead of being a secondary finding. The oral health-related quality of life of patients with LP is also seriously affected by the presence of HCV infection, which has been evidenced by observational studies. Chronic mouth sores are painful, frequent, and debilitating to the daily activities of the patients, their eating habits, and their mental health (9). However, the relationship is not convincing, and some investigations are warning against exaggerating the relationship based on regional differences, genetic factors and heterogeneity in the studies (10). Additionally, rare clinical presentations have been used to illustrate the complexities of the interaction between LP and HCV, in addition to the involvement of other extrinsic triggering factors like vaccinations, further complicating the clinical scenario and supporting the theory of a multifactorial pathogenesis of LP (11).

The developments of antiviral treatment have given more insights into this association. The results of patients with HCV treated with direct-acting antivirals (DAAs) hardly suggest that active viral replication is a crucial factor in disease retention, evidenced by the subsequent improvement or even clearing of emphasis lesions (12). Meta-analyses have also established that there is a correlation between hepatic disorders (such as HCV and hepatocellular carcinoma) and LP, thus exposing LP patients to increased risks of developing severe liver disorders and reiterating the importance of early diagnosis and medication (13). Initial evidence has shown that DAAs-mediated HCV eradication has once again shown benefits capable of reducing liver-related complications, but also potential reduction in incidences of oral LP, pointing towards a treatment benefit that impacts beyond the hepatic system (14). Further studies support the idea that treatment with DAA results in favourable outcomes in terms of the reduction of extrahepatic manifestations like LP, advancing the viral causality line of argument (15). Cutaneous evidences of the HCV-related LP also expand the numerical range of the disease. Case reports have also reported presentations like lichen planus

pigmentosus as a separate extrahepatic case of skin manifestations of chronic HCV infection, and this point highlights disparate clinical phenotypes (16).
Epidemiological studies involving large populations of people also have shown that HCV infection predisposes to chronic flesh diseases that have a propensity to develop as an inflammatory skin disease (LP), creating a wider lens of dermatological burden of HCV (17). Interestingly, not every patient responds to HCV cure with equal success, with complete remission and disappearance of lesions, variable clinical courses of LP occurring after HCV cure, some resulting in persistence or even worsening of lesions, which may reflect the presence of additional immunological or genetic factors that predispose patients to different clinical outcomes (18). The relationships between LP and HCV have significant implications for clinical management, and the burden of HCV in Southern Punjab continues to be one of the highest worldwide. Pakistan is known to be a high-burden country in terms of HCV, and since LP is fairly prevalent as a mucocutaneous disorder, the chances of an overlap are high (12). Understanding the relationship between these conditions is important for clinicians as it affect diagnostic strategies, management decisions and long-term management strategies.
In contrast, surveillance of HCV-positive patients by dermatological appearance safeguards a comprehensive management process that accommodates the hepatic and extrahepatic aspects of disease (14). The relationship between hepatitis C virus infection and lichen planus has been repeatedly found in various populations in different study designs and clinical settings. Although the controversy is ongoing about the intensity and universality of this correlation, the mounting data support that LP is a significant extracapsular expression of HCV infection. The introduction of DAAs has transformed the management of HCV and provides an opportunity to enhance the outcomes in people with both diseases. Nevertheless, clinical case-to-case differences necessitate further studies to inform about the immunological and molecular pathways between LP and HCV (16). In areas of high prevalence, like Southern Punjab, this association is not only a medically necessary concern, but it is a high-priority public health issue, with opportunities to minimise disease burden, enhance patient quality of life, and forestall long-term hepatic diseases.

Objective: To establish the relationship between hepatitis C virus infection and lichen planus in the Southern Punjab population by assessing clinical patterns, prevalence, and implications on diagnostic, therapeutic, and patient outcomes.

MATERIALS AND METHODS

Study Design: Cross-sectional observational study

Study Setting: Department of Oral Medicine, Nishtar Institute of Dentistry, Multan, Pakistan

Duration of the Study: January 2025 to June 2025.

