

FREQUENCY OF HEPATITIS C VIRUS IN PATIENT WITH LICHEN PLANUS PRESENTING TO TERTIARY CARE HOSPITAL IN KHYBER PAKHTUNKHWA, PAKISTAN

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Abstract *Lichen Planus (LP) is a chronic inflammatory condition that affects the skin, mucous membranes, or both. The present study aimed to determine the frequency of hepatitis C virus in patients with lichen planus. This cross-sectional study was conducted at the Department of Medicine, Medical Teaching Institute, Lady Reading Hospital Peshawar. The study duration was from July 2021 to December 2021. A thorough medical history and a comprehensive physical examination were obtained, including an evaluation of the affected skin and mucous membrane areas. A consultant dermatologist took Skin biopsies from the lichen planus lesions and sent them to the hospital laboratory for histopathological analysis. Hepatitis C virus infection was confirmed through PCR testing in the hospital laboratory. All collected data was documented on a specially designed form containing demographic information. The data was then analyzed using the Statistical Package for the Social Sciences (SPSS), version 23. Post-stratification chi-square tests were applied, with a significance level set at $p \leq 0.05$ to determine statistical significance. In this study, we included a total of 101 patients who had lichen planus. The ages of these patients ranged from 18 to 50 years, with a mean age of 36.410 years and a standard deviation of 9.362 years. Among these patients, 23.8% were found to be infected with the Hepatitis C virus. The patients' mean Body Mass Index (BMI) was 25.78 kg/m², with a standard deviation of 4.087 kg/m². An interesting finding was a statistically significant association (with a p-value of 0.002) between BMI and the occurrence of Hepatitis C virus among lichen planus patients. This suggests a positive significant association between BMI and the presence of HCV in patients with lichen planus. These findings highlight the importance of considering age, gender, and BMI when assessing the risk of HCV infection in lichen planus patients. Furthermore, the relatively high prevalence of HCV among lichen planus patients in this population emphasizes the importance of regular screening for Hepatitis C in individuals with lichen planus, particularly in the fifth decade of life, and those with lower BMIs. This information may improve clinical management and patient care in lichen planus and its potential comorbidities.*

Keywords: Lichen Planus (LP), Hepatitis C Virus (HCV), chronic inflammation, Body Mass Index (BMI)

Introduction

Lichen Planus (LP) is one of the most common dermatological diseases that affects the skin, mucosa, or both. It is recurrent, of unknown etiology, and can adopt different clinical appearances depending on its time of evolution, localization, and severity. LP generally evolves with unpredictable spells of remission and intensification (Mostafa and Tarakji, 2015). Lichen planus (LP) is a condition that affects the lining of the mouth, with an estimated prevalence of 0.5% to 3%. It tends to occur more frequently in females, with a ratio of 1.5 to 3 females for every male affected. This condition typically begins between the ages of 30 and 60 years. It is also the subject of ongoing debate regarding its potential to

progress into a precancerous state (Robledo-Sierra and van der Waal, 2018). *Lichen Planus (LP)* is a chronic inflammatory disease that can impact the skin, mucous membranes, or both. The condition tends to recur, and its exact cause is still unknown. The appearance of LP can vary depending on how long it has been present, where it's located on the body, and its severity. This condition often follows an unpredictable pattern, with periods of remission and flare-ups (Mostafa and Tarakji, 2015).

LP is notably the most common dermatological condition with oral manifestations. It affects the oral mucosa, and its prevalence is estimated to be between 0.5% and 3%. It tends to affect more



women than men, with a female-to-male ratio ranging from 1.5 to 3. LP typically emerges in individuals between the ages of 30 and 60. Moreover, ongoing debate exists about its potential to develop into a premalignant condition (Robledo-Sierra and van der Waal, 2018). The exact cause of lichen planus (LP) remains unknown, although several theories have been proposed. These hypotheses include viral, immunological, and emotional stress as potential triggers.

