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Research Article

Evaluation Of Serum Cortisol And Psychological Factors In Patients With Oral Lichen Planus

Dr. Jigna S. Shah¹, Dr. Anand J Patel²

¹Professor & Head, Dept of Oral Medicine & Radiology, Govt. Dental College & Hospital, Ahmedabad-16, Gujarat, India.

² Post Graduate Student, Dept of Oral Medicine & Radiology, Govt. Dental College & Hospital, Ahmedabad, Gujarat, India.

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ABSTRACT

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Background and aim: Oral lichen planus is a chronic mucocutaneous disease characterized by bilateral white striations on buccal mucosa, tongue, and gingiva with multifactorial etiology. Psychosomatic factors and their association with dermatological disorders are well recognized. The present study was conducted to assess the psychological status of the patient having oral lichen planus by evaluating depression, anxiety and stress by various standard questionnaire as well as by evaluating serum cortisol level and to compare with controls.

Material and methods: Study included total 41 patients of OLP and 20 normal control patients. All cases were studied in detail to analyze evaluation of serum cortisol & psychological factors in patients with Oral Lichen Planus & normal Controls. The psychometric evaluation using the DASS 21 Questionnaire was carried out, by the same investigator on all cases of OLP & Controls. All OLP cases were selected after histopathological confirmation.

Results: Study indicates DASS – 21 scale mean value and Serum Cortisol were higher in OLP patients as compare to Control Group.

Conclusion: The study concluded that a definitive relationship between depression, anxiety, stress and serum cortisol with Oral lichen planus. It plays important role in pathogenesis of OLP.

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Corresponding Author: Dr. Anand J Patel, Post Graduate Student, Dept of Oral Medicine & Radiology, Govt. Dental College & Hospital, Ahmedabad, Gujarat, India.

INTRODUCTION:

Many systemic diseases manifest in the oral cavity. In some conditions oral cavity provides the first clue for the detection of underlying systemic disease. Dermatological disorders are one such class of diseases that have oral manifestations. Thus, the dentist may be in a position to establish the diagnosis of a dermatologic disease before the cutaneous lesions become apparent. Lichen planus, pemphigus, pemphigoid and psoriasis are a few examples of dermatologic diseases that have oral manifestations. (^[1])

Lichen planus is a common dermatological disorder, which may affect the skin and oral mucosa. The condition was first described by Erasmus Wilson in 1869 who characterized the patients as anxious, high strung, and sensitive with a tendency to worry excessively and with periods of undue emotional stress. (^[2]) The World Health Organization (WHO) has defined OLP as a potentially precancerous disorder, representing a generalized state associated with a significantly increased risk of cancer. OLP affects 0.5% to 2.2% and is more frequent in women than men, from 2:1 to 3:1. (^[3]) In India the prevalence rate is 2.6%. (^{[4],[5]})

There is now ample evidence of interactions between the central nervous system and the immune system. Both stress and psychiatric illness have been associated with impairment in immune function. Because cortisol has often been suspected of playing a major role as a link between the central nervous system and the immune system. Cortisol is a 21-carbon glucocorticoid secreted by the adrenal cortex that regulates carbohydrate, protein, fat and water metabolism, maintains vascular reactivity, affects the sensitivity of the nervous system, regulates blood cell numbers, and affects the human stress response. Serum cortisol levels are increased in response to a stressful situation, a well-known fact. (^[1]) Therefore it can be a useful aid in not just understanding the pathogenesis of oral lichen planus but also in determining the progression of these lesions.