Inclusion Criteria: All patients diagnosed clinically with lichen planus, independent of age and gender, could be included. Participants with clinically confirmed oral, cutaneous, or mucocutaneous lichen planus were included. All the patients who provided informed consent and were willing to be tested regarding serology of the hepatitis C virus antibodies were recruited.

Exclusion Criteria: Patients with lichenoid lesions secondary to drug use, dental restorative materials or systemic causes were excluded. People with a history of autoimmune disorders, hepatitis B, or previous antiviral treatment for hepatitis C were omitted. Also, patients who were not ready to participate or could not give blood samples to be analysed through serological observation were excluded.

Methods: Each of the participants was examined based on the broad history and clinical inspection with the purpose of establishing that it was the cause of lichen planus. Demographic data was

recorded, such as age, gender, and interests in medication. Clinical assessment of oral and cutaneous lesions and histopathological confirmation in case of diagnostic ambiguity were conducted. Clinical assessment was followed by the collection of venous blood samples, which were tested to identify anti-HCV antibodies using enzyme-linked immunosorbent assay (ELISA). Positive samples were further confirmed by polymerase chain reaction (PCR) of active HCV infection. The data were collected and analysed to reveal how common HCV is among lichen planus patients, and the relationship between the two disorders was also assessed statistically. Strict confidence was ensured, and ethical approval was taken by the institutional review board of Nishtar Institute of Dentistry, Multan.

RESULTS

A sample of 150 patients was studied, consisting of patients with clinically and histologically established lichen planus. The average age of the participants is 42.7 ± 12.3 years, with a minimum age of 18 years and a maximum age of 70 years. These were 94 (62.7%) females and 56 (37.3%) males.

Table 1. Demographic Characteristics of Patients with Lichen Planus (N=150)

Variable	Categories	Frequency (n)	Percentage (%)
Gender	Male	56	37.3
	Female	94	62.7
Age group	18–30	38	25.3
	31–50	74	49.3
	51–70	38	25.3
Residence	Urban	88	58.7
	Rural	62	41.3

Anti-HCV antibodies were found in 54 patients (36%), whereas 96 patients (64%) were negative, among the study population. Out of the 54 antibody-positive cases, active infection was confirmed in 47 patients (31.3%).

Table 2. Prevalence of Hepatitis C Virus (HCV) in Lichen Planus Patients

HCV Status	Frequency (n)	Percentage (%)
Anti-HCV Negative	96	64.0
Anti-HCV Positive	54	36.0
PCR Confirmed HCV	47	31.3

When stratified by gender, HCV infection was more common in females (38.3%) compared to males (32.1%). However, this difference was not statistically significant ($p > 0.05$).

Table 3. Association of Gender with Hepatitis C Virus Positivity

Gender	HCV Positive (n=54)	HCV Negative (n=96)	Total	Percentage Positive (%)
Male	18	38	56	32.1
Female	36	58	94	38.3

