Journal of Pakistan Association of Dermatologists. 2022;**32(2)**:373-377.

Original Article

Frequency of positive anti hepatitis C virus antibodies among lichen planus patients

Madiha Iqbal, Sana Aslam*, Shaista Umbreen, Rabia Mukhtar, Sadia Qayyum, Bushra Bashir, Lamees Mahmood Malik

Department of Dermatology, Allama Iqbal Medical College, Jinnah Hospital Lahore.
* Department of Dermatology, District Health Quarter, Layyah.

Abstract

Objective The purpose of this study was to determine frequency of positive Hepatitis C virus in lichen planus patients.

Methods It was a cross-sectional survey which was carried out from 06-08-2014 to 05-02-2015 at the Department of Dermatology, Jinnah Hospital, Lahore. Total 100 patients of lichen planus were enrolled. Antibody titre of Hepatitis C were measured by enzyme-linked immunosorbant assay of third generation.

Results Patients of age between 20-70 years were selected. Mean age was 40.55±14.38 years. Out of total 100 patients, 58 were male (58%) while remaining 42 were female (42.0%). Skin involvement was seen in 96 patients (96.0%), mucous membrane involvement in 21 patients (21.0%) and nails involvement in 8 patients (8.0%). Distribution of patients by type of lesions was as follows: nonerosive mucosal 13%, hypertrophic 80%, annular 1%, follicular 8%, nonerosive palmoplantar 5%, nail lesions 6%, atrophic 9%, erosive mucosal lesions 10%, guttate form 6%, actinic 8% and erosive palmoplantar lesions 1%. Hepatitis C antibody was positive in 23 patients (23.0%).

Conclusion We discovered high frequency of positive HCV in lichen planus patients. We need a case-control study on a larger population to clarify our results.

Key words
Lichen planus, hepatitis C virus, lichenoid eruption.

Introduction

Lichen planus (LP) is characterized as a chronic inflammatory disease with an automimmune etiology. It can have cutaneous as well as mucosal manifestations. There is also evidence of scalp, hair and nail involvement. These lesions are plane topped, purplish, polygonal and pruritic papules and plaques. The onset is mostly acute that affects flexor aspect of wrist, forearm and leg. The lesions show reticular, lacy, white lines called Wickham striae. The classical lichen planus cases are diagnosed clinically, but punch biopsy of 4mm is often helpful. Biopsy is required for atypical lesions.[1] Lichen planus (LP) is chronic disease affecting oral cavity in almost 2% of population. Its oral manifestations can be asymptomatic or severely painful. Its features are similar to diseases of autoimmune etiology although pathogenesis of lichen planus still remains unclear. Stress causes exacerbations. Dental materials and medications may lead to lichenoid reactions.[2] Hepatitis C virus (HCV) is currently considered as most

Address for correspondence
Dr. Madiha Iqbal
Department of Dermatology,
Allama Iqbal Medical College,
Jinnah Hospital Lahore.
Email: madihadrjinnah@gmail.com

common cause of blood-borne hepatitis and chronic liver disease all over the world. Morbidity due to HCV infection is not only because of chronic liver disease but also due to its various extra hepatic manifestations (EHM).[3] A wide geographical variation is reported in Hepatitis C Virus prevalence in lichen planus patients. England has 0% prevalence in contrast to 63% in Japan.[4] Ukonu and Augustine reported positive anti-HCV antibodies in 21.4% patients of lichen planus.[5] Ghods *et al.* reported anti-HCV antibodies in 4.8% of patients.[4] Halawani carried out a study at University of King Saud, University of King Khalid Hospital at Saudi Arabia. He demonstrated that 12.76% of lichen planus patients had positive anti-HCV antibodies.[6] Therefore, different geographical regions show difference in Hepatitis C Virus prevalence in lichen planus cases. The rationale of our study is that geographical origin of the patients can significantly affect frequency of HCV in LP patients. Our study aimed to identify frequency of positive HCV infection in LP cases of our setting.

