RELATIONSHIP OF ORAL LICHEN PLANUS WITH SERUM TRANSAMINASE LEVELS AND ANTI-HCV STATUS

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Abstract

Background:
Oral lichen planus (OLP) is a chronic disease of established immune-mediated pathogenesis. It mostcommonly, protractedly, and persistently involves the mucosa of the oral cavity. Antigen-specific and nonspecificmechanisms play a role in its pathogenesis, leading to T-cell accumulation in superficial lamina propria, intraepithelial T-cell migration, and keratinocyte apoptosis in OLP. In recent control studies, anti-hepatitis C virus (anti-HCV) circulating antibodies were more common in patients with lichen planus than in controls.The controversies and uncertainties regarding the association of HCV and the liver function status (transaminase levels) in oral lichen planus transpired this study design and implementation.
Aims: To determine andcompare the serum transaminase levels and anti HCV status in OLP patients and healthy controls, to inquire into the possible association of OLP and to determine if the clinical characteristics of OLP differed with alterationsin serum transaminase profile patterns.
Subjects and Methods: Forty patients comprising 20 cases and 20 controls were enrolledfor the study. Twenty cases of clinically and pathologically diagnosed OLP and twenty age- and sex-matched controls weresubjected to blood examination for the assessment of serum transaminase level, i.eSGPT and SGOT. Theobtained data were compared with standard values to assess any alterations of the serum transaminase levels. Further, the anti HCV status was assessed in in patients demonstrating elevation of serum profile. Statistical Analysis used Pearson's correlation and student's unpaired t-test. A $P \leq 0.05$was considered statistically significant.
Results: Pertainingto individual serum lipid levels in cases and controls, the association was found to be statistically insignificantand the anti HCV status was negative in the entire selected sample.
Conclusions: The current study suggested an evident association between elevated serum transaminase levels and OLP; elevated levels were significator for severity of OLP symptoms. We recommendimminent studies on a larger population of geographical interest to additionally substantiate a positive association between the two.

Keywords: Oral Lichen Planus, Serum transaminase, SGPT, SGOT, HCV

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1. Introduction

Lichen planus (LP) is a commonplace immunological disorder manifesting on the skin, mucous membranes, nails, and hair. Oral LP (OLP) is the oral counterpart of the same, is recalcitrant and implicates the mucosa of the oral cavity. It commonly affects middle-aged females, and the frequency of malignant transformation ranges from 0% to 5.3%.1

The prevalence in accordance with the data assessed on global scale, was 1.01%, with a characteristic geographical difference ($p<0.001\%$). The highest was determined to be from Europe (1.43%) and lowest in India (0.49%).[2]This disorder can manifest on the oral cavity, skin, nails, hair, eyes, esophagus, and other mucous membranes. As clinicians, one should be attuned to various clinical features of all clinical subtypes for LP.[2] A concrete flawless pathogenesis has not yet been arrived upon, however, both antigen specific and non-specific mechanisms have been hinted at. There is T-cell accumulation in superficial lamina propria, intra-epithelial T cell migration and keratinocyte apoptosis in OLP. The etiologies span from dental materials allergies, medical side effects, genetics' predisposition, and systemic diseases, inclusive of autoimmune and nutritional deficiencies. Additionally, other reports suggest OLP and viruses, such as Varicella-Zoster Virus (VZV), Epstein Barr Virus (EBV), Human Herpes Virus-6 (HHV-6), Hepatitis C Virus (HCV), and Human Papilloma Virus (HPV) .[3]

Chronic hepatitis C virus (HCV) infection is a health care problem of concern and a primary cause of chronic liver disease. Hepatitis C virus (HCV) is an enveloped single stranded, positive sense RNA virus. It is a blood borne pathogen with routes of transmission including blood transfusion, percutaneous exposure from contaminated needles and occupational exposure to blood as well as other body fluids. After an acute HCV infection, the proportion of patients continue to remain chronically infected is estimated to be as high as 85% to 90%.4 According to 2019 data, 58 million people live with chronic hepatitis C infection and results in about 400,000 deaths each year. While good progress has been made in several champion countries, there remains a major testing and treatment gap.[5]

An association between OLP and HCV is suspected, yet controversial. The prevalence of this association is a conundrum in the literature. In recent control studies, anti-hepatitis C virus (anti-HCV) circulating antibodies were more common in patients with lichen planus than in controls. Elevation of transaminase levels was reported in 40 of 187 patients with oral lichen planus.[6,7]The controversies and uncertainties regarding the association of HCV and the liver function status (transaminase levels) in oral lichen planus transpired this study design and implementation. In this vein, the study was taken up to probe into the possible correlation between OLP and serum transaminase level as well as HCV status. Additionally, the derangements would also be checked for an association with the difference in clinical characteristics of OLP.

