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**Original Article**

# Assessment of Anxiety, Depression and serum cortisol levels in oral submucous fibrosis and leukoplakia patients

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## ABSTRACT

**Background:** Modern hectic lifestyle caused stressed and get addicted to various harmful habits such as smoking, gutka chewing, tobacco chewing etc, resultant so many oral lesions and severity of these lesions depended on increases with frequency of chewing tobacco, arecanut, smoking etc. Cortisol is a "stress hormone" and has been used as an indicator in stress evaluation in various studies. There is good evidence of many studies where stress and anxiety are related to increase resting levels of cortisol. Anxiety and Depression are psychological behaviours associated with stress, As stress increases there is increase in the frequency of deleterious habits and increase in the serum cortisol level. **Objective:** to assess and co-relate the anxiety, depression and serum cortisol levels in habit associated oral lesions like Oral Submucous Fibrosis and Leukoplakia and compare with that of healthy subjects.

**Material and Methods:** Total of 90 subjects was included in the study who were divided into different groups, GROUP I (OSMF), GROUP II (Leukoplakia) and GROUP III (Control group). All the patients were assessed for serum cortisol level, severity of anxiety and depression by (HAM‐A) questionnaire and (HAM‐D) questionnaire respectively.

**Results:** A significant co-relation was seen between serum cortisol level, anxiety level and depression level in OSMF patient and leukoplakia patients when compared with the control group.

**Conclusion:** A strong co-relation exists between of serum cortisol level, anxiety level and depression level in patients with habit oriented diseases. Assessing anxiety and depression in patients with OSMF and leukoplakia and comparing with the serum cortisol level may reveal the level of stress.

**Keywords:** Oral Submucous Fibrosis, Leukoplakia, Anxiety, Depression, Serum Cortisol.

## INTRODUCTION

Anxiety can be defined as "an emotional state, characterized by uneasiness, discomfort and fear about some defined or undefined threat" while depression is "a state of unhappiness or sadness" which is experienced from time to time.[1] Stress utilizes two mechanisms to deteriorate our immune system to facilitate disease process. One is the biological mechanism which is mediated through the "hypothalamic- pituitary-adrenal (HPA) axis" and the

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production of "cortisol". Second is the behavioral mechanism which promotes the poor health behaviors like smoking, alcoholism, consuming unhealthy diet, poor oral hygiene habits, Para functional habits etc. The Patient's oral health deteriorates in response to these unhealthy habits, and causes variety of oral diseases.[1] Stress is one of the main etiology and predisposing factor in many diseases.[2]

Pre-malignant lesions such as Oral submucous fibrosis(OSMF), leukoplakia, squamous cell carcinoma(SCC), Oral lichen planus are one of the most common oral mucosal diseases in human beings and constitute entities that deserve to be investigated as psychosomatic diseases. In many studies it is found that 20% to 40% of cancer patients have significant levels of distress.2 Cortisol "stress hormone" has been used as an indicator in stress evaluation in various studies. Cortisol is the major glucocorticoid in humans and has influences on metabolism, immunoregulation, vascular responsiveness, cognition, and behavior. In stressful situations, there is an activation of the HPA (hypothalamus–pituitary–adrenal) axis, causing the release of cortisol, a hormone which shows a complex action on the metabolism of carbohydrates, proteins and lipids, besides acting on inflammatory and immunological responses.[2]

Many studies have shown association between psychiatric morbidity and chronic disorders such as cardiovascular diseases, cancers, asthma, arthritis, chronic obstructive pulmonary disease, diabetes mellitus, temporomandibular disorders, burning mouth syndrome, oral lichen planus and recurrent aphthous stomatitis. But, literature on psychiatric morbidity in OSMF and leukoplakia remains scarce.[3]

Hence the present study was aimed to assess the anxiety, depression and serum cortisol levels in oral submucous fibrosis and leukoplakia patients and to co-relate serum levels of cortisol with anxiety and depression in pre-malignancy (Oral sub-mucous fibrosis and leukoplakia).

## MATERIAL & METHODS

This cross sectional comparative study done in the Department of psychiatry, GCRG Medical College Lucknow with diagnosed patients of Oral Submucous fibrosis and oral Leukoplakia in the age range of 20 to 45 years taken from dental department, were included in the study after obtaining a written informed consent from the patient. The study included 90 patients who were divided as: GROUP I consist of patients diagnosed clinically OSMF. GROUP II consists of patients diagnosed clinically leukoplakia. GROUP III is the control group. In this study, assessment of anxiety and depression by Hamilton Anxiety Rating Scale (HAM‐A) questionnaire 4and Hamilton Depression Rating Scale (HAM‐D) questionnaire5 respectively. The HAM‐A scale comprised 14 items (anxious mood, tension, fears, insomnia, intellectual, depressed mood, somatic complaints muscular, somatic complaints sensory, cardiovascular symptoms, respiratory symptoms, gastrointestinal symptoms, genitourinary symptoms, autonomic symptoms, behavior at interview) and 5 responses (with scores 0, 1, 2, 3, and 4 indicating not present, mild, moderate, severe, very severe, respectively) to each item. A patient has to select one response (answer) for each item (question) and then the total score (range from 0 to 56) is calculated.