Psychodermatology is an interesting area for interface between psychiatry and dermatology, as there is a bidirectional interaction between skin and mind. Psychologically, skin is an erogenous zone and

channel for emotional discharge so that troubled skin could be a manifestation of unexpressed anger or an inner conflict due to external stress. Lichen planus (LP) may represent the manifestation of a mucosal reaction to a variety of etiological factors. The cause is unknown, but it is classified as an autoimmune disorder which may be precipitated or exacerbated by psychosocial stressors. (^[6]) The Depression Anxiety Stress Scale (DASS) is a 21-item self-report measure of anxiety, depression and stress. It requires no special skills to administer. Each of the three subscales of DASS is intercorrelated with one another. (^{[7],[8]}) The purpose of this study was to assess depression, anxiety and stress and serum cortisol levels in patients with oral lichen planus.

MATERIALS AND METHODS:

A clinical study was undertaken in the department of OMR, GDCH during the period of 2016-2017 after obtaining institutional ethical clearance. The study included a total of 41 patients with OLP and 20 normal control patients. All patients with lesions morphologically showing Wickham's striae / papules, erosion, ulceration & skin lesions with or without systemic disease e.g. diabetes mellitus and hypertension were included in the study irrespective of their complaint. Age and sex matched apparently healthy 20 subjects who had no history of systemic conditions and no oral lesions were included in the control group. Individuals suffering from diseases that can alter serum cortisol such as Cushing and Addison's disease, individuals taking systemic steroids, severe mental illness like schizophrenia and other psychological disorders, patients with lichenoid reactions evidenced by histopathological examination, drug intake or other predisposing conditions & patients who had received any medications for Lichen Planus were excluded from the study. After selection of the patients, all patients were included in the study and subjected to a detailed case history, clinical examination and various investigations and DASS-21 scale. The psychometric evaluation using DASS-21 was carried out by the same investigator in all patients. DASS-21 is a self-report questionnaire consisting of 21 symptoms divided into three subscales of 7 items: Depression

scale, anxiety scale, and stress scale. Participants rated the extent to which they had experienced each symptom over the previous week on a four-point scale ranging from 0 [did not apply to me at all] to 3 [applied to me very much, or most of the time].

After routine blood investigation, all the patients were subjected to serum cortisol investigation. Patients were called in the morning and fasting blood samples (12-14hrs) of about 5ml was collected in morning at 8 to 9 a.m. The blood sample was collected for the purpose and was sent to the Pathology laboratory, where the serum cortisol was carried out by fully automated machine and reports were analyzed in detail.

Method for estimation of serum cortisol

- Serum cortisol levels were estimated using fully automated electrochemiluminescence (ECL) method.

After all blood investigation All patients were subjected to Punch biopsy procedure. After histopathology confirmation of Oral Lichen Planus patients were treated by topical steroid Fluocinolone acetonide (0.025%) and when associated with skin lesion, systemic steroid (tab prednisolone 1-2 mg /Kg were given. All patients were kept on follow up for 8 weeks. All the patients were analyzed in detail & following results were obtained.

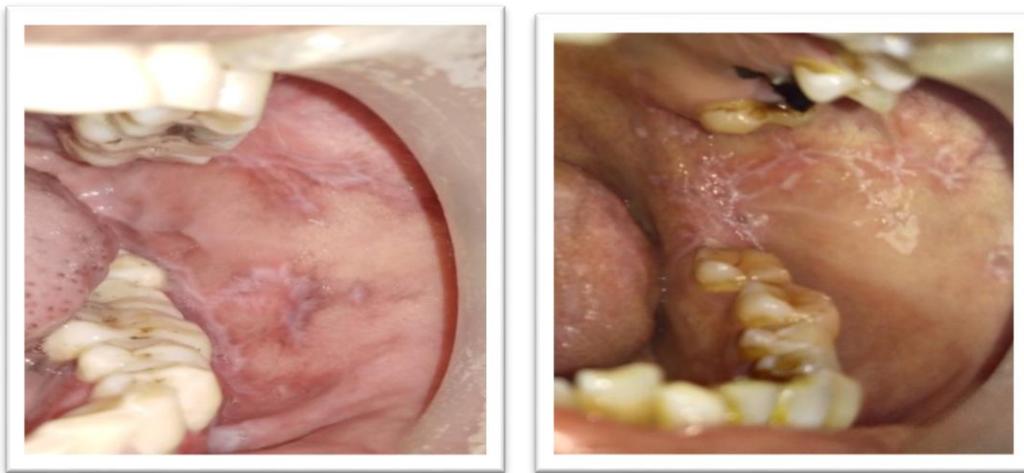


Fig 1 shows Intra Oral Photograph of OLP showing reticular form on left buccal mucosa