2. Materials and Methods

Ethical clearance was obtained from the Institutional Ethical Committee before conducting the study. The study group comprised 40 patients, irrespective of age, presenting to the institution as outpatients who were examined and selected by three investigators. Using purposive sampling method, the study was conducted from January 2019 to July 2020. Based on the prevalence of OLP , keeping confidence limit (Z) at 95% and allowable error (d) at 5%, the sample size for the study was fixed at 20 cases and 20 controls. They were classified into two groups:

1. Cases - 20 individuals with clinically and histopathologically diagnosed OLP.
2. Controls - 30 age- and sex-matched individuals with apparently healthy oral mucosa.

[Figure 1] and [Figure 2] were the clinical photographs of the cases selected. The selected participants were explained in detail about the procedures involved and written informed consent was obtained from them. A detailed history wasrecorded and a thorough general physical examination was performed wherein the relevant history (age, gender) andclinical and histopathological details were noted in an especially prepared pro forma.[8] This was followed by a detailedexamination of the OLP lesions. Clinically diagnosed OLP lesions were then subjected to histopathological evaluationfor confirmation following which symptomatic cases were managed by conventional therapy. The criteria for the caseand control group selection were as follows.

Inclusion criteria:

1.Patients with clinically and histopathologically diagnosed OLP – modified WHO criteria 2003 (cases)

2.Patients with apparently healthy oral mucosa on complete oral examination (controls)

3.Patients not known to be suffering from any other endocrine or metabolic disorders

4.Patients not on any medications that are known to alter serum lipid levels in the body.

Exclusion criteria

1.Pregnant patients

2.Patients known to be suffering from any medical condition that precludes them from undergoing an oral biopsyprocedure.
3.Patients on dyslipidemia therapy and on therapy for OLP
4.Patients with any other coexisting oral lesions.

Venous blood samples were collected from the patients in the case and control group for the assessment of individualserum transaminase levels (SGPT-Serum glutamic pyruvic transaminase and SGOT-serum glutamic-oxaloacetic transaminase). The normal ranges were standardized at:

- SGOT levels – 5 to 40 units per liter of serum
- SGPT levels – 7 to 56 units per liter of serum

It was assessed using modified IFCC method. The anti HCV status was evaluated using Rapid Detection Method (Oraquick).[9,10]The values were subsequently recorded in the respective pro forma. If the patient were found observed with deranged serum levels, they were referred to general physicians for further management.[11]
The data were tabulated and subjected to statistical analysis. Descriptive statistical procedures suchas means, standarddeviations, medians, minimum, maximum, and percentages were used to summarize all variables. Chi square test was applied to assess the variables in the study and Student's t test were applied to assess the mean of case and control groups. $P \leq 0.05$ was considered statistically significant.Microsoft Excel was used for data registration, and IBM SPSS Statistics (version 20.0, SPSS Inc., IBM) was used forstatistical analyses.

RESULTS

Of the 20 OLP patients in the case study group, 12 (60%) were women and 8 (40%) were men. And in the 20 patients in control group, 10(50%) were women and 10(50%) were men. The predominant age range was 35 to 49 years for women in the case group.

Table 1: Prevalence of OLP in gender and age stratification with SGPT,SGOT and Anti-HCV results

Case group					
Age in years	**Female**	**Male**	**SGPT**	**SGOT**	**Anti-HCV**
15-34	1	2			Negative
35-49	6	4	1 (M)	1(M)	Negative
50-60	2	2	1(M)		Negative
61-80	3	0			Negative
Control group					
Age in years	**Female(F)**	**Male(M)**	**SGPT**	**SGOT**	**Anti-HCV**
15-34	7	8			Negative
35-49	1	2	1(M)	1(M)	Negative
50-60	2	0			Negative
61-80	0	0			Negative

