

Association between Hepatitis C Virus Infection and Oral Lichen Planus in Israeli Patients

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Abstract

Background: Oral lichen planus is a cell-mediated immune condition of unknown etiology. A possible association of OLP with hepatitis C virus infection has been documented in specific populations. However, no such possible association has been studied in Israel.

Objectives: To assess the prevalence of HCV antibodies among patients with OLP in Israel.

Methods: The prevalence of HCV seropositivity was studied in OLP patients (n=62) and compared with that of a control group (n=65) and with the prevalence among healthy volunteer blood donors (n=225,452) as representatives of the general population.

Results: The prevalence of HCV, as detected by the presence of anti-HCV antibodies screened by enzyme-linked immunosorbent assay, and confirmed by recombinant immunoblot assay, was 4.8%, 1.5% and 0.1%, respectively. HCV seropositivity in the OLP patients was significantly higher than in the healthy blood donors ($P < 0.001$).

Conclusions: A possible association between OLP and HCV is suggested. Therefore, screening OLP patients for antibodies to HCV is recommended.

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Figure 1. Erosive lesions of oral lichen planus on the buccal mucosa of patient with HCV infection

Oral lichen planus, a cell-mediated immune condition of unknown etiology, affects the oral mucosa in 1–2% of the general population [1]. Clinically, one of three forms is presented: reticular lichen planus, atrophic lichen planus, or erosive lichen planus. The reticular form of OLP includes white, usually asymptomatic, striated lines or white plaques on the oral mucosa. The atrophic and erosive forms contain erythema with no ulcerations (atrophic) or an ulcerated mucosa (erosive) in addition to the white or white red changes. Atrophic lichen planus and erosive lichen planus are usually associated with some discomfort or pain [Figure 1].

OLP may involve any site of the oral mucosa, usually bilaterally, most commonly involving the buccal mucosa, gingivae, and lateral borders of the tongue [2,3]. OLP is notoriously associated with premalignant risk, and with malignant transformation rate ranging between 0.4 and 5.6% [4].

The association of OLP with hepatitis C virus infection is well

documented [Table 1], and has been observed in Italy, Japan, Brazil and the United States [5], with an unidentified cause and effect association. In northern European countries such an association has not been reported, probably reflecting a low prevalence of HCV infection in those populations [5].

The overall prevalence of HCV seropositivity in the Israeli population was approximately 0.5% when determined by non-confirmed enzyme-linked immunosorbent assay testing [6,7], ranging from 0.06% in native-born Israelis [8] to 3.6% among individuals born in other countries who immigrated to Israel, mostly from the former Soviet Union [9].

The co-occurrence of OLP and anti-HCV antibodies has never been studied in the Israeli population. The purpose of the present study was to assess the correlation between OLP and confirmed HCV seropositivity.

Patients and Methods

The study group consisted of 62 clinically and histopathology confirmed OLP patients (48 women and 14 men), treated

OLP = oral lichen planus

HCV = hepatitis C virus

consecutively in the Oral Medicine Clinic of our dental school. Two groups served as controls: group A included 65 (47 women and 19 men) age and gender-matched participants with non-OLP oral mucosal disorders who were treated in the same clinic for various mucosal lesions such as hyperkeratosis, oral candidiasis, recurrent aphthous stomatitis, pemphigus vulgaris, mucous membrane pemphigoid and benign oral growths. The second group, group B, included 225,452 volunteer blood donors of Magen David Adom National Blood Services (59,261 women and 165,401 men), ranging in age from 17 to 65, who represented the general healthy Israeli population. Serum samples were screened for anti-HCV antibodies using a third-generation ELISA, Abbott Diagnostika, Weisbaden, Germany). Repeat reactive samples were confirmed using a recombinant immunoblot assay (HCV 3.0 SIA, Ortho Clinical Diagnostics, USA).

Pearson chi-square test and ANOVA were used with the BMPD stratified software (BMPD Software, University of California Press 1993). Significance was set at P value lower than 0.05.

Results

The study group ranged in age from 27 to 82 years (mean 60.1 years) compared with 25 to 80 years (mean 63.3) in control group A. The native Israelis comprised 51.6% of participants in the study group ($n=32$) compared to 36.9% ($n=24$) and 73% ($n=164,580$) in control groups A and B, respectively.

In the study group, three patients (4.8%) were seropositive for HCV compared to only one patient (1.5%) in control group A and 240 (0.1%) among the blood donors [Table 1]. HCV seropositivity was significantly higher in the OLP patients than in group B representing the general Israeli population ($P < 0.001$). There was no statistically significant difference in finding HCV antibodies between control groups A and B. Neither was there a significant difference between the prevalence of HCV antibodies detected in patients from the study group (3/62) compared with control group A (1/64).

