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Serum cortisol levels in erosive & non-erosive oral lichen planus subjects & associated stress factors – A case control study

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Type of Publication: Case Study

Conflicts of Interest: Nil

Abstract

Background & objectives: LP is a chronic inflammatory mucocutaneous disorder which can manifest in oral mucosa. 75% of the patients with cutaneous lichen planus also experience oral lesions[1]. The prevalence of Oral lichen planus is 1.01% . It most often affects buccal mucosa and tongue and usually has erosive and non-erosive forms. Non erosive form is often asymptomatic; the erosive forms are commonly sensitive and painful and affect the quality of life. Many patients often report a worsening of disease during periods of emotional stress. This study has been conducted to evaluate the biological aspect, namely cortisol level, and psychological aspects, that is anxiety and depression, in patients with erosive & non-erosive OLP with healthy controls.

Method: A case control study was conducted on 30 cases each of NEOLP, EOLP and 30 controls. The serum cortisol levels of all 90 patients were estimated by using electrochemiluminescence. GHQ was administered to all subjects and controls. After that HADS questionnaire was administered to subjects and controls that have higher score of > 3 to evaluate the psychological status.

Interpretation: The mean serum cortisol level of the OLP group showed high values with a significant

statistical difference (p=0.0001) from the controls. The mean anxiety and depression scores of the OLP group showed very high significant difference (p=0.0001) from the controls. The difference in mean cortisol level between NEOLP group and control was not significant (p=0.0576), whereas the difference was highly significant between the EOLP group and controls (p=0.0001). The difference between the anxiety and depression scores between the NEOLP group and EOLP group were not very significant (p=0.5716 for anxiety & p = 0.1374 for depression).

Conclusion: These findings suggest that psychological factors contribute to pathogenesis of OLP and increase serum cortisol could be a possible indicator for the lesion.

Keywords: Oral Lichen Planus, Cortisol, Erosive, Psychologic, Electrochemiluminescence

Introduction

Lichen planus is a chronic inflammatory mucocutaneous disorder which can manifest in oral mucosa. 75% of the patients with cutaneous lichen planus also experience oral lesions[1]. The global pooled prevalence of Oral lichen planus is 1.01% and prevalence in India was reported 0.49%[2]. It usually affects middle aged females, with a ratio of 1.4:1[3]. It most often affects buccal mucosa and tongue and usually has erosive and non-erosive forms.

Non-erosive form is often asymptomatic while erosive forms are commonly sensitive and painful and affect the quality of life. Meta-analysis of OLP lesions reported 1.37% of malignant transformation erosive type, female and tongue site were considered as risk factors for the transformation[4]. Current concepts of pathogenesis include immunologic and genetic factors, emotional stress, hepatic diseases and drugs as causative factors. Many patients often report a worsening of disease during periods of emotional stress. A few researchers have shown that the association exists between stress and erosive disease, but not with asymptomatic variants.

Serum cortisol levels are increased in response to stressful situations. It can be a useful aid in not just understanding the pathogenesis of OPL but also in determining the progression of these lesions. There have been few studies done in the area of stress as a predisposing factor in OLP lesions. Thus, there is a great need to understand the etiopathogenesis and progression of these lesions.

Material and Methods

Data for the study was collected from 90 out-patients in the age group between 18 – 80 years, fulfilling inclusion criteria. 30 subjects with clinically non-erosive, histopathologically confirmed OLP patients without skin involvement grouped into group A. 30 subjects with clinically erosive, histopathologically confirmed OLP patients without skin involvement grouped into group B. Group C consisted of 30 subjects with no apparent lesions of the oral mucosa & the skin.

Exclusion criteria were the subjects who were treated for OLP or undergoing treatment, subjects with oral lichen planus as well as cutaneous lichen planus, subjects with lichenoid reactions, subjects who had undergone chemotherapy or radiotherapy, and subjects with systemic diseases & on medications. Controls with history of stress, depression and systemic illness were excluded.

5ml of venous blood was obtained from the median cubital vein between 8.00 - 10.00 am on empty stomach. Then serum cortisol estimation was done by the Electrochemiluminescence method on the same day.