Of the20 patients in the case group, two subjects reported increased levels of SGOT values and 1 patient showed increased levels of SGPT value, and in the control group incidentally there was increased levels of SGOT value in 2 of 20 patients and increased levels of SGPT value in 1 patient.Anti-HCV status was found to be negative in all the patients both in case and control group.(Table 1)

Table2: Average Age-wise and gender wisedistribution of OLP clinical type in cases group

Sample Group	**Average age(yr.)**	**Female Gender (%)**	**Clinical Types (%)**		**Location (%)**		
			Reticular	**Erosive**	**Buccal Mucosa**	**Gingiva**	**Tongue**
Case	44.08	60	85	12.5	80	7.5	12.5
Control	33.70	50	N/A				

The average age was 44.08 years in case group and 33.70 in control group.60% of the diagnosed Case group reported women subjects. 85% of subjects in Case group were diagnosed as reticular type of

OLP and 12.5% in erosive type. 80% of the lesions were reportedon the buccal mucosa, 7.5% of the lesions were seen in thegingiva and 12.5% of lesions seen in the tongue.

Table3 (a) SGOT Values

			GROUP		Total
			CASE	CONTROL	
SGOT	NORMAL	Count	38	18	56
		% within GROUP	95.0%	90.0%	93.3%
	ABNORMAL	Count	2	2	4
		% within GROUP	5.0%	10.0%	6.7%
	Total	Count	40	20	60
		% within GROUP	100.0%	100.0%	100.0%

TABLE 8(b): Chi-square tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.536a	1	.464		
Continuity Correction b	.033	1	.855		
Likelihood Ratio	.507	1	.476		
Fisher's Exact Test				.595	.407
Linear-by-Linear Association	.527	1	.468		
N of Valid Cases	60				

2 cells (50.0%) have expected count less than 5. The minimum expected count is 1.33.

Computed only for a 2x2 table

TABLE 9(a): SGPT Group

			GROUP		Total
			CASE	CONTROL	
SGPT	NORMAL	Count	39	19	58
		% within GROUP	97.5%	95.0%	96.7%
	ABNORMAL	Count	1	1	2
		% within GROUP	2.5%	5.0%	3.3%
Total		Count	40	20	60
		% within GROUP	100.0%	100.0%	100.0%

TABLE 9(b): Chi-square tests

Chi-Square Tests

	Value	Df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.259[a]	1	.611		
Continuity Correction[b]	.000	1	1.000		
Likelihood Ratio	.244	1	.621		
Fisher's Exact Test				1.000	.559
Linear-by-Linear Association	.254	1	.614		
N of Valid Cases	60				

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .67.

b. Computed only for a 2x2 table

Tables 8(a), 8(b), 9(a), 9(b) - The following were inferred. Using X2and t-tests it was found out that the relationship between altered transaminase levels and OLP was significant with SGOT liver enzyme and of less significance with SGPT liver enzyme and severity of lesion was linked to raised serum transaminase levels.

Chartno: 1

CASE	20.65	6.585
CONTROL	25.25	8.522

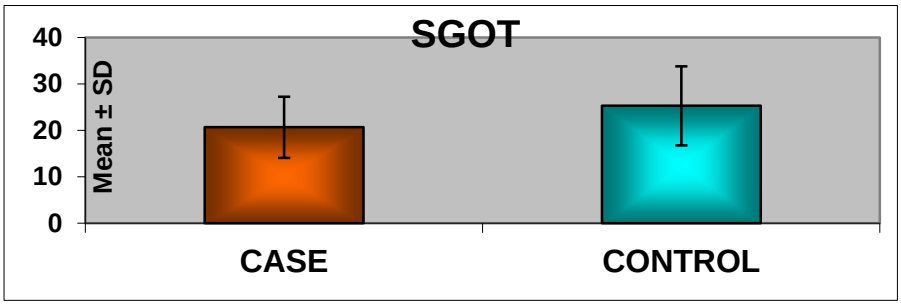

Chart no 1 gives mean +/- SD for case group for SGOT as 20.65, for Control group the value for Mean+/- SD is 25.25, The std. error for Case group-SGOT is 6.585 and for control group is 8.522.