Fig:2 Intra Oral Photograph of OLP showing Erosive form on left and right buccal mucosa in 75-year-old patient



Fig:3 Intra Oral Photograph of OLP showing Ulcerative form on ventral surface of tongue in 10-year-old patient



Fig:4 Intra Oral Photograph of OLP showing Desquamative Gingivitis

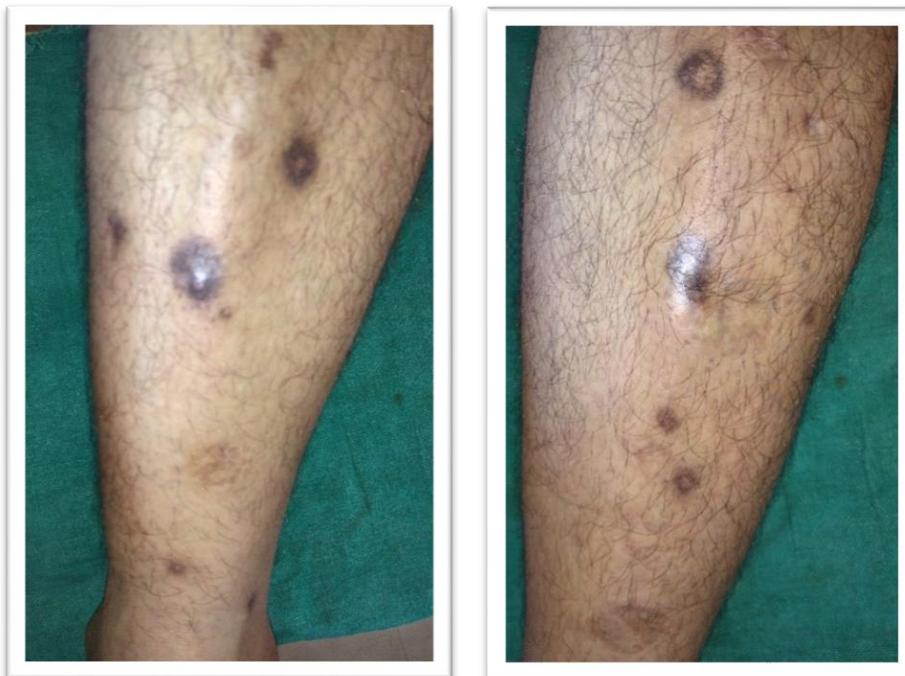


Fig 5 showing Superficial brownish Macular lesion on extensor surface of legs.

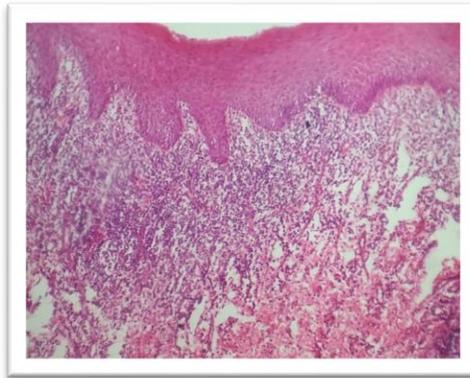


Fig 6 Shows Photomicrograph of OLP showing Hyper parakeratosis, saw tooth rete pegs and band of infiltrated lymphocytes in connective tissue. (HE stains 10x)