GHQ was given to all subjects which consisted of 12 questions with 4 possible answers to assess the general

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health of the individual in the last 2 weeks. If the scoring was above 3, then the patients were assessed for anxiety & depression using HADS scale. In this scale there are 14 groups of questions all together for anxiety & depression with 4 possible options which describes the way individual feels in the last 2 weeks. Then the scores were added up to interpret the condition.

After estimating serum cortisol levels and assessment of anxiety & depression status, these three variables were correlated under 3 groups to assess the significant difference if present using statistical analysis.

Anova & Chi square test were applied to test the difference between the groups. Student's *T* test and Tukey's HSD test were applied for statistical evaluation. Direct logistic regression was used to calculate odds ratios (OR) with 95% confidence intervals (CI). Level of significance was set at 0.05 and 0.001 the results was considered statistically significant with $p<0.05$.

Results

Demographic data analysis of Group A

In this group the age of the subjects were ranged from 20 to 63 years. Majority (33%) of these cases were within 41-50 years. Males comprised 43 % of this group, while females formed the remaining 57%. Commonest site of occurrence was on buccal mucosa followed by gingiva.

Demographic data analysis of Group B

In this group the age of the subjects were ranged from 27 to 75 years. Majority of the patients (40%) were in the age group of > 50years. Males comprised 40% of this group while females comprised the remaining 60%. Commonest site of occurrence were on buccal mucosa followed by gingiva and on labial sulcus.

Demographic data analysis of Group C

Majority of the patients (33%) in this group were in the age group of 41-50 years. Males comprised 50% of this group while females formed rest 50%.

Analysis of mean cortisol values, mean anxiety and mean depression scores of the groups in the study:

Mean cortisol value analysis (table 1)

The mean cortisol value in Group A was calculated to be 8.65 ± 1.2813 mg/dl, lower than the mean cortisol levels of Group B - 11.19 ± 1.5951 mg/dl but higher than the mean cortisol value of Group C - 7.806 ± 1.3602 mg/dl. The combined mean cortisol value of Group A and Group B was calculated to be 9.92 ± 1.4382 mg/dl higher than that of Group C - 7.2100 ± 1.62717 mg/dl.

Table 1: Comparison of Mean Cortisol Level

Groups	Number of participants	Mean	Std dev	Odds ratio(95% CI)
NELP	30	8.65	1.2813	1.34(1.06-1.54)
ELP	30	11.19	1.5951	1.89(1.46-2.01)
CONTROL	30	7.806	1.3602	1
F Value (Anova Test)	46.54			
P Value	<0.0001*	Tukey HSD Post-hoc Test… Group A vs Group B: Diff=2.5400 p=0.0000* Group A vs Group C: Diff=-0.8500, p=0.0576 Group B vs Group C: Diff=-3.3900, p=0.0000*		

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Mean GHQ score analysis (table 2)

The mean GHQ score in Group A was calculated to be 2.507 ± 0.836, lower than mean GHQ score in Group B - 2.877 ± 0.754 but higher than the mean GHQ score in Group C - 1.747 ± 0.876. The combined mean GHQ scores of Group A and Group B was 2.692 ± 0.876 higher than that of Group C 1.747 ± 0.876.

Mean anxiety score analysis (Table 3,Graph 1)

The mean anxiety score in Group A was calculated to be 10.105 ± 1.991, lower than that of mean anxiety score in Group B - 10.105 ± 1.7292 but higher than the mean anxiety score in Group C - 4.75 ± 1.707. The combined mean anxiety scores of Group A and Group B was 10.461 ± 1.891 was higher than that of Group C - 4.75 ± 1.707.

Table 2: Comparison of Mean GHQ Score

Groups	Number of participants	Mean	Std dev	Odds ratio (95% CI)
NELP	30	2.507	0.836	1.57(1.23-1.92)
ELP	30	2.877	0.754	1.89(1.22-2.07)
Control	30	1.747	0.876	1
F Value (Anova Test)	17.91			
P Value	<0.0001*	Tukey HSD Post-hoc Test... Group A vs Group B: Diff=0.7130, p=0.5716 Group A vs Group C: Diff=-5.3550, p=0.0001* Group B vs Group C: Diff=-6.0680, p=0.0000*		

