Original Article

A study of lichen planus and its association with hepatitis C infection

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Abstract

Objectives: The association of lichen planus with chronic hepatitis C virus (HCV) has been widely reported in the literature. However, there are wide geographical variations in the reported prevalence of HCV infection in patients with lichen planus. This study was conducted to determine the association of lichen planus with HCV in Iraqi patients in Basra governorate (southern Iraq).

Methods: From January 2008 to October 2009, 97 cases of lichen planus, 47 women (48.5%) and 50 men (51.5%) were diagnosed on the basis of characteristic clinical features, and if necessary, typical histological findings on biopsy. The patients were screened for the presence of anti-HCV antibodies by third generation ELISA. The control group (2070 person) consisted of healthy blood donors who were screened for HCV in the Central Blood Bank of Basra.

Results: Anti-HCV antibodies were detected in 3 (3.1%) cases of the patients. This was significantly higher in blood donors (p value = 0.002). A statistically significant association was demonstrated between lichen planus and hepatitis C virus infection. Liver function tests, plasma glucose and gender were not significantly different between HCV infected and non-infected patients.

Keywords: lichen planus; hepatitis C; correlation.
Introduction

Lichen planus (LP), which was firstly described in 1869 by Jonathan Hutchinson, is a unique inflammatory cutaneous and mucous membrane reaction pattern of unknown aetiology characterized by small violaceous flat angular scaly shiny pruritic papules and plaques on the skin and white papules in the mouth.1,2 There are several clinical forms of LP; actinic, annular, atrophic, erosive, follicular (lichen planopilaris), guttate, hypertrophic, linear, papular and vesiculobullous. Skin lesions are characterized by a white lace-like pattern (Wickham's striae) on papules and are almost pathognomonic of lichen planus. Mucous membrane involvement is seen in 40–60% of patients with skin lesion. Twenty percent of patients have mucous membrane lesions only.1 The mucosal lesion is usually asymptomatic and women outnumber men by more than 2:1.3 Ulcerative mucosal lesions are characterized by small violaceous flat angular scaly shiny pruritic papules and plaques on the skin and white papules in the mouth.1,2

The cause of LP is unclear. The most acceptable hypothesis implies a viral cause, immunological or emotional stress. Lichenoid eruptions include drug induced, chemical, bacterial and post bone marrow transplantation. Lichenoid drug eruptions are morphologically similar to LP and can be differentiated by drug history only.3,6

Hepatitis C virus (HCV) is a single-stranded RNA flavivirus that replicates in hepatocytes and peripheral blood mononuclear cells.5

The diagnosis is based on detection of antibodies against HCV (anti-HCV). The third-generation enzyme-linked immunosorbent assay (ELISA) has 99% sensitivity in detecting total antibodies with 94% specificity and can be confirmed by direct detection using HCV RNA.4

In recent years it has become known that HCV induces a broad spectrum of extrahepatic manifestations including porphyria cutanea tarda and LP. These dermatological manifestations may serve as an early marker for HCV that may save lives. Therefore, evaluating the potential clinical role of LP in diagnosing HCV infection seems to be an extremely practical and pivotal task.8

The association of LP and HCV is uncertain and controversial in literature because the prevalence of HCV infection in patients with LP varies considerably from one geographical area to another ranging from 4% in northern France to 62% in Japan while studies from Great Britain failed to reveal any association.6–11 It has been suggested that the geographical origin of patients would be an important factor in HCV prevalence among patient with LP.12

The pathogenesis of this association is uncertain and there are several explanations that had been suggested by several researchers. One of the more often cited explanation is the suggestion that HCV infection precipitates an autoimmune process.13 LP appears to be related to the pattern of immune dysregulation induced by HCV. The mechanism of HCV induced lichen planus is possibly related to the viral replication in lymphocytes14 and it is well known that one of the characteristic histological features of LP is band like lymphocytic infiltration in the papillary dermis or possibly HCV is related in a way or another to the basal cell layer of the epidermis to which the lymphocytic band like infiltrate seems to be directed and once these cells are destroyed, the infiltrate descends down to the upper dermis. This point needs to be further clarified in more specified studies.

The controversies and uncertainties regarding the association of LP and chronic HCV inspired us to conduct this study in a group of patients in Basra (southern Iraq).

Materials and Methods

From January 2008 to October 2009, a total of 97 patients with lichen planus were enrolled in a case control study, 50 males (51.5%) and 47 females (48.5%) with an age ranging from 5 to 77-year-old (mean age 34.2 ± 14.7 years). Male: female was 1:1.06.