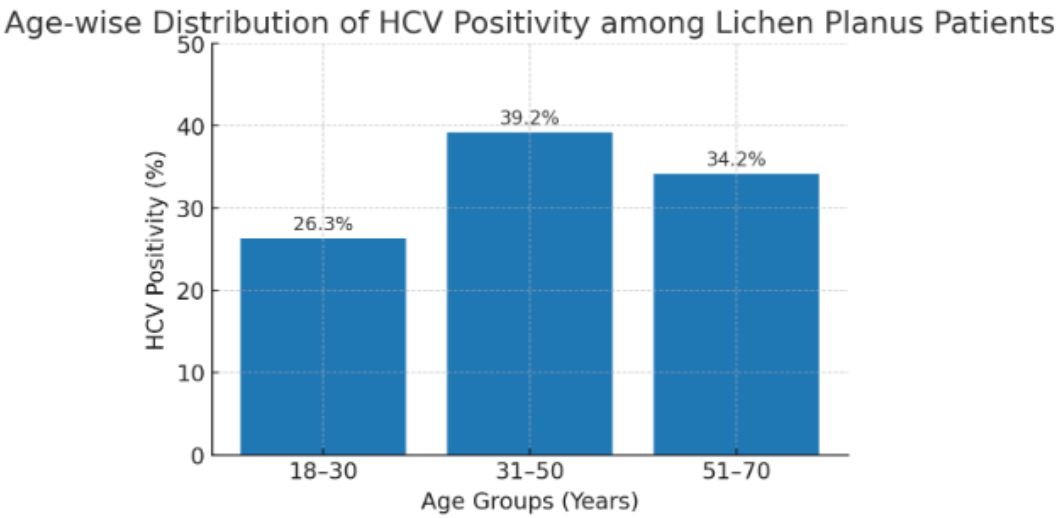
Regarding clinical manifestations, the most predominant oral format of lichen planus was apparent in 102 patients (68%), followed by cutaneous (28%) and mucocutaneous (4%). The oral lesions had a statistically significantly higher percentage (40.2%) of CAV positivity than the cutaneous involvement (25.0%).

Table 4. Association Between Clinical Type of Lichen Planus and HCV Status

Clinical Presentation	Total Cases (n)	HCV Positive (n)	HCV Negative (n)	Percentage Positive (%)
Oral LP	102	41	61	40.2
Cutaneous LP	42	10	32	23.8
Mucocutaneous LP	6	3	3	50.0

The distribution of HCV positivity across age groups is shown in **Figure 1**. The prevalence was highest among patients aged 31–50 years (39.2%), followed by those aged 51–70 years (34.2%). Younger patients (18–30 years) had a comparatively lower prevalence (26.3%).

Figure 1. Age-wise distribution of HCV positivity among Lichen Planus patients



Collectively, the study results indicate a high rate of hepatitis C infection in lichen planus patients, especially those with oral manifestations and those in the middle-aged population, which indicates a major risk factor for both conditions.

Discussion

The study aimed to determine the relationship of lichen planus (LP) to hepatitis C virus (HCV) infection in patients attending a tertiary care dental institute in Southern Punjab. Results showed that 36 per cent of the LP patients tested positive for anti-HCV antibodies, and 31.3 per cent had active infection determined by PCR. The association was highly significant, particularly in patients with oral lichen planus, where 40.2 per cent were positive. These findings confirm the increasing literature stating that LP is an extrahepatic result of chronic HCV that is most pronounced in high viral-burden areas. Earlier research studies have proven unequivocally that the prevalence of HCV antibodies is increased in LP patients as compared to a normal population (1). The observed prevalence is comparable with the national trends since Pakistan reports a high endemicity of HCV that contributes to a considerable number of nationwide morbidity and mortality (2). Multiple systematic reviews and meta-analyses have validated a two-way association, indicating that LP not only occurs more frequently in HCV-positive individuals but could also serve as a clinical indicator of unrecognised viral infection (3). Case-control studies further prove this association, where HCV was found to be higher in the LP patients than in the controls, indicating that LP might be an early indication of the presence of a hepatic disease (4).

Stratification analysis of LP cases by clinical form showed a very strong association between oral lesions and HCV infection. This observation supports the findings of large-scale cohort studies that have found oral LP is the most common extrahepatic manifestation of HCV, and was commonly associated with more severe or persistent disease (5). A study in an Indian tertiary care hospital also showed a significant correlation between oral LP and HCV seropositivity, which adds weight to the

fact that HCV should also be screened in patients with oral LP (6). Case reports also underline that unique or extended distribution of lesions may be a common feature in HCV-positive individuals with LP and indicate the clinical value of screening routine (7). Further, the comparative studies on both the hepatitis B and C virus indicate that the LP is associated more with HCV than hepatitis B and portrays a differentiated viral pathogenesis (8). A significant clinical value of the results is that HCV-related LP is associated with oral health-related quality of life. Patients mention pain that occurs chronically, burning sensations, and limitations in dietary intake, which are both negative impacts on the way of living (9).