Methods

It was a cross-sectional survey which was carried out from 06-08-2014 to 05-02-2015 at the Department of Dermatology, Jinnah Hospital, Lahore. The calculated sample size was 100.Confidence level of 95%, margin of error 6.5% and probable percentage of positive anti HCV antibody titres of 12.7%[6] in patients of lichen planus was taken. Non-probability/ purposive sampling technique were used for sample selection. Diagnosis of lichen planus (LP) was made in patients on basis of clinical evaluation. Lesions include recurrent, violaceous, pruritic, plane topped, polygonal papules which may coalesce to form rough hypertrophic plaques, mostly accompanied by mucosal lesions of oral cavity and genitalia. Patients suffering from lichen planus of age 20-70 years, both genders and with lesions for more than 2 weeks duration involving skin, mucous membranes or nails were included. Patients with suspected drug-induced lichenoid reactions (assessed by medical record) were excluded from the study.

After taking informed written consent from each patient, 100 patients of lichen planus fulfilling the inclusion criteria were selected. Lichen planus was diagnosed by clinical examination. Demographic data like age, gender, disease duration was stratified according to types of lesions and sites of involvement to address the effect modifiers. Antibody titres of HCV were measured by Enzyme-Linked Immunosorbant Assay of third generation (ELISA Testing System of 3.0 Ortho® HCV; Clinical Ortho Diagnostics, NJ, Raritan, USA) and was labeled as per 62 operational definitions.

The analysis of collected data was done by software of SPSS (version 20). Patient's age as well as duration of illness was presented as mean±SD. The percentage and frequency for qualitative data like gender, HCV positivity, types of lesions (nonerosive mucosal, hypertrophic, annular, follicular, nonerosive palmoplantar, nail lesions, atrophic, erosive mucosal lesions, guttate form, actinic, erosive palmoplantar lesions), sites of involvement (skin, mucous membrane, nails) were calculated. Data was stratified for site of involvement, age and gender. We applied Chi-square test and considered p value <0.05 as significant in post stratification.

Results

The patients had mean age of 40.55±14.38 years. Out of 100 patients, 58 were male patients (58.0%), whereas remaining 42 were female patients (42.0%) **(Table 1)**. Distribution of

Table 1 Baseline demographics of the study population (n=100).

Characteristics	*n (%age)*
Age mean years	40.55±13.38
Age Groups	
20-40 years	49 (49%)
41-70 years	51 (51%)
Gender	
Male	58 (58%)
Female	42 (42%)
Duration of disease mean months	17.23±23.55
Hepatitis C positive	23 (23%)

Table 2 Distribution of patients by type of and site of lesions (n=100).

Lesion type and site	*N (%age)*
Type of lesions	
Nonerosive mucosal	13(13%)
Hypertrophic	80(80%)
Annular	01(01%)
Follicular	08(08%)
Nonerosive palmoplantar	05(05%)
Nail lesions	06(06%)
Atrophic	09(09%)
Erosive mucosal lesions	10(10%)
Guttate form	06(06%)
Actinic	08(08%)
Erosive palmoplantar lesions	01(01%)
Site of lesion	
Skin	96(96%)
Mucous membrane	21(21%)
Nails	08(08%)

Table 3 Stratification of study population with Hepatitis C.

Characteristics	*Hepatitis C*		*p value*
	+ve	*-ve*	
Age			<0.120
20-40 years	08	41	
41-70 years	15	36	
Gender			<0.037
Male	09	49	
Female	14	28	
Skin involved			<0.923
Yes	22	74	
No	01	03	
Mucous membrane			<0.015
Yes	09	12	
No	14	65	
Nails			<0.310
Yes	03	05	
No	20	72	

patients by type of lesions was as follows: nonerosive mucosal 13%, hypertrophic 80%, annular 1%, follicular 8%, nonerosive palmoplantar 5%, nail lesions 6%, atrophic 9%, erosive mucosal lesions 10%, guttate form 6%, actinic 8% and erosive palmoplantar lesions 1% **(Table 2)**. Skin involvement was seen in 96 patients (96.0%), mucous membrane involvement in 21 patients (21.0%) and nails involvement in 8 patients (8.0%) **(Table 2)**. Hepatitis C virus positivity was seen in 23 patients (23.0%) **(Table 1)**. Stratification according to patients age, gender and site involved presented in **Table 3**.