Table 3: Comparison of Mean Anxiety Level

Groups	Number of participants	Mean	Std dev	Odds ratio (95% CI)
NELP	30	2.507	0.836	1.57(1.23-1.92)
ELP	30	2.877	0.754	1.89(1.22-2.07)
Control	30	1.747	0.876	1
F Value (Anova Test)	17.91			
P Value	<0.0001*	Tukey HSD Post-hoc Test... Group A vs Group B: Diff=0.7130, p=0.5716 Group A vs Group C : Diff=-5.3550, p=0.0001* Group B vs Group C: Diff=-6.0680, p=0.0000*		

Mean depression score analysis (table 4)

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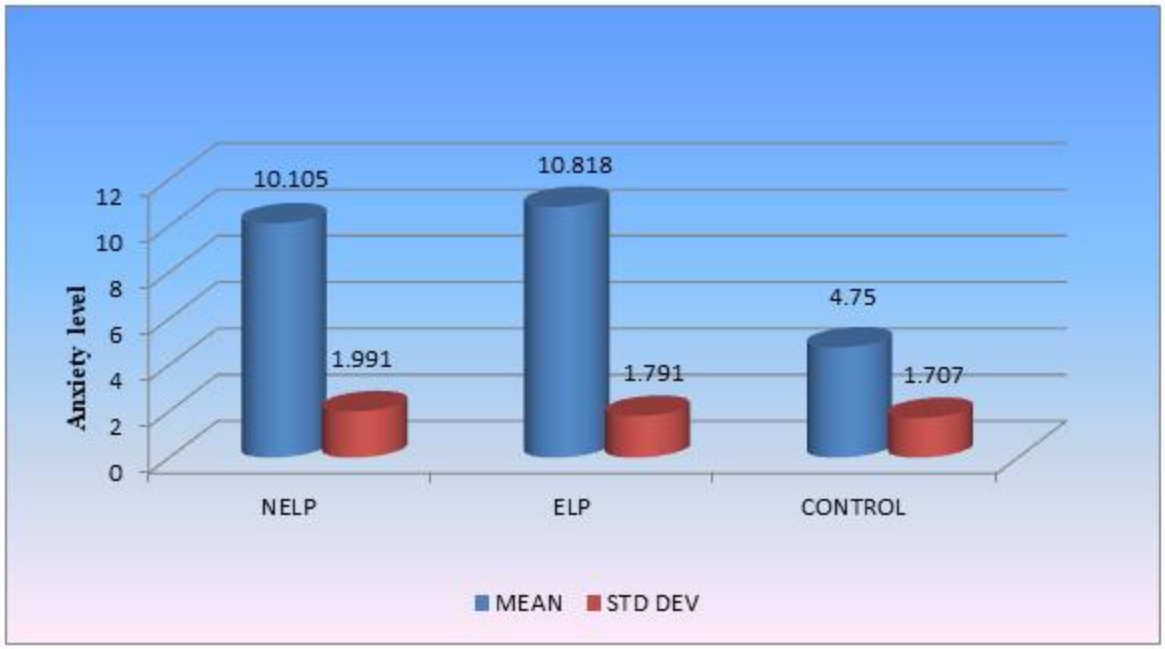
Graph 1: Mean of Anxiety Scores



The mean depression score of Group A was calculated to be 8.909 ± 1.446 , lower than that of mean depression score of Group B - 10.818 ± 1.791 but higher than mean depression score of Group C - 3 ± 0.8165. The combined mean depression score of Group A and Group B 8.507 ± 1.619 was higher than that of Group C - 3 ± 0.8615. The Combined HADS score of Group B was higher than that of group A and group C.

Table 4: Comparison of Depression Level

Groups	Number of participants	Mean	Std dev	Odds ratio (95% CI)
NELP	11	8.909	1.446	2.87(1.67-3.81)
ELP	19	10.105	1.792	3.68(2.44-4.31)
Control	4	3	0.8165	1
F Value	32.123			
P Value(Anova Test)	<0.0001*	Tukey HSD Post-hoc Test... Group 1 vs Group 2: Diff=1.2000, p=0.1374 Group 1 vs Group 3: Diff=-5.9000, **p=0.0000*** Group 2 vs Group 3: Diff=-7.1000, **p=0.0000***		