Chart No: 2

CASE	23.28	5.32
CONTROL	25.4	9.944

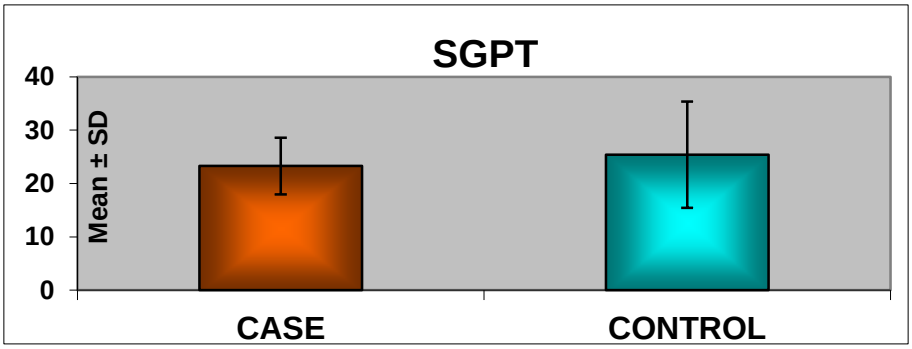

Chart no 2 gives mean +/- SD for case group for SGPT as 23.28, for Control group the value for Mean+/- SD is 25.4 The std. error for Case group-SGPT is 5.32 and for control group is 9.944

3. Discussion

Oral lichen planus (OLP) is a chronic inflammatory disease.[1]An array of factorshave been proposed in contributing etiology inclusive of genetic background, dental materials, drugs, infectious agents (virus), autoimmunity, immunodeficiency, food allergies, stress, habits, trauma, diabetes, hypertension, malignant neoplasm, and bowel disease. [12] It is interesting to note that quite a few dermatologic disorders such as lichen planus itself and psoriasis have been inseverable linked to malignant risk factors.[13]

The SGOT and SGPT levels are normally present in the serum in low concentration. The level of these enzymes is usually raised in hepatic disorders like hepatitis and primary biliary cirrhosis. These enzymes are released into the blood in greater amounts when there is damage to the liver cell membrane resulting in increased permeability.[14]

The current interest is the associated serum transaminase and anti HCV status of note in OLP patients, which in turn has been linked to increased risk of malignancy and liver failure.

The prevalence of liver diseases in patients with oral lichen planus differs extensively in literature, ranging from 0.1% to 35% based on assessments of serum transaminase activity.[6] In the present study, 2 patients (10 %) with oral lichen planus showed elevated transaminase levels. Only one patients (5%) were detected with elevated enzyme levels in the control group. Thus, an association was expected between elevated transaminase levels and detection of oral lichen planus. Similar findings were reported by Alaizari, N et al in a systematic review and meta-analysis (1807 cases of OLP and 2519 controls).[14] One study attributed that the pathogenesis of OLP in HCV infection was not conducive of the virus but as a response by host factors, insulin resistance, genetics, and immunologic factor.[15]The study by Nagao, Y et al.observed 9396 liver disease patients, 522were HCV antibody positive. After exclusion criteria, 87 patients withHCV-related diseases had oral and medical exams. Of these 87 patients,the presence of LP, including oral lesions, was 19.5% patients. It was contrived that subjects who have HCV and any form of LP should be closely monitoredfor extrahepatic malignancy.[16] Another case report demonstrated a complete healing of OLP post liver transplant and direct-acting antiviral medication.[17]In a prospective study with 7 subjects with HCV associated OLP,four subjects demonstrated a total resolution, and three showed lesion improvementafter continual use of direct-acting antivirals.[18]

Anti HCV status was found to be negative for all the patients in both case and control group by rapid detection method (OraQuick).Although, there is slight elevation of SGPT level in OLP patientscompared with control group in our study but there is no statistically significant difference observed.However, it was gleaned that the presence of greater liver alterations, there is correspondingly greater tendency toward development of more aggressive oral lesions.The geographic differences in the prevalence ofOLP associatedwith HCV infection might simply reflect overall differences in HCV epidemiology against a background of similar prevalence of OLP from country to country.20,21,22

4. Conclusion

The interpretation of elevated SGOT and SGPT levels depends upon the entire clinical evaluation of a patient.Many studies conducted worldwide at various centres showed varied results, regarding the relationship between chronic liver disease and Oral Lichen Planus with special reference to Anti-HCV status. In conclusion, this study does not report statistically significant association of chronic liver disease in patients with oral lichen planus. It is attributed to the limited sample size and the geographical nature of HCV manifestation in the area of sample size recovery. Further larger samples with PCR based analysisfor HCV has to be

done to find the correlation between oral lichen planus and liver disease.

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