More females were more positive for Hepatitis C as compared to males p<0.037.

Discussion

A wide geographical variation in relation to lichen planus and positive anti HCV antibodies has been observed. The studies conducted in England[7] and India[8] did not show any relationship between these two diseases. Whereas, a Japanese study determined 37.8% of lichen planus patients out of 45 showed positive serology for hepatitis C virus.[9] In Nigeria, 9% of lichen planus patients had positive anti HCV antibodies.[10] Italy, Germany and Spain were the countries with high frequency of positive anti HCV serology in lichen planus patients.[11-13] Erkek *et al.*[14] found in Turkey, 12.9% of LP patients had positive anti HCV antibodies as compared to control group 3.7% had positive HCV serology. However, this difference was insignificant statistically. Another study conducted in Turkey at Gaziantep region by Kirtak *et al.*[15] showed significant statistical difference in both case and control groups. In Nigeria, Daramola *et al.*[10] found 9% prevalence of HCV in 57 lichen planus patients, although no significant association of HCV infection was noticed statistically. The results of our study

showed (23%) of lichen planus patients had positive anti HCV antibodies. This percentage was higher than most of the above mentioned studies. Most of the cases of our study were of hypertrophic lichen planus, and it was similar to previous observations.[10] In other studies,[16,17] erosive mucosal lesions were more prevalent in patients of HCV ($p<0.001$). It is still not clarified that whether HCV infection plays any role in the development of lichen planus lesions or not. It has been proposed that activated T-cells, particularly CD+8 T-cells are directed towards basal keratinocytes through a response that is immune mediated.[18] Th 1 associated cytokines like TNF alpha, interleukin IL-1 , IL-6, IL-8, ICAM-1 and interferon gamma also play vital role in pathogenesis of lichen planus.[19] Role of Hepatitis C virus infection in pathogenesis of LP is still disputed. Lesions of lichen planus can help to diagnose Hepatitis C infection earlier. Some authors believe that if HCV RNA is identified in epithelial cells of involved skin and mucosa of LP patients, then only we can hypothesize the role of hepatitis C virus in development of LP lesions. Otherwise, merely, HCV positive serology or even PCR positive in LP patients is insufficient to support association between them. Criber *et al.*[21] emphasized the importance of determining frequency of HCV in lichen planus patients as compared to general population. Criber *et al.*[21] argued that there is 1% prevalence of HCV in general population, in comparison to 3.8% prevalence of HCV in lichen planus patients which was quite significant. Limitation of our study was descriptive study design and small sample size. Hepatitis C virus has higher prevalence in our region. Therefore, in order to make a better policy, we need a larger multicentre study. It is evident that HCV screening in LP patients, even with normal liver function tests, will be helpful. Skin specialists should particularly advise hepatitis C virus screening before taking skin biopsy of lichen planus cases.

Conclusion

We observed high frequency of positive HCV serology in patients of lichen planus. To clarify these findings a case-control study on a larger population is needed.