Graph 2: Mean Depression Score

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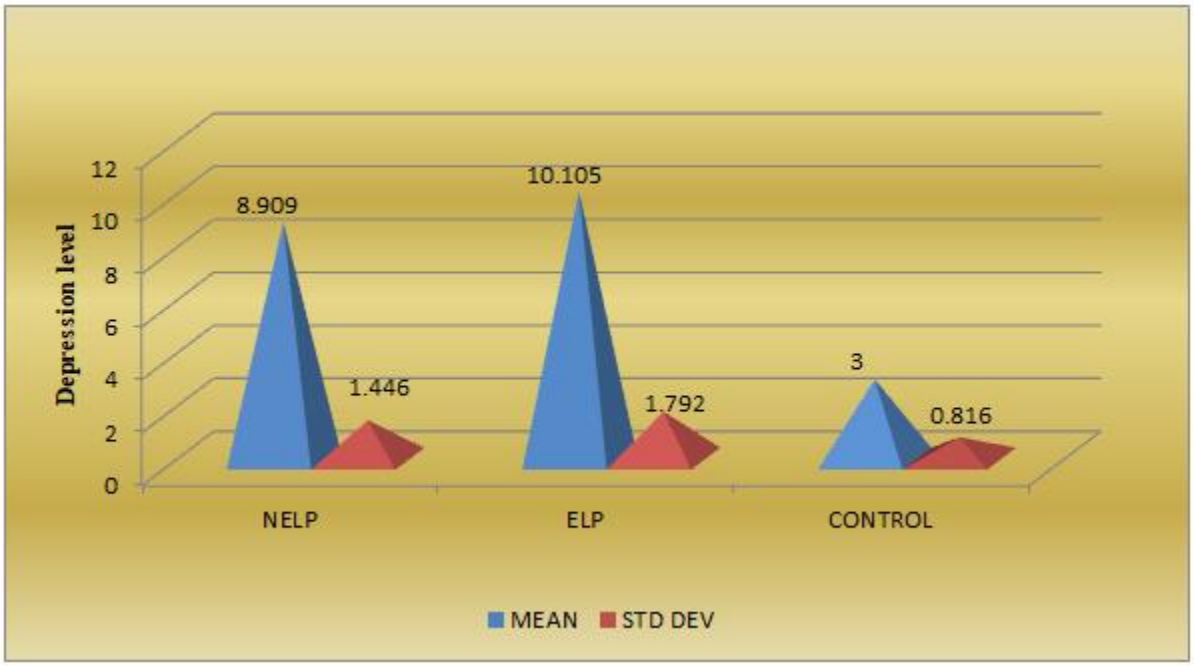

Analysis of statistical significance

Serum cortisol levels

When statistical comparison was made between the three study groups for the serum cortisol levels, a very highly significant statistical difference (p=0.0001) was noted. When Group A was compared with Group B for serum cortisol levels, it was found to be highly significant (p =0.0001). No statistically significant difference was noted between Group A and Group C serum cortisol values (p =0.0576). On comparison of Group B with Group C serum cortisol values revealed a very highly statistically significant difference (p =0.0001). When comparison of combined mean serum cortisol value of Group A and Group B was done with Group C a very highly statistically significant difference was noticed (p=0.0001).

GHQ scores

When an intergroup comparison was made between the three groups for the GHQ scores, a very highly statistically significant difference (p = 0.0001) was noted. On comparison of Group A and Group B no statistical significant difference was noticed (p=0.5716). A statistically significant difference was observed between Group A and Group C when GHQ scores were compared (p=0.0001). 0n comparison of the mean GHQ scores of group B with Group C a very highly statistically significant difference (p=0.0001) was detected. When comparison of combined mean GHQ scores of Group A and Group B was done with Group C a very highly statistically significant difference was noticed (p=0.0001).

Anxiety scores

When an intergroup comparison was made between the three groups for the anxiety scores, a very highly statistically significant difference (p = 0.0001) was noted. On comparison of Group A and Group B no statistical significant difference was noticed (p=0.5716). A statistically significant difference was observed between Group A and Group C when anxiety scores were compared (p=0.0001). 0n comparison of the mean anxiety scores of group B with Group C a very highly statistically significant difference (p=0.0001) was detected. When comparison of combined mean anxiety

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scores of Group A and Group B was done with Group C a very highly statistically significant difference was noticed (p=0.0001).