This study was carried out at the dermatology clinic of both Al-Sadir teaching and Basra general hospitals.

The demographic data such as age, gender and information including type of lesion, site of involvement and other associated lesions were collected using a checklist after taking the patients’ consent.

Patients with a possible drug induced lichenoid eruptions, those who have chronic hepatitis B infection and a history of alcohol consumption were excluded from the study. All of the 97 patients were screened for the presence of serological evidence of HCV using the 3rd generation ELISA kit for detection of antibodies to human HCV, Murex anti-HCV ELISA version 4.0 (Abbott corporation, Kyalami Business pork, South Africa). All of the patients were also screened for hepatitis B infection using a detection kit for hepatitis B antigen, Murex HBs Ag version 4.0 (Abbott corporation, Kyalami Business pork, South Africa).

A total of 2070 apparently healthy Iraqi blood donors from both sexes were selected from the records of Central Blood Bank of Basra and have been used as a control group. They had already been tested for HCV antibodies using the same technique that was used in testing the cases.

All of the patients were diagnosed clinically by a dermatologist. In suspicious cases 27 patients (27.8%), the diagnosis was confirmed by skin biopsy. All of the specimens were examined by the same histopathologist. The histological confirmation was based on the presence of degeneration of the basal layer with band like lymphocytic infiltration of the papillary dermis.

Conclusions: The prevalence of HCV among Iraqi patients with lichen planus (3.1%) was significantly higher than in the control group (0.14%). It seems that there is an association between HCV and lichen planus among Iraqi patients in Basra city; however, liver function tests are not pivotal means in screening for HCV in lichen planus patients.

Keywords: Association; Hepatitis C; Lichen planus
Blood samples were obtained from all patients for estimation of plasma glucose and liver enzymes.

The control group was selected by systemic random sampling method. The total number of healthy blood donors from both sexes and of different age groups, who donated blood in the Central Blood Bank of Basra during the same period of cases, collection (103,450 people), were divided into groups of fifties In each group, the number 6 was selected by chance and the 6th of each 50 was taken as a control. The number of controls that had been extracted by the aforementioned statistical method was 2070.

Pooled data were analysed using Statistical Package for the Social Sciences (SPSS) (ver.15) software. Fisher’s exact test was used to test the significance of association between lichen planus and HCV. In the comparison between cases and controls, p value less than 0.05 was considered as significant.

Results

Three patients (3.1%) out of 97 with LP had positive serological test for anti-HCV antibody compared with the control group in which the prevalence of anti-HCV antibody was estimated to be 0.14%, p value = 0.002.

The peak of LP was in the age group 30–39 years in both sexes and represents 36 (37.1%) of total cases followed by the age group 40–49 in 10 males (10.3%) and 20–29 in nine females (9.3%). The lowest prevalence of LP 1 (1%) was recorded in the age group 70–79 as shown in Table 1. There were 16 patients under 20 and represented (16.5%) of the total cases.

The skin condition predominated over other sites of involvement in both sexes; females 6 (75%) presented with oral lesions more than males 2 (25%) while males 13 (76.5%) had generalized LP compared to females 4 (23.5%). The sex distribution of patients and the site of LP are shown in Table 2.

The commonest type of LP encountered during this study was the classical type which accounts for 36 cases (37.1%) followed by the hypertrophic and oral types with frequency of 20 (20.6%) and 9 (9.3%), respectively. The sex distribution of patients in reference to the type of LP is shown in Table 3. Classical LP is the commonest type in both sexes, 19 males (38%) and 17 females (36.2%). The oral type is seen more in females 7 (14.9%) compared with their male counterparts only 2 (4%) of whom were affected. The Atrophic and annular types were seen exclusively in males while the hypertrophic type was seen more in males.

All the patients with positive serological test of HCV were males 3 (6%). No significant differences were found between both sexes in those with negative serology, p value = 0.24. Two of the three cases with serological evidence of HCV had oral reticulate lesions.

Only one (33.3%) of the three patients who were HCV positive had elevated plasma glucose compared to 13 (13.8%) out of 94 who were HCV seronegative; however, there is no significant difference between the two groups, p value = 0.37.

Abnormal liver function test (LFT) were found in 23 (23.7%) of patients with LP none of whom were anti-HCV positive. The distribution of LFT in different age groups is shown in Table 4. Those younger than 20 years had the highest incidence of abnormal LFT, 12 (52.1%) compared to 11 (47.9%) from other age groups. This abnormality was due to isolated elevation in ALP in the first group and in aminotransferases in the second group.