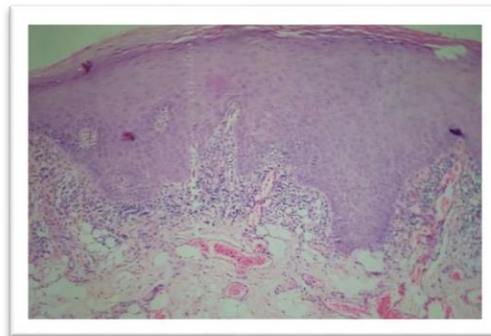


Fig 7 shows Photomicrograph of OLP showing hyper parakeratosis, acanthosis, epithelial dysplasia and band of infiltrated lymphocytes in connective tissue. (HE stains 10x)

RESULT

Table 1 shows Out of 41 study subjects, reticular OLP was present in 36.6%, erosive in 46.3%, ulcerative in 7.3%, popular in 7.3% and mixed in 2.4% of the study subjects. Reticular, erosive, papular and mixed type of

OLP was more common in 31-50 years of age group while ulcerative was more common in 51-75 years of age group. Statistically, no significant difference was present between age groups and various types of OLP.

Table: 1 Age wise distribution of the patients						
Clinical forms of OLP cases n=41						
Age in yrs	Reticular/ Linear (n= 15) (36.6%)	Erosive (n= 19) (46.3%)	Ulcerative (n=3) (7.3%)	Papular(n= 3) (7.3%)	Mixed(n=1) (2.4%)	Total (n=41) (100%)
10-30	5 (33.3%)	5 (26.3%)	0 (0%)	0 (0%)	0 (0%)	10 (24.4%)
31-50	6 (40%)	10 (52.6%)	1 (33.3%)	2 (66.7%)	1 (100%)	20 (48.8%)
51-75	4 (26.7%)	4 (21.1%)	2 (66.7%)	1 (33.3%)	0 (0%)	11 (26.8%)
Chi square Value = 5.731, P Value > 0.05 NS						

Table 2 shows Reticular (73.3%), erosive (84.2%) and mixed type (100%) of OLP was more common in female subjects while ulcerative (66.7%) and papular

(66.7%) was more common in male subjects. Statistically, no significant difference was present between gender and various types of OLP.

Table: 2 Sex Wise Distribution Of The Patients						
Clinical forms of OLP cases n=41						
Sex	Reticular/ Linear (n=15) (36.6%)	Erosive (n=19) (46.3%)	Ulcerative (n=3) (7.3%)	Papular (n=3) (7.3%)	Mixed (n=1) (2.4%)	Total (n=41) (100%)
Male	4 (26.7%)	3 (15.8%)	2 (66.7%)	2 (66.7%)	0 (0%)	11 (26.8%)
Female	11 (73.3%)	16 (84.2%)	1 (33.3%)	1 (33.3%)	1 (100%)	30 (73.2%)
Chi square Value = 6.397, P Value > 0.05 NS						

Table 3 shows Subjects with reticular, erosive, ulcerative, papular and mixed OLP, buccal mucosa (97.56%) was mostly affected site in oral cavity.

Table: 3 Different site wise distribution of the patients in clinical forms of olp						
Clinical forms of OLP cases n=41						
Sites	Reticular/ Linear (n=15) (36.6%)	Erosive (n=19) (46.3%)	Ulcerative (n=3) (7.3%)	Papular (n=3) (7.3%)	Mixed (n=1) (2.4%)	Total (n=41) (100%)
Buccal mucosa	15 (100%)	19 (100%)	2 (66.66%)	3 (100%)	1 (100%)	40 (97.56%)
Labial mucosa/lip	2 (13.33%)	6 (31.57%)	1 (33.33%)	1 (33.33%)	1 (100%)	11 (26.82%)
Tongue	3 (20%)	3 (15.78%)	2 (66.66%)	1 (33.33)	1 (100%)	10 (24.39%)
Hard palate	0 (0%)	1 (5.26%)	0 (0%)	0 (0%)	0 (0%)	1 (2.43%)
Attached gingiva	1 (6.66%)	7 (36.84%)	1 (33.33%)	0 (0%)	0 (0%)	9 (21.95%)

Table 4 shows mean value depression score; anxiety score and stress score were higher in ulcerative and erosive forms as compared to reticular/linear and

papular form. mean value of serum cortisol was higher in ulcerative and erosive forms as compared to papular and reticular/linear forms.