References

1. Usatine RO, Tinitigan M. Diagnosis and treatment of lichen planus. *Am Fam Physician*. 2011;**84**:53-60.
2. Czerninski R, Pikovsky A. Update and review of oral lichen planus. *Refuat Hapeh Vehashinayim*. 2013;**30**:31-7.
3. Lodi G, Pellicano R, Carrozzo M. Hepatitis C virus infection and lichen planus: a systematic review with meta-analysis. *Oral Dis*. 2010;**16**:601-12.
4. Ghodsi SZ, Daneshpazhooh M, Shahi M, Nikfarjam A. Lichen planus and Hepatitis C: a casecontrol study. *BMC Dermatology*. 2004;**4**:6
5. Ukonu AB, Augustine U. The prevalence of hepatitis C Virus (HCV) among lichen planus patients and its clinical pattern at the University of Abuja Teaching Hospital, Gwagwalada, Abuja, Nigeria. *Glob J Health Sci*. 2012;**4**:113-9.
6. Halawani M. Hepatitis C virus genotypes among 82 patients with lichen planus in the Kingdom of Saudi Arabia. *Int J Dermatol*. 2014;**53**:171-7.
7. Tucker SC, Coulson IH. Lichen Planus is not associated with Hepatitis C Virus Infection in Patients from North West England. *Acta Academy Venereology*. 1999;**79**:378-9.
8. Prabhu S, Pavithran K, Sobhanadevi G. Lichen Planus and Hepatitis C Virus (HCV). Is There an Association? A Serological study of 65 cases. *Indian J Dermatol Venereol Leprol*. 2002;**68**:273-4.
9. Tanei R, Wantanbe K, Nishiyama S. Clinical and Histopathological Analysis of the Relationship between Lichen Planus and Chronic Hepatitis C Virus. *J Deramtol*. 1995;**22**:316-23.
10. Daramola OOM, George AO, Ogunbiyi AO. Hepatitis C Virus and Lichen Planus in

Nigerians: Any Relationship? *Int J Dermatol*. 2002;**41**:217-9.
11. Sanchez-perez J, De Castro M, Buezo GF, Fernandez-Herrera J, Borque MJ, Garcia-Diez A. Prevalence and Clinical Presentation of Patients with Lichen Planus and Hepatitis C Virus Infection. *Br J Dermatol.* 1996;**134**:715.
12. Foti C, Novielle G, Coviello C, Vella F, Vera, GA, Volpe A. *et al*. Lichen Planus and Hepatitis C Virus. *G Ital Dermatol Venereol*. 1994;**129**:93-6.
13. Inhof M, Popal H, Lee JH, Zenzen S, Milbradt R. Prevalence of Hepatitis C Virus Genotypes in Patients with Lichen Planus. *Dermatology*. 1997;**195**:1-5.
14. Erkek E, Bozologan O, Olut AI. Hepatitis C Virus Infection Prevalence in Lichen Planus: Examination of Lesional and Normal Skin of Hepatitis for the Presence of Hepatitis C Virus RNA. *Clinical Exp Dermatol*. 2001;**26**:540-4.
15. Kirtak N, Inalöz HS, Ozgöztasi, Erbağci Z. The prevalence of hepatitis C virus infection in patients with lichen planus in Gaziantep region of Turkey. *Eur J Epidemiol*. 2000;**16(12)**:1159-61.
16. Carrozzo M, Gandolfo S, Carbone M. Hepatitis C virus infection in Italian patients with oral lichen planus: a prospective case-control study. *J Oral Pathol Med*. 1996;**25**:527-33.
17. Dupin N, Chosidow O, Lunel F, Fret C, Szpirglas H, Frances C. Oral Lichen Planus and Hepatitis C Virus Infection: A Fortuitous Association? *Arch Dermatol 1997*;**133**:1052-3.
18. Hussein MR. Evalaution of Angiogenesis in Normal and Lichen Planus Skin by CD 34 Protein Immunohistochemistry: Preliminary Findings. *Cell Biol Int*. 2007;**31**:1292.
19. Chen X, Liu Z, Yue Q. The Expression of TNF-Alpha and ICAM-1 in Lesions of Lichen Planus and Its Implication. *J Huazhong Univ Sci*. 2007;**27**:739.
20. Arrieta JJ, Rodriguez Inigo E, Casqueiro M, Bartolon J, Manzarbeita F, Herrero M, *et al.* Detection of Hepatitis C Virus Replication by In Situ Hybridization In Epithelial Cells of AntiHepatitis C Virus-Positive Patients with and without Oral Lichen Planus. *Hepatology*. 2000;**32**:97103.
21. Criber B, Garnier C, Laustriat O *et al*. Lichen planus and hepatitis C virus infection an epidemiologic study. *J Am Acad Dermatol*. 1994;**31**:1070-2.