All of the three patients who were HCV positive had normal LFT compared to 71 (75.5%) of the HCV negative group with 23 (24.5%) abnormal LFT.

Discussion

LP is a pruritic, purplish, plane, polygonal papular eruption. It is seen most commonly on the flexor surface of the wrist and legs, genitalia and mucous membranes. More than 50% of cutaneous lesions resolve within 6 months and 85% of cases resolve within 18 months. However, oral lesions have a mean duration of 5 years.

In recent years it has become known that HCV induces a broad spectrum of extrahepatic manifestations including LP. The first case was reported in France in 1991. The prevalence of HCV antibodies in patients with oral and cutaneous LP was found to be significantly higher than...

| Table 1: Distribution of patients with LP in relation to their age and sex. |
|---|---|---|---|---|---|
| Age (years) | Total | 0–9 (%) | 10–19 (%) | 20–29 (%) | 30–39 (%) | 40–49 (%) | 50–59 (%) | 60–69 | 70–79 |
| Males | 34 (48.6) | 5 (2.1) | 8 (2.9) | 20 (58.8) | 10 (29.4) | 2 (5.9) | 2 (5.9) | 2 (5.9) | 50 (100) |
| Females | 36 (51.4) | 4 (5.6) | 9 (12.5) | 16 (23.7) | 5 (7.4) | 5 (5.6) | 3 (5.6) | 0 (0) | 47 (100) |
| Total | 70 (100) | 10 (14.3) | 17 (24.3) | 36 (51.4) | 15 (21.4) | 7 (10) | 5 (7.1) | 1 (1.4) | 97 (100) |

<p>| Table 2: Sex distribution of various sites of LP among all patients. |
|---|---|---|---|---|---|</p>
<table>
<thead>
<tr>
<th>Sex</th>
<th>Skin (%)</th>
<th>Generalized (%)</th>
<th>Oral (%)</th>
<th>Scalp (%)</th>
<th>Genital (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>34 (48.6)</td>
<td>13 (76.5)</td>
<td>2 (25)</td>
<td>0 (0)</td>
<td>1 (100)</td>
</tr>
<tr>
<td>Females</td>
<td>36 (51.4)</td>
<td>4 (23.5)</td>
<td>6 (75)</td>
<td>1 (100)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>70 (100)</td>
<td>17 (100)</td>
<td>8 (100)</td>
<td>1 (100)</td>
<td>1 (100)</td>
</tr>
</tbody>
</table>
that in the control group in Jordan, Kingdom of Saudi Arabia, Turkey and Iran.

In this study HCV antibody prevalence in patients with LP was 3.1%. It was significantly higher in the blood donors (0.14%) who were in the control group ($p$ value = 0.002). However, the prevalence of HCV among the control group was substantially lower than in other countries like north Egypt (38%) and USA (1.4%). This may be attributed to the highest prevalence of intravenous drug users in developed countries like USA and the use of infected parenteral antimony treatment for schistosomiasis in Egypt. In addition to this, no studies have been carried out in Basra to estimate the real prevalence in the general population. One of the limitations of this study is that the control group was non-representative of the general population as they were healthy individuals.

For some authors the association of LP and positive serology for HCV, even positive RNA, is not a substantive enough reason to determine the role of HCV in the pathogenesis of LP. Nevertheless, demonstration of HCV RNA in epithelial cells of oral mucosa and skin lesions of patients with LP would lead to the theory that direct action of the virus is involved.

It was found that 36 patients (37.1%) were in their 4th decade which matches what had been written in studies. LP is rare in children. An interesting finding in our study is that 16 patients (16.5%) were under the age of 20. This may be attributed to the hepatitis B vaccine and there are reported cases of LP secondary to hepatitis B vaccination keeping in mind that the hepatitis B vaccine has been included in the expanded programme of immunization (EPI) in Iraq since 1992.

