

# Prevalence of Hepatitis C Virus in Oral Lichen Planus and the Levels of Aminotransferase Hepatic Enzymes in Patients with Oral Lichen Planus.

Imran Malik<sup>1</sup>, Daya K Jangam<sup>2</sup>, Anies Ahmed<sup>3</sup>, Faheem Muzaffar Mir<sup>4</sup>, Jasdeep Kaur<sup>5</sup>, Gulnaaz Anjum<sup>6</sup>

<sup>1</sup>MDS, Community Health Center Kandi, J&K Govt. Health Dept.

<sup>2</sup>Prof & HOD Deptt of Oral Medicine & Radiology, Sinhgad Dental College & Hospital Pune.

<sup>3</sup>MDS, Dj College of Dental Sciences & Rsearcch Modinagar Delhi/NCR.

<sup>4</sup>MDS, Lecturer, Dept. of Biomedical Dental Sciences, University of Dammam College Of Dentistry, Saudi Arabia.

<sup>5</sup>MDS, Senior Lecturer, Oral Medicine & Radiology, Shaheed Kartar ingh Sarabha Dental College, Sarabha.

<sup>6</sup>PG Student, AME'S Dental College, Raichur Karnataka.

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## ABSTRACT

**Background:** Oral lichen planus (OLP) is a relatively common skin and oral disease that manifests as a mucous reaction to a variety of etiologic factors, including autoimmune disease, drug reaction, diabetes mellitus (DM), hypertension, hepatitis C virus (HCV), urolithiasis, psychogenic factors, and bacterial infection. It is one of the most frequent oral lesion found in patients with hepatitis C virus (HCV) infection. **Objective:** The purpose of this study was to investigate the relationship between HCV infection and OLP as there is a high prevalence of HCV infection in India, and to assess the levels of aminotransferase enzymes (SGPT/SGOT) in patients with OLP. **Methods:** The study consisted of 25 histopathologically confirmed patients of OLP and 25 subjects with age and sex matched healthy volunteers visiting the outpatient department of a dental hospital over a period of 1 year. All subjects in both groups were subjected to serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT) and HCV antibodies detection. **Results:** The average HCV antibody between study and control group was statistically non-significant with  $p=0.965$ . The percentage of patients with elevated SGOT and SGPT values was higher among the OLP patients in the study group ((32.0%) i.e.  $>45$  IU/L) in comparison to subjects in the control group (0%). Hence, SGOT and SGPT value was statistically significant ( $p$  value= 0.002). **Conclusion:** OLP in certain populations can be used as a marker for HCV infection in addition to transaminase hepatic enzymes level.

**Keywords:** Hepatitis C virus, Oral Lichen planus, SGOT /SGPT.

## INTRODUCTION

Lichen Planus (LP) is a chronic inflammatory muco-cutaneous disease or a common dermatological disorder occurring on the skin and oral mucous membrane appearing as a lace like pattern.<sup>[1]</sup> It is characterized by shiny, flat-topped, pruritic, violaceous, and papulosquamous eruptions varying in size from pin point to larger than a centimeter, mainly involving the extremities, genitalia, or oral cavity.<sup>[2]</sup> It is estimated to occur in 0.2-2.3% of the general population and it represents about 0.6% of all diseases that the

dentists frequently meet.<sup>[3]</sup> Lichen planus was first described in the year 1869 by Erasmus Wilson. Later in 1895, Wickam's described the characteristic appearance of whitish Striae and punctuations that develop on the top of the flat-surfaced papules and termed them as "Wickham's striae."<sup>[4]</sup>

The etiology of LP is largely unknown. Its association with human leukocyte antigen (HLA)-BW16, B8, and DRI suggests the possibility of genetic predisposition.<sup>[5]</sup> A number of investigators have reported a correlation between LP and certain liver diseases, particularly primary biliary cirrhosis, active chronic hepatitis, and cryptogenic liver cirrhosis, and a common pathogenic basis has been suggested in a number of cases.<sup>[6]</sup> A possible association between oral lichen planus (OLP) and hepatitis C virus (HCV) infection has been documented in certain populations such as Japan and Southern Europe; however, the issue remains controversial. Although many studies demonstrated

### Name & Address of Corresponding Author

Dr.Imran Malik  
MDS,  
Community Health Center,  
Kandi,  
J&K Govt. Health Dept.  
Jammu and Kashmir

a significant association between HCV and OLP, Where as some reported the opposite.<sup>[7]</sup> Altered liver function tests, i.e., elevated serum glutamic oxaloacetic transaminase (SGOT)/serum glutamic pyruvic transaminase (SGPT), have been detected especially in erosive type of oral lichen planus (OLP).<sup>[8]</sup>

Aminotransferase elevated results could be used as a clue to clinical signs of asymptomatic hepatopathies, and as a marker to check the OLP cases for the relevant Hepatic Viruses. It is well known that the OLP patients with normal hepatic enzyme levels are usually HCV negative but they might be suffering other hepatopathies.<sup>[9]</sup> A number of studies have investigated the relationship between HCV and LP in the last two decades with variable results. Geographical heterogeneity of the association between HCV and LP has been clearly noted.<sup>[10]</sup> The association of HCV and the liver function status (transaminase levels) in OLP, have always remained a controversial subject Considering all the previous observations, this study was carried out to investigate the possible epidemiological relationship.