Since OLP is usually diagnosed in patients over 50 years old, the prevalence of HCV antibodies in the study group was compared to the prevalence among the 24,738 blood donors over the age of 50 (22 HCV seropositive = 0.088%). The same level of significance was found ($P < 0.001$).

The prevalence of HCV antibodies was significantly higher ($P < 0.001$) in the Israeli-born patients diagnosed with OLP (6.25%) than among the native Israeli blood donors (0.026%).

Discussion

Lichen planus is a chronic mucocutaneous disease with unknown etiology. The accumulating data suggest a possible association between cutaneous and oral lichen planus and HCV infection. This occurrence has

ELISA = enzyme-linked immunosorbent assay

Table 1. HCV seropositivity in the different groups

Group	No.	Seropositive	
		No.	%
OLP patients	62	3	4.8*
Non-OLP patients	65	1	1.5
Blood donors	225,452	240	0.1*

* $P < 0.001$

never been studied in the Israeli population. The present study aimed to investigate the possible association in OLP patients in Israel. Since the prevalence of HCV infection in Israel is low compared to other populations [6,7], the difference in occurrence between the study group and the first control group failed to reach statistical significance. However, when the study group was compared with a large sample of healthy volunteer blood donors who represented the general population in Israel, a significant difference was found in the occurrence of HCV infections.

Although control B group consisted of blood donations collected during 2003, it may be considered a representative figure for the current prevalence (0.1%). Anti-HCV antibodies detected among blood donors in Israel in the last decade remain relatively constant (E. Shinar, personal communication). This lower prevalence results from screening for HCV by more sensitive, third-generation ELISA tests, and from confirmation of the positive results. The occurrence of anti-HCV antibodies in different countries and geographic areas may vary, with prevalence up to 5% [Table 2]. In addition, differences in prevalence of anti-HCV antibodies may differ among different ethnic groups in the same country [7,9], ranging from 0.06% in native-born Israelis [8] to 3.6% among individuals born in other countries who immigrated to Israel, mostly from the former USSR [9]. However, in the study group, where a high prevalence of HCV was detected among patients with OLP, 51.6% of the participants were native-born Israelis as compared to 36.9% in the

Table 2. The prevalence of anti-HCV antibodies in patient with OLP in different geographic areas

Study	Country	LP		Control		Significance
		No.	HCV Ab (%)	No.	HCV Ab (%)	
Dupin et al. [13]	France	102	4.9	306	4.5	No
Lodi et al. [14]	Italy	303	19.1	278	3.2	Yes
Mignogna et al. [15]	Italy	263	28.8	100	3	Yes
Nagao et al. [16]	Japan	45	62	–	–	–
Bagan et al. [17]	Spain	100	23	100	5	Yes
Ingafou et al. [18]	UK	55	0	110	0	No
Chainani-Wu et al. [19]	USA	31	45	–	–	–
Eisen [20]	USA	195	0	–	–	–
Figueiredo et al. [21]	Brazil	68	8.8	1059	1.4	Yes
van der Meij & van der Waal [22]	Netherlands	55	0	–	–	–
Present study	Israel	62	4.8	65	1.5	No
				225,452	0.1	Yes

control group A. This further supports a possible association between HCV and OLP.

In the present study, the possible association between OLP and HCV infections should be carefully interpreted. It is well known that once diagnosed with HCV, seropositive individuals cannot donate blood. Therefore, the choice of blood donors as representative of the general population may portray a selection bias and underestimates the actual prevalence of anti-HCV antibodies in the general healthy population.

The erosive form of OLP was diagnosed in 23 of the 62 patients (37%) and only one (4%) was HCV seropositive compared to 2 (5%) of the 39 non-erosive OLP patients. Although other studies suggest that HCV infection associates mainly with the erosive form of OLP [10,11], a recent controlled study reports that the reticular clinical form may also be highly associated with positive HCV antibodies [12]. This higher occurrence in a non-erosive form of the disease was shown in the present analysis.

In conclusion, the present study suggests a possible correlation between OLP and HCV infections in the Israeli population. However, no relation was found between this association and a specific clinical form of the disease. Due to the higher occurrence of HCV seropositivity in OLP patients, it is suggested that all Israeli patients diagnosed with OLP be regularly screened for HCV antibodies.

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It came to be that reform should begin at home, and since that day I have not had time to remake the world

Will Durant (1885-1981), American philosopher, historian, and writer. He is best known for his authorship and co-authorship with his wife Ariel Durant of *The Story of Civilization*