Furthermore, lichenoid eruptions encompass a range of conditions, such as drug-induced, chemical-related, bacterial, and those occurring after bone marrow transplantation. Drug-induced lichenoid eruptions resemble LP but can be differentiated by a patient's medication history. Hepatitis C virus (HCV) belongs to the single-stranded RNA flavivirus family and primarily replicates in hepatocytes and peripheral blood mononuclear cells. The association between Lichen planus (LP) and Hepatitis C Virus (HCV) has been uncertain and debated in the scientific literature. This uncertainty largely arises from the considerable variation in the prevalence of HCV infection among patients with lichen planus in different geographic regions. The initial connection between HCV and LP was noted by Mokni et al. in 1991. They reported a case involving a patient who had developed violaceous papules on their arms and trunk. Laboratory tests revealed elevated transaminases, and subsequent investigations confirmed the presence of HCV infection. A cutaneous biopsy confirmed the diagnosis of LP. It's worth noting that these studies emerged shortly after the discovery of HCV in 1989 (Cassol-Spanemberg et al., 2019). In a study conducted by Ukonu AB et al., it was found that 21.4% of patients with lichen planus tested positive for Hepatitis C Virus (Bob and Augustine, 2012). Another study it has been reported a higher prevalence of HCV positivity, with 40.5% of lichen planus patients testing positive for the virus.

Additionally, a study by Donempudi P et al. indicated a substantially higher frequency of 88% for Hepatitis C Virus positivity among patients with lichen planus (Tariq et al., 2020). Although the pathogenesis of LP is controversial because of its diverse etio-pathogenecity, chronicity, and more malignant potentiality, it has become a subject of interest for research studies regarding various aspects of this lesion and its link with viral diseases. Previous studies have shown variability in results in different populations; therefore, their results cannot be generalized to our population. So, this study was planned to determine the frequency of Hepatitis C Virus in patients with lichen planus in our local population. Results of this study will be helpful for future researchers in this subject.

Materials and Methods

This Cross-Sectional Study was conducted in the Department of Medicine, Lady Reading Hospital, Peshawar from 1st July 2021 to 31st December 2021. Sample size was calculated 101 by using the expected frequency of Hepatitis C Virus 21.4% with 85 Margin of error and 95% Confidence level. Sampling technique was non-probability consecutive sampling. All patients aged 18-50 years, including males and females with lichen planus for more than 03 weeks, were included in the study, while patients with history of diabetes, hypertension, and renal disease were excluded from the study, and patients who refused informed consent.

For study purposes, approval was taken from CPSP, and after successfully accepting our research proposal a total of 101 patients were included in this study. Before enrollment in the study, informed consent was taken from all study cases. Detailed history of each patient with their physical examination was done. Examination of the lesions if present, was noted specifically. Blood investigations like LFTs and viral profiles were also done. The consultant dermatologist took Biopsy from lichen planus lesions and sent for histopathology testing to the hospital laboratory. For Hepatitis C virus, samples were sent from the hospital laboratory for PCR testing. For this purpose, Blood samples (3 ml in fluoride tubes) were drawn from all the patients by a 4th year resident student. The samples were transported to hospital laboratory of Lady Reading Hospital, Peshawar within half an hour of collection for HCV detection. Data was recorded for HCV as per operational definition. We collected all the information using a specially designed form, which included details about the participants' demographics. The data was then analyzed using the statistical software SPSS version 23. For quantitative variables like age and the duration of lichen planus, we presented the results as Mean \pm SD. Qualitative variables, such as gender, family history of HCV, and Hepatitis C Virus positivity, were analyzed by calculating frequencies and percentages. We conducted stratified analyses based on age, gender, family history of HCV, and the duration of lichen planus to examine their potential influence on Hepatitis C Virus positivity. To assess the statistical significance of these findings, we applied the post-stratification chi-square test, considering $p \leq 0.05$ as the threshold for statistical significance.

Results

A total of 101 study cases were included in this study. The majority of study cases (63.4%) were male. Age of the patients ranged from 18 to 50 years. The maximum number of patients (43.6%) were from the age group 41 to 50. Family history showed that 6.9% of patients have fatty liver in family member. Based on Body mass index (BMI), study

cases were divided into three groups i.e., Healthy individuals with BMI = 18.5-25kg/m², overweight with BMI=25.1-30kg/m² and Obese with BMI=>30kg/m². Results showed that 54.5% were healthy, whereas 14.9% were obese. The main objective of the study was to know the presence of Hepatitis C virus, and results showed that 24 (23.8%) of the study cases were Hepatitis C virus positive results (Table 1)