The aim of this study is to see the possibility of any association between Oral Lichen Planus with hepatitis C virus and the levels of aminotransferase hepatic enzymes like Serum alanine aminotransferase (ALT/SGPT), Serum aspartate aminotransferase (AST/SGOT) in patient with oral lichen planus.

## MATERIALS AND METHODS

The study was conducted after the research protocol was approved by the Ethics Committee of M. A. Rangoonwala College of dental sciences and research center. The study was performed on 50 subjects divided into two groups: Study group and control group. All the participants were explained the need and design of the study and the need for undergoing a thorough clinical examination, biopsy and blood investigations at the start of the study. Only those patients, who gave a signed informed consent on an institutionally approved document, participated in the study.

Patients in both the study and control group were asked about their medical history. Exclusion factors included previous history of viral hepatitis, Lichenoid reactions and any chronic liver disorders, blood transfusion and other systemic diseases were excluded from the study. The study group consisted of 25 patients with clinical lesion of OLP, later Incisional biopsy of the lesion was done to confirm histopathologically. The histological confirmation is based on the following criteria:<sup>[11]</sup>

- Hyperparakeratosis or Hyperorthokeratosis.
- Thickening of the granular cell layer and a saw-toothed appearance to the rete pegs.

- “Liquefaction degeneration” or necrosis of the basal cell layer, which is often replaced by an eosinophilic band.
- Isolated epithelial cells, shrunken with eosinophilic cytoplasm and one or more pyknotic nuclear fragments (Civatte bodies),
- A dense subepithelial band of lymphocytes.
- The linear sub-basilar lymphocytic infiltration is composed largely of T cells.

After histological confirmation, the patients were subjected for venous blood collection.

Control group of 25 age and sex matched apparently healthy subjects.

### Laboratory procedure

The blood samples were collected from both groups and subjected to biochemical analysis- HCV antibody titre, ELISA, SGOT and SGPT. HCV antibodies were detected by third generation by TMB HCV Microlisa (ELISA kit) (Fig 1). The serum samples and the reconstituted reagent were maintained at room temperature prior to experiment.

SGPT was estimated by ALT/SGPT (IFCC/KINETIC) ENZOKIT (RANBAXY Fine Chemicals Limited Diagnostic Division Formerly Ranbaxy Diagnostics). This is a quantitative estimation of Serum alanine amino-transferase (SGPT) also known as Alanine aminotransferase (ALT).

SGOT was estimated by AST/SGOT (IFCC/KINETIC) ENZOKIT (RANBAXY Fine Chemicals Limited Diagnostic Division Formerly Ranbaxy Diagnostics). This is a quantitative estimation of Serum Glutamic Oxalacetic Transaminase (SGOT) also known as Aspartate aminotransferase (AST), a tissues enzyme that catalyzes the exchange of amino acids and keto groups between alpha-amino acids and alpha-keto acids.

Chi-square test was used to test the statistical significance of difference of categorical variables. The statistical significance of difference of average age and several biochemical parameters (such as SGPT, SGOT etc) between cases and controls, has been tested using Mann-Whitney U test, non-parametric test procedure to compare two independent groups. The entire data was analyzed using Statistical Package for Social Sciences (SPSS ver 20).

## RESULTS

The present study included 50 subjects: 25 OLP patients and 25 healthy subjects as controls. OLP patients were clinically divided into Non-erosive and Erosive types. Age and sex matched healthy controls selected as per the inclusion and exclusion criteria. The average age difference between the

study and control group was statistically non-significant with  $p=0.457$ . The sex distribution between study and control group was statistically non-significant with  $p= 1.000$  (Chi-square test). No statistically significant difference was noted between both the groups regarding mean age, sex. [Table 1]

While considering the type of OLP - Out of 25 OLP patients, 11 patients (44.0%) were presented with erosive type of OLP (8 males and 3 females), whereas 14 patients (56.0%) were presented with non erosive type of OLP (9 males and 5 females). Regarding the site distribution, 23 patients (92.0%) were presented with lesions on buccal mucosa, 1 patient (4.0%) presented lesion on gingiva and 1 patient (4.0%) presented lesion on labial mucosa.