Depression scores

When an intergroup comparison was done for the depression score between the three groups in the study, a very highly significant difference (p=0.0001) was noted. No statistically significant difference (p=0.1374) was observed between the mean depression scores between Group A and Group B.A statistical significant difference (p=0.0001) was noticed when Group A was compared to Group C. On comparison with Group B scores to Group C scores a very highly significant difference (p=0.0001) was observed. When comparison of combined mean depression scores of Group A and Group B was done with Group C a very highly statistically significant was noted (0.001).

Discussion

OLP is a fairly common disease of adults and has a worldwide distribution. Many patients often report of worsening of disease during periods of emotional stress. Few researchers have shown that the association exists between stress and erosive disease, but not with asymptomatic variants. In this study an attempt was made to analyze the anxiety, depression levels and the serum cortisol levels in erosive and non-erosive oral lichen planus patients. Also an attempt was made to compare these parameters between oral lichen planus patients and normal patients.

Analyzing the results of our study, it can be noted that both in Group A (Non erosive) & Group B (Erosive) majority of the patients were within the age range of 41 to 50 years. The age distribution was similar as in most of the studies [5, 6, 7, 8, 9]. The gender distribution (female to male ratio) in the present study for Group A and Group B was 1.3:1 & 1.5:1 respectively. This ratio was similar in most of the studies reviewed [6, 7, 9].

The occurrence and distribution of lesion in the oral mucosa is 80% in the buccal mucosa, 65% in the tongue, 20% lips, <10% seen on the floor of mouth and palate[10]. In our study we found that buccal mucosa (73%) was the commonest site of occurrence in cases of non-erosive lichen planus subjects followed by gingival (20%). Whereas in erosive OLP subjects commonest site of occurrence was buccal mucosa (63%) followed by gingiva (13%). Buccal mucosa is most common site as discussed by Kruppa et al [10]], Lavanya et al [7] , Gowri et al [6], Nogueira [11]and other reviewed article.

The mean serum cortisol analysis between oral lichen planus patients (Group A & Group B combined) and controls (Group C) revealed a significant difference in our study. Similar results were found by Prolo P et al [12], Miricescu D et al [13], Jethna et al [14]& Ivanoski K et al [15]Prolo P et al & Ivanoski K et al; both these studies showed that there was a significant alteration in the CD4/CD8 ratios. In the present study we have not taken into consideration of the CD4/CD8 ratios but this could probably the factor linking the altered serum cortisol levels with oral lichen planus.

In our study it was found that environmental factor like stress plays a role in OLP. Odds ratio within 95 % of confidence interval limits suggests that the risk of having high levels of cortisol in group A and group B (1.34 & 1.89) is higher as compared to controls that is 1.

In the present study, two scales were used to measure stress, anxiety and depression. The GHQ-12 was used because of its simplicity in consultant settings and for detecting psychosocial stressors in those with a diagnosable psychiatric disorder [10]. The HADS was used for identifying and quantifying the two most common

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forms of psychological disturbances in patients, namely anxiety and depression [16]. The results with these questionnaires confirmed the presence of psychosocial stressors, namely, stress, anxiety and depression in the OLP patients.

Recent research has confirmed skin both as an immediate stress perceiver and as a target of stress responses. As the largest organ of the body, skin plays important barrier and immune functions, maintaining homeostasis between external environment and internal tissues [17]. Cortisol is a stress hormone and cortisol levels tested in this study represents only one possible mechanism for psychobiological interactions in OLP patients. These data suggest that cortisol and psychological status may play a role in the pathogenesis of OLP. Taken together, these may represent possible avenues by which the psychological status of an individual may impact on immune system homeostasis during onset and progression of lichen planus.

Conclusion

From this it was concluded that Oral lichen planus can be considered as a psychosomatic disorder, more commonly observed in the middle age group of 40-50 years, with female predominance in ratio of 1.4: 1. The anxiety and depression scores of the erosive group were significantly higher than that of scores of the controls. This suggests that stress can act as an aggravating factor for oral lichen planus. Some articles have suggested that stress may not initiate the OLP development, rather than OLP can lead to psychological stress by altering patient's self-image and influencing their public interactions. Changes in serum cortisol levels correlates with psychological changes and may be predictor of oral presentation. Therefore, psychological well-being is an important factor that should be considered in the treatment of these patients.

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