Table 1. Baseline characteristics of study cases

Characteristics	Frequency	Percentage
Gender		
Male	64	63.4
Female	37	36.6
Age group (Years)		
18 – 30	32	31.7
31 – 40	25	24.8
41 – 50	44	43.6
Family History of Fatty Liver		
Yes	7	6.9
No	94	93.1
BMI Status		
Healthy (BMI = 18.5-25kg/m ²)	55	54.5
Overweight (BMI=25.1-30kg/m ²)	31	30.7
Obese (BMI=>30kg/m ²)	15	14.9
Presence of Hepatitis C Virus		
Yes	24	23.8
No	77	76.2

The mean age of study cases was 36.410 ± 9.362 years, the mean weight 75.54 ± 11.342 kg, the mean height was 171.44 ± 9.270 cm, the mean BMI was 25.78 ± 4.08789 kg/m², the mean duration of lichen planus at the time of the study was 18.89 ± 10.006 months (Table 2).

Table 2. Mean ± SD of different characteristics of study cases (months) N = 101

Demographics & Baseline Characteristics	Mean ± Standard Deviation
Age (years)	36.41 ± 9.362
Weight (kg)	75.54 ± 11.342
Height (cm)	171.44 ± 9.270
BMI (kg/m ²)	25.78 ± 4.08789
Lichen Planus Duration (months)	18.89 ± 10.006

This study also studied the stratification of HCV with other characteristics of study cases. Results showed that no significant positive association (p-value 0.390) was found between the presence of HCV and gender. Similarly, negative significant association (0.563) existed among the presence of HCV virus with age of the cases and a similar

association (0.760) existed among HCV and family history of HCV positive members.

Positive significant association (0.002) was found among HCV presence and BMI of the study cases (Table 3).

Table 3. Stratification of HCV with respect to other characteristics

Characteristics		HCV		Total	P-value
		Yes	No		
Gender	Male	17 (26.6%)	47 (73.4%)	64	0.390
	Female	7 (18.9%)	30 (81.1%)	37	
	Total	24 (23.8%)	77 (76.2%)	101	
Age	18 – 30 years	7 (21.9%)	25 (78.1%)	32	0.563
	31 – 40 years	5 (20.0%)	20 (80.0%)	25	
	41 – 50 years	12 (27.3%)	32 (72.7%)	44	
	Total	24 (23.8%)	77 (76.2%)	101 (100.0%)	
Family History of HCV	Yes	2 (28.6%)	5 (71.4%)	7	0.760
	No	22 (23.4%)	72 (76.6%)	94	
	Total	24 (23.8%)	77 (76.2%)	101 (100.0%)	
BMI Status	Healthy (BMI=18.5-25kg/m ²)	7 (12.7%)	48 (87.3%)	55	0.002
	Overweight (BMI=25.1-30kg/m ²)	10 (32.3%)	21 (67.7%)	31	
	Obese (BMI=>30kg/m ²)	7 (46.6%)	8 (53.4%)	15	
	Total	24 (23.8%)	77 (76.2%)	101	

Discussion

Lichen Planus, one of the most characteristic lichenoid dermatoses, is a chronic, inflammatory skin condition of unknown origin that affects both the skin and mucosal membranes. It often follows a pattern of relapses and remissions. The prevalence of Lichen Planus (LP) varies across different regions, and there is no specific target population for its occurrence. Various global studies have reported an approximate LP prevalence of 0.5% in the general population. Similarly, the presence of Hepatitis C Virus (HCV) in LP patients varies, with different studies showing specific prevalence rates (Lodi et al., 2010; Nagao and Sata, 2012). Some studies conducted in developed countries like the USA,

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Germany, Italy, Spain, and Iran have found associations between HCV and LP, suggesting that HCV may trigger LP (Deguchi et al., 2002; Musso et al., 2008; Yamamoto et al., 2000; Zhou et al., 2001; Zhou et al., 2002). However, studies from other regions, including France, India, and England, have failed to establish a clear link between Lichen Planus and Hepatitis C Virus. These varying results highlight the complex relationship between HCV and LP, and while some studies suggest an association, the exact nature of this relationship remains uncertain (Ammar et al., 2008). Further research is needed to understand the role of HCV in triggering LP and clarify the underlying mechanisms contributing to this connection. The divergent findings underscore the importance of considering geographical and regional factors in LP and HCV, emphasizing the need for a comprehensive and global perspective on this dermatological condition (Abell et al., 1975).