In both the study group and control group none of the patients showed HCV seropositivity [Table 2]. SGPT (IU/l) levels were altered in 8 patients (32.0%) in the study group and none out of 25 subjects in the control group.[ Graph 1].

Moreover, the mean value of SGOT (Graph 2) and SGPT (Graph 3) was found to be higher in the study group compared to the control group, and the difference in the mean between them was found to be statistically significant ( $p < 0.05$ ).[Table 3].

**Table 1: Sex and age distribution in the study and control group.**

		Study Group n =25	Control Group n =25
SEX	Males	17 (68.0%)	17 (68.0%)
	Females	8 (32.0%)	8 (32.0%)
Age range (years)		17-70 years	17-70 years
Average age (years)		34.7	34.7

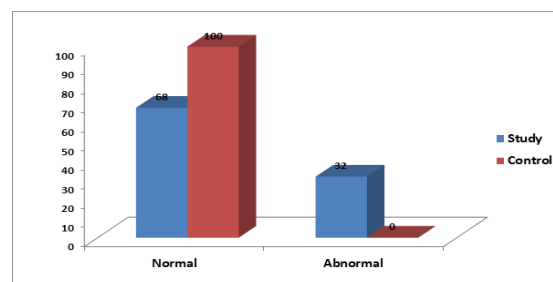
**Table 2: The distribution of HCV antibody status among Study group and Control group using Chi-square test.**

Parameters	Study (n=25)	Control (n=25)	P-value
HCV Antibody (S/CO)‡	0.28 (0.030)	0.28 (0.028)	0.965
HCV Antibody status			
Positive ( $\geq 1.0$ )	0	0	1.000
Negative ( $< 1.0$ )	25 (100.0)	25 (100.0)	

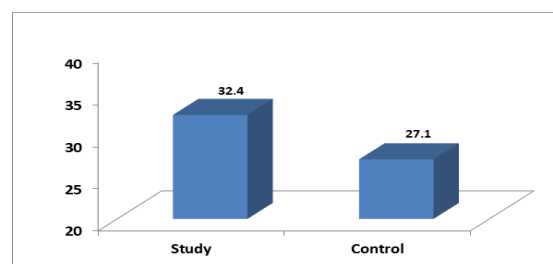
**Table 3: SGPT and SGOT distribution between Study and Control group.**

Parameters	Study (n=25)	Control (n=25)	P-value
SGPT (IU /L) ‡	35.3 (9.9)	29.9 (1.9)	0.011
SGPT Status			
Normal (5 - 45)	17 (68.0)	25 (100.0)	0.002
Abnormal ( $>45$ )	8 (32.0)	0	
SGOT (IU /L)‡	32.4 (10.1)	27.1 (1.9)	0.014
SGOT Status			
Normal (5 - 45)	17 (68.0)	25 (100.0)	0.002
Abnormal ( $>45$ )	8 (32.0)	0	

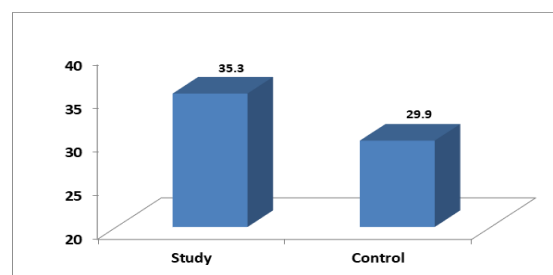
‡Values are Mean (Standard Deviation) whose p-values are obtained by Mann-Whitney U test



**Graph 1: The distribution of SGPT status between Study and Control group**



**Graph 2: The distribution of average SGOT between Study and Control group**



**Graph 3: The distribution of average SGPT between Study and Control group**



**Figure 1: ELISA kit (TMB Microlisa) with micropipettes.**

## DISCUSSION

OLP is a fairly common disease of adults and has a worldwide distribution. Among Indians the prevalence is found to be 0.02 to 0.22%, as per recorded in 30,000 dental outpatients. Considerable high prevalence of 1.5% has been reported from door-to-door investigations in 7,369 villagers in a district of Kerla. Etiopathogenesis of OLP appears

to be complex, interactions with genetic, environmental and lifestyle factors are reported.<sup>[12]</sup> During recent years an increased prevalence of chronic-liver disease has been reported in patients with OLP, including primary biliary cirrhosis and chronic hepatitis especially Hepatitis C virus (HCV). Many studies demonstrated a significant association between HCV and OLP, Where as some reported the opposite however, the issue remains controversial.<sup>[13]</sup> The prevalence of HCV in patients with OLP infections varies widely ranging from 1.6 to 16.1%. Whereas, the prevalence in India is 1.5-2.2%.<sup>[14]</sup>