Table 3: sex distribution of patients in relation to the type of LP.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Oral (%)</th>
<th>Classical (%)</th>
<th>Actinic (%)</th>
<th>Follicular (%)</th>
<th>Pigmented (%)</th>
<th>Annular (%)</th>
<th>Hypertrophic (%)</th>
<th>Acute (%)</th>
<th>Guttate (%)</th>
<th>Bullous (%)</th>
<th>Atrophic (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>2 (4)</td>
<td>19 (38)</td>
<td>1 (2)</td>
<td>1 (2)</td>
<td>3 (6)</td>
<td>4 (8)</td>
<td>13 (26)</td>
<td>1 (2)</td>
<td>1 (2)</td>
<td>1 (2)</td>
<td>1 (2)</td>
<td>50 (100)</td>
</tr>
<tr>
<td>Females</td>
<td>7 (14.9)</td>
<td>17 (36.2)</td>
<td>7 (14.9)</td>
<td>1 (2.1)</td>
<td>1 (2.1)</td>
<td>0 (0)</td>
<td>7 (14.9)</td>
<td>4 (8.5)</td>
<td>2 (4.3)</td>
<td>1 (2.1)</td>
<td>0 (0)</td>
<td>47 (100)</td>
</tr>
<tr>
<td>Total</td>
<td>9 (9.3)</td>
<td>36 (37.1)</td>
<td>8 (8.2)</td>
<td>2 (2.1)</td>
<td>4 (4.1)</td>
<td>4 (4.1)</td>
<td>20 (20.6)</td>
<td>8 (8.2)</td>
<td>3 (3.1)</td>
<td>2 (2.1)</td>
<td>1 (1)</td>
<td>97 (100)</td>
</tr>
</tbody>
</table>

Table 4: distribution of LFT in regard to age groups.

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>LFT</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal (%)</td>
<td>Abnormal (%)</td>
</tr>
<tr>
<td>0–9</td>
<td>1 (16.7)</td>
<td>5 (83.3)</td>
</tr>
<tr>
<td>10–19</td>
<td>3 (30)</td>
<td>7 (70)</td>
</tr>
<tr>
<td>20–29</td>
<td>16 (94.1)</td>
<td>1 (5.9)</td>
</tr>
<tr>
<td>30–39</td>
<td>32 (88.9)</td>
<td>4 (11.1)</td>
</tr>
<tr>
<td>40–49</td>
<td>12 (80)</td>
<td>3 (20)</td>
</tr>
<tr>
<td>50–59</td>
<td>5 (71.4)</td>
<td>2 (28.6)</td>
</tr>
<tr>
<td>60–69</td>
<td>4 (80)</td>
<td>1 (20)</td>
</tr>
<tr>
<td>70–79</td>
<td>1 (100)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Total (%)</td>
<td>74 (76.3)</td>
<td>23 (23.7)</td>
</tr>
</tbody>
</table>

LFT: liver function tests.

The majority of patients with LP in this study 70 (72.2%) had skin involvement which was similar to that found in other studies. However, two studies found that 46.6% and 53.4% had generalized LP (skin and oral), respectively. Another study found oral lesion being the commonest.

In oral LP, women outnumber men by more than 2:1 which concords with the findings in this study where the majority of patients were females. Furthermore, females were more likely to be affected by erosive oral LP in contrast to males who more commonly suffered from reticulate oral lesions. Mechanical injury from dental procedures and poor fitting appliances may trigger or exacerbate gingival LP probably via the Koebner’s phenomenon. Al-Hamdi found that chewing of deram (juglans) which is a herbal remedy used widely by women in the southern part of Iraq for cosmetic purposes plays a role in the pathogenesis of LP. This may explain the above findings, at least among Iraqi female patients.

No significant association was found between high plasma glucose and HCV seropositivity, however, Al-Tarawneh et al. found that RBS were significantly higher in HCV positive patients and recommended its use as a routine investigation in every patient afflicted by LP.

In this study 23 patients (32.7%) with LP had abnormal LFT and none of them had HCV antibodies.
these patients were under 20 and had isolated hyperphosphatase (elevated alkaline phosphatase). This can be explained by the normal finding of hyperphosphatase encountered in the growing bone. On the other hand, two of the 11 patients (48%), who were over 20 and presented abnormal LFT, had elevation in all the three enzymes. One of these two patients was a 37-year-old female suffering from Hodgkin’s disease and undergoing chemotherapy. The remaining nine patients had elevation in either two or one of the transaminases. This may be attributed to agents causing hepatic insult other than hepatitis B or C.

**Conclusion**

A statistically significant high prevalence of HCV (3.1%) is detected in Iraqi patients living in Basra with LP.

**Recommendation**

It seems that screening for HCV would be cautious in patients with LP even in those with normal LFT. Dermatologists should request hepatitis screening before attempting skin biopsy for every patient with LP.

**Conflict of interest**

The authors have no conflict of interest to declare.

**Acknowledgement**

We would like to thank the workers in the Blood Bank of Basra, Central Lab in Basra Teaching Hospital, Dermatology outpatient clinic and the pathologist Dr. Sawsan Salih for their kind help.

**References**