Nevertheless, the linkage between LP and HCV is still controversial in certain groups. Some studies have claimed that the association is unreliable and that they are dependent on geographical differences, genetics of hosts and environmental cofactors (10). Moreover, special case observations, e.g., development of atrophic LP following COVID-19 immunisation in an HCV-positive patient, point to the possibility of the viral infection being a preconditioning background factor, with other external factors mediating disease manifestation (11). The release of direct-acting antiviral medications (DAAs) has offered essential perspectives on the pathogenesis of LP linked with HCV. Several reports suggest that, in the context of successful clearance of HCV with DAAs, clearance or regression of LP lesions continues to point towards active viral replication as a sustaining mechanism of LP pathology (12).

Systematic reviews and meta-analyses have also uncovered relationships between LP, liver disease, and hepatocellular carcinoma, requiring liver disease to be a consideration during the monitoring of patients with LP (13). Literature points to HCV eradication having therapeutic benefits beyond liver health to liver-related outcomes and the prevention of extrahepatic complications, including LP (14, 15). Cutaneous LP linked with HCV presence has been reported in literature as well, including lichen planus pigmentosus, which can serve as a particular extrahepatic cutaneous manifestation of a chronic infection (16). Epidemiological studies have also shown that HCV infection predisposes people to chronic inflammatory skin disorders such as LP, making HCV-related extrahepatic morbidity much broader (17). However, post-HCV cure results are inconsistent. Some patients achieve complete remission of LP subsequent to viral clearance, but others have persistent or recurring lesions, indicating that other immunological or genetic factors contribute to the persistence of disease in the face of viral clearance (18).

The overlap between LP and HCV also cannot be ignored in high-prevalence areas like Southern Punjab. Since one-third of the LP patients tested positive with HCV, viral screening must be included in the routine battery of tests used in the investigation of LP. The early diagnosis of HCV enables early antiviral therapy and lessens the danger of liver-associated hazardous events like liver cirrhosis and hepatocellular carcinoma (14). In contrast, routine dermatology examination and check-ups with oral examinations in HCV patients can aid in early diagnosis of LP to treat it symptomatically and allow patients to have a higher quality of life. Although the study has several strengths, including confirmation of HCV by both serological and PCR methods, several limitations need to be mentioned. The study was single-centred, which means that the results cannot be applied to the whole population of Southern Punjab.

However, the cross-sectional design does not allow one to make causal inference. Multicenter, longitudinal studies with larger cohorts are needed to further define the temporal relationship and determine whether the resolution of LP is universal after HCV eradication (15). The study further supports the existence of a relationship between LP and HCV infection amongst the population of the Southern Punjab. Notably, oral LP demonstrated a great degree of association with HCV positivity. These results support the necessity of regular HCV screening in LP patients and show the possible benefits of the antiviral treatment, not limited to hepatic disease control but also aimed at improving dermatological symptoms.

Conclusion

This report emphasizes a strong correlation between lichen planus and hepatitis C virus in the South Punjab inhabitants, where 36 per cent of the patients had anti-HCV antibody status, and 31.3 per cent

tested positive in the form of active infection through PCR. The interaction was also strongest in patients with oral lichen planus, indicating a possible extrahepatic manifestation of HCV. These results are consistent with the literature, which consistently finds HCV as one of the major factors in the pathogenesis of lichen planus. Notably, the findings emphasize the necessity of regular screening for HCV in lichen planus patients, especially in regions with high frequency, like in Pakistan. Early diagnosis and implementation of antiviral treatment can even salvage the hepatic disease and benefit the dermatological and oral outcomes. This association can help take a comprehensive approach to patients and reduce the dual burden of chronic HCV infection and lichen planus among vulnerable populations.

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