There is an elevation of the hepatic enzymes (Serum Alanine-Amino Transferase SGPT/ALT) and (Serum Aspartate-Amino Transferase SGOT/AST) in many cases of OLP. The elevated transaminase hepatic enzymes levels might be related to the development of oral lichen planus lesions. There by giving a clear evidence of the association of chronic HCV infection and other liver diseases with the OLP.<sup>[15]</sup>

There are conflicting results about the association of HCV infection with OLP. Many studies did not find a relationship between the two diseases while others have demonstrated a correlation.<sup>[16]</sup> In the present study, all patients in the study group and subjects in the control group who were subjected to the estimation of anti-HCV titer by the highly sensitive

ELISA technique were found to be seronegative. Similar finding of no correlation between OLP and HCV infection has also been reported by many other authors.<sup>[16-17]</sup>

The seronegativity found in the present study may be due to the fact that these patients may be either in the initial phase or in the chronic phase of HCV infection at the time of visit. During the early phase of HCV infection, adequate antibodies are not formed and in the chronic phase antibodies decline in their number, which cannot be easily detected in the serum or the patient may be really seronegative where the transaminase elevation may be caused by factors other than HCV, which might trigger the development of OLP.<sup>[18]</sup>

Studies based on SGPT and SGOT levels in the prevalence of liver diseases in lichen planus was found to be varied widely in literature, (range of 0.1% to 35%).<sup>229-232</sup> In present study SGPT and SGOT levels were elevated in 8 patients (32.0%) i.e. >45 IU/L in study group whereas; all subjects in control group had normal SGPT and SGOT levels i.e. 5-45 IU/L. Higher proportion of patients from study group had abnormal SGPT compared to control group with  $p=0.002$  which was statistically significant. The average SGPT was higher between the study and control group with  $p=0.011$  which was statistically significant. Thus, an association can be expected between elevated transaminase levels and detection of OLP.

In relation to SGPT/SGOT levels with type of oral lichen planus, out of 11 erosive types 8 patients (72.7%) had elevated levels of SGPT and SGOT. All 14 non erosive types had normal values of SGPT and SGOT. Mean  $\pm$ SD range of SGPT in erosive types was  $42.8 \pm 7.1$  whereas; mean  $\pm$ SD range of SGPT in non erosive types was  $29.4 \pm 1.5$ . Similar observations were reported by Ali .A A, Suresh C. S (2007),<sup>[8]</sup> and Altaf Hussain Chalkoo (2010)[19] reported the elevation of transaminase levels (SGPT/SGOT) in erosive type of OLP. These elevated levels may indicate that in presence of great liver alterations there is a correspondingly greater tendency towards the development of aggressive oral lesions and also it can be suggested that there is a clear and strong association between increased levels of SGPT/SGOT and formation of erosive type of OLP. From these observations, it can be inferred that the association of OLP with liver diseases is not a mere coincidence. However, a direct relationship between liver function and the pathogenesis or persistence of OLP is unclear.

There are two main hypotheses regarding the mechanism of HCV induced OLP:

1. HCV may replicate within oral epithelium, thus directly contributing to development of OLP lesions.
2. HCV is a virus that has a high rate of mutation. This results in the repeated activation of immune cells, increasing the likelihood of cross reaction with self tissue and therefore heightening the risk of developing autoimmune diseases. Certain genotypes may be more likely to result in the cross reaction of activated immune cells against oral epithelium.<sup>[4]</sup>

In present study an attempt was made to find the correlation, if any, between HCV and OLP. All subjects included in the study and control groups were subjected to anti-HCV titer by ELISA technique and all were found to be HCV negative [Table 2].

HCV infection is an asymptomatic disease which in many cases leads to severe consequences. So, extrahepatic manifestations in the form of OLP may help identify asymptomatic patients infected with HCV infections. Although the correlation between HCV and OLP is still controversial, more studies are necessary for a better understanding of the relationship between HCV infection and OLP especially taking into consideration high mutative nature of the HCV virus and also subtypes of HCV and genotypes which could explain the prevalence of HCV in various geographic locations.

## CONCLUSION

Lichen planus could be a stereotypic cell-mediated reaction to either a specific virus or several viruses, some of them hepatotropic. Moreover, as LP can be



the first extrahepatic manifestation of HCV infection and because of HCV's significant morbidity and mortality, it is important for the clinician to subject the patients suspected of OLP, especially the erosive form, and those residing in areas where the prevalence of HCV infection is high to estimation of liver function tests and hepatitis C antibodies detection to prevent any incidental transmission of HCV to health workers.<sup>[18]</sup> So, liver disease or hepatitis C can be considered a risk factor for LP although not a specific marker of it and may lead to diagnosis, early treatment, and possibly a better prognosis in asymptomatic OLP patients.

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