We conducted a study with a similar objective, and our results indicated a significantly higher prevalence of Hepatitis C Virus (HCV) among patients with Lichen Planus (LP), with an observed rate of 23.8% among these patients. It's worth noting that while these findings are specific to the geographic region of Pakistan, it's essential to recognize that other demographic groups may have an elevated risk of HCV infection, such as individuals with a history of blood transfusion, hemophiliacs, and intravenous drug users (Shahzadi et al., 2019). Different studies suggest that the association between LP and HCV infection is less likely to be a random occurrence, particularly given that the general population's prevalence of LP is less than 1%.

Unfortunately, there is no specific reason to know the exact causes of HCV infection in patients with Lichen Planus (LP), and they are not yet fully understood. To find this reason, different studies were conducted and one important conclusion was drawn that a history of alcohol consumption, which was found to be associated with Hepatitis C virus was also found in 20% of patients affected both with LP and HCV (Donempudi et al., 2016; Gamil et al., 2008).

In the present study, the association between Lichen Planus (LP) and Hepatitis C Virus (HCV) infection was most frequently observed in individuals in their fifth to sixth decades, encompassing 75% of the patients. Interestingly, men were affected 1.5 times more often than women. In eight cases, LP was diagnosed simultaneously with HCV infection, while in five patients, the diagnosis of LP occurred 5 to 10 years after the onset of liver disease. From a clinical standpoint, the manifestations of HCV-related LP closely resembled those of classic LP. Notably, mucous membrane involvement was common in

cases of HCV-related LP (Donempudi et al., 2016). While many researchers suggest that cellular immunity plays a significant role in the development of LP, the exact role of HCV in LP's pathogenesis remains uncertain. Further research is needed to corroborate these findings. It is important to note that the replication of HCV in skin and mucosal LP lesions has not been reported in the existing literature. Therefore, LP should be considered among dermatological conditions, such as porphyria cutanea tarda, cryoglobulinemia-related vasculitis, and erythema multiforme, potentially associated with HCV infection.

Our study's results suggest no substantial correlation between gender and the prevalence of Hepatitis C Virus (HCV) infection among individuals with Lichen Planus (LP). In other words, our statistical analysis, as indicated by a p-value of 0.390, did not reveal a significant positive association between gender and HCV infection in LP patients. This implies that the likelihood of having HCV in LP patients does not significantly differ between males and females in our study population, highlighting that gender alone may not be a significant factor in the occurrence of HCV in individuals with LP.

Similarly, a notable negative correlation (0.563) was observed between the presence of HCV virus and the age of the cases. An earlier study mentioned that in regions with a higher prevalence of HCV, the infection is more common in individuals over 40 years of age and less prevalent in those under 20. This observation implies that the prevalence of HCV infection may be linked to the duration of exposure to activities or procedures associated with a risk of virus transmission. Our study has uncovered a significant and robust relationship between the presence of Hepatitis C Virus (HCV) and the Body Mass Index (BMI) of patients with Lichen planus (LP). The statistical analysis, indicated by a low p-value of 0.002, demonstrates that higher or lower BMI values are associated with a notably increased or decreased likelihood of HCV infection in LP patients. This novel finding underscores the role of BMI as a potential indicator and contributor to the prevalence of HCV in individuals with LP. This association suggests that monitoring the BMI of LP patients can be an important aspect of their medical care. Individuals with LP who exhibit variations in BMI, especially those with a lower BMI, may be at a higher risk of HCV infection. By regularly assessing and maintaining a healthy BMI, healthcare providers can potentially aid in the early diagnosis and timely intervention for HCV in LP patients, ultimately enhancing their clinical management and overall well-being.

In a broader context, these findings may also offer insights into the potential underlying mechanisms connecting BMI and HCV susceptibility,

highlighting the need for further research to elucidate the specific pathways through which these factors interact. This knowledge could potentially lead to more effective strategies for preventing and managing HCV infection in the context of LP, offering a valuable contribution to dermatology and viral infections.

Conclusion

These findings highlight the importance of considering age, gender, and BMI when assessing the risk of HCV infection in lichen planus patients. Furthermore, the relatively high prevalence of HCV among lichen planus patients in this population emphasizes the importance of regular screening for Hepatitis C in individuals with lichen planus, particularly in the fifth decade of life, and those with lower BMIs. This information may improve clinical management and patient care in lichen planus and its potential comorbidities.

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Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

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Conflict of Interest

Regarding conflicts of interest, the authors state that their research was carried out independently without any affiliations or financial ties that could raise concerns about biases.



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