Table 4 Association with DASS -21 scale & serum cortisol						
Clinical forms of olp cases n=41 (Mean value ± SD)						
	Reticular/ Linear (n=15) (36.6%)	Erosive (n=19) (46.3%)	Ulcerative (n=3) (7.3%)	Papular (n=3) (7.3%)	Mixed (n=1) (2.4%)	F Value and P Value
Depression Score	5.07 ± 1.66	6.63 ± 1.11	6.67 ± 0.57	4.67 ± 0.57	8 ± 0	4.481 ≤ 0.05 S
Anxiety Score	6.20 ± 1.52	7.05 ± 1.26	7.67 ± 1.15	7 ± 1	7 ± 0	1.228 > 0.05 NS
Stress Score	9.13 ± 2.03	11.74 ± 1.59	12.67 ± 2.08	10 ± 1	13 ± 0	5.954 ≤ 0.05 S
DASS 21 Scale Score	19.93 ± 4.60	25.58 ± 2.73	27 ± 2.64	21.67 ± 1.52	28 ± 0	6.787 ≤ 0.05 S
Serum Cortisol	8.05 ± 4.70	12.66 ± 2.08	12.82 ± 0.87	11.3 ± 1.20	13.5 ± 0	4.550 ≤ 0.05 S

Table 5 shows mean value depression score; anxiety score, stress score and DASS – 21 scale score were higher in OLP patients as compare to Control Group.

Serum Cortisol level was higher in OLP patients as compare to Control Group

Table: 5 Association with DASS -21 scale score & serum cortisol between groups						
Cases n=61(cases & controls)						
	Case Groups OLP (n=41)		Control Groups (n=20)		Difference and 95%CI	t Value and P Value
	Mean	SD	Mean	SD		
Depression Score	5.95	1.15	1.45	1.05	4.50 (3.74, 5.26)	11.828 ≤ 0.05 S
Anxiety Score	6.78	1.37	2.50	1.05	4.28 (3.58, 4.97)	12.302 ≤ 0.05 S
Stress score	10.76	2.17	3.50	0.82	7.25 (6.24, 8.26)	14.358 ≤ 0.05 S
DASS 21 scale score	23.39	4.44	7.45	1.70	4.28 (13.87, 18)	15.446 ≤ 0.05 S
Serum Cortisol	10.90	3.84	8.94	1.49	1.96 (0.17, 3.75)	2.196 ≤ 0.05 S

Table 6 shows A multiple regression was run to predict DASS from depression, anxiety, stress and serum cortisol. Combined four variables were

statistically significant to predict DASS. Depression, anxiety and stress were statistically significant to predict DASS while serum cortisol was not significant to predict DAS

Variable	B Value	Significant Value	CI (95%)		R and R ² Value	Overall P Value
			Lower Bound	Upper Bound		
Depression	1.004	S	0.759	1.250	0.981 0.962	≤ 0.05 S
Anxiety	0.968	S	0.682	1.255		
Stress	0.945	S	0.740	1.150		
Serum Cortisol	0.083	NS	-0.002	0.169		

DISCUSSION

In present study out of 41 patients most of patients of reticular, erosive, papular and mixed form of OLP fall in 31-50 years of age group except in ulcerative form which is seen in 51-75 years of age group. The youngest patient was 10 years old and the oldest was 75 years old. According to literature, OLP predominantly involves middle age population. ([3],[5],[10],[11],[13],[14],[15],[16],[17],[18]) But according to Shklar and McCarthy oral mucosal lesion of lichen planus can occur at any age.([9])

In present study most of form of OLP fall in 31-50 years age this may be due to hormonal imbalance, nutritional deficiency, local factors like constant irritation from 3rd molars and consumption of tobacco. In youngest patient with reticular form of OLP, exam stress and hormonal changes were found. In oldest patient with ulcerative form of OLP, constant trauma from attrited sharp cusp on lateral margin of tongue was found.

The present study showed female predominance in all form of OLP except in ulcerative and papular form. This is similar to studies by many authors who have reported female predominance. ([5],[10],[11],[13],[14],[15],[17],[18]) Considering different clinical forms of OLP, reticular/linear, erosive were common among females whereas ulcerative and papular lesions were common in male than female. Erosive form was more commonly associated with stress, anxiety and hormonal disturbances, which is again more commonly seen in females.

Various literatures showed the most frequent intraoral site involved with OLP was buccal mucosa. ([4], [5], [12], [22], [23], [24]) Labial mucosa, tongue, gingiva and hard palate were the next frequent site. ([4], [5],[12],[22],[24]) This may be due to the fact that buccal mucosa is subjected to mechanical trauma, irritation by sharp cusps, sharp filling margins or rough surfaces and even poorly fitting dental prostheses. This phenomenon is termed as Koebner phenomenon or isomorphic response characterized by the occurrence of LP changes in areas subjected to trauma.

Considering various clinical forms of OLP in the present study, reticular/linear, erosive, ulcerative, papular forms were more commonly found on buccal mucosa/vestibule. This is very similar to other studies. ([4], [5], [12], [22], [24]) as seen only in 7.3% patients in this study. Papular lesions may be thought to be initial presentation of the disease that gradually enlarge and come together to form reticular pattern, this was very similar to other study. ([5], [13])

In present study according to DASS – 21 scale mean value depression score; anxiety score and stress score were higher in ulcerative and erosive forms as compared to reticular/linear and papular form. DASS – 21 scale mean value was higher in OLP patients as compare to Control Group. This is very similar to other studies. ([1], [2], [6], [19], [21], [25])

This may be due to the fact that OLP is often associated with pain & patient may find difficulty to ingest certain types of food, a fact influencing their

daily life and interfering directly with their quality of life.

Stressful situation causes the HPA-axis to release corticosteroids, simultaneously there are psychoneuro-immunologic interactions at the nerve terminals with the lymphocytes and haemopoietic system. An altered lymphocytic state is produced which is directly linked to the occurrence of lichen planus. but other literature does not support relationship of stress, anxiety and depression to oral lichen planus. ⁽¹²⁰⁾ In present study mean value of serum cortisol was higher in ulcerative and erosive forms as compared to papular and reticular/linear forms. Serum Cortisol level was higher in OLP patients as compare to Control Group. This is very similar to other studies. ^(11, 12, 121) In conditions involving pain, anxiety, fright or acute tissue damage, many metabolic and endocrine changes occur, and among these a rise in the levels of blood cortisol is one of the most important physiological effects. Cortisol is the major glucocorticoid in human and has a wide range of influences on metabolism, immunoregulation, vascular responsiveness, cognition and behavior. In stressful situations, there is an activation of the HPA (Hypothalamus-pituitary-adrenal) axis, with release of cortisol, a hormone that shows a complex action on inflammatory and immunological responses. So, with OLP initiation and progression serum cortisol level increased.

CONCLUSION

It is concluded that DASS – 21 scale mean value depression score; anxiety score and stress score were higher in ulcerative and erosive forms as compare to reticular/linear and papular forms. DASS – 21 scale mean value was higher in OLP patients (23.39 ± 4.44) as compare to Control Group (7.45 ± 1.70). Mean value of serum cortisol was higher in ulcerative and erosive forms as compare to papular and reticular/linear forms. Serum Cortisol level was higher in OLP patients (10.90 ± 3.84) as compared to Control Group (8.94 ± 1.49).

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