0 = Not present, 1 = Mild, 2 = Moderate, 3 = Severe, 4 = Very severe.

| Normal range | Mild | Moderate | Severe |
|---|---|---|---|
| 0-13 | 14-17 | 18-24 | 25 and over |

The HAM‐D scale comprised 17 items (depressed mood, feeling of guilt, suicide, insomnia early, insomnia middle, insomnia late, works and interests, retardation, agitation, anxiety psychic, anxiety somatic, somatic symptoms gastrointestinal, somatic symptoms general, genital symptoms, hypochondriasis, loss of weight, and insight) and 3–5 responses (with

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scores between 0 and 4) for each item. The interviewing clinician had to select one response (answer) for each item (question) and then the total score (range 0–52) was calculated.

| NORMAL | MILD | MODERATE | SEVERE | VERY SEVERE |
|---|---|---|---|---|
| 0-7 | 8-13 | 14-18 | 19-22 | >23 |

Followed by blood examination with due consideration of aseptic precaution, venepuncture was done and 5 ml of venous blood was drawn using 5ml syringe. The sample was sent for laboratory diagnosis. The serum cortisol level was estimated using Electro-chemilumunescence Immunoassay (ECLIA) ROCHE COBA E 411. The normal serum cortisol level ranges from 138 to 600 nmol/L (fasting 8 AM to 12 noon).

**RESULTS**

Among all the study patients 13 (14.4%) patients were between age group of 21-25yrs , 22(24.4%) patients between 26-30 yrs, 12(13.3%) patients between 31-35 yrs, 29(32.3%) patients between 36-40 yrs and 14(15.6%) patients between 41-45 yrs respectively. The mean age was 33.56±6.45 yrs. Gender distribution of patients 81(90%) were males and 9(10%) were females. Distribution of tobacco habit revealed 60(66.6%) patients had tobacco related habits and 30(33.3%) had no tobacco habits. The study subjects showed various tobacco habits, About 29(48.3%) patients had gutka/betelnut habit, 21(35%) patients had cigarette smoking habit and 10(16.7%) patients had beedi smoking habit.

**Comparison of Anxiety levels among the study groups (Table 1)**

Distribution of study subjects according to the level of anxiety by HAM-A Scale revealed 22(24.4%) patients had normal anxiety, 43(47.8%) patients had mild anxiety,25 (27.8%) had moderate anxiety. None of them had severe anxiety. The mean serum cortisol level in patients with normal anxiety was 167.73 ± 30.55nmol/L, Mild anxiety was 350.18 ± 94.02 nmol/L , Moderate anxiety was 478.55 ± 86.81nmol/L and was statistically significant with a P value of 0.0001. Among patients suffering, from Normal Anxiety 22 (100%) were from GROUP III. Among patients suffering from Mild Anxiety 15(34.9%) were from GROUP I, 20(46.5%) were from GROUP II and 8(18.6%) were from GROUP III. Among patients suffering from Moderate Anxiety 15(60%) were from GROUP I and 10(40%) were from GROUP II and was statistically significant with a P value of 0.001.

**Comparison of Depression levels among study groups (Table 2)**

Distribution of study subjects according to the level of depression by HAM-D Scale revealed 38(42.3%) subjects had recorded normal, 25(27.8%) patients had mild depression,22(24.4%) patients had moderate depression, 3(3.3%) had severe depression, 2(2.2%) patients had very severe depression. The mean cortisol level in patients with Normal Depression was 226.97 ± 82.50nmol/L, Mild Depression 362.44 ± 74.45nmol/L , Moderate Depression 462.05 ± 92.56nmol/L, Severe Depression 512.18 ± 101.14nmol/L , Very Severe Depression 662.06±39.01nmol/L respectively and was statistically significant with a P value of 0.0001. Among patients suffering from Normal Depression 8(21%) were from GROUP I, 3(7.9%) were from GROUP II and 27(71.1%) were from GROUP III. Among patients suffering from Mild Depression 9(36%) were from GROUP I, 13(52%) were from GROUP II and 3(12%) were from GROUP III. Among patients suffering from Moderate Depression 11(50%) were from GROUP I and 11(50%) were from GROUP II. Among patients suffering from Severe Depression in 1(33.3%) were from GROUP I and 2(66.7%) were from GROUP II. Among patients suffering from Very Severe Depression in 1(50%) were from GROUP I and 1(50%) were from GROUP II and was statistically significant with a P value of 0.001.

**Comparison of serum cortisol level among study groups (Table 3)**

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The mean serum cortisol level in GROUP I (OSMF) 467.11 ± 93.89 nmol/L, GROUP II (Leukoplakia) 369.07 ± 81.24 nmol/L and GROUP III (control) 187.54 ± 43.33 nmol/L respectively and was statistically significant with a P value of 0.0001. The mean serum cortisol level among tobacco users was 418.09 ± 100.11 nmol/L and 187.54 ± 43.32 nmol/L in nonusers and was statistically significant with a P value of 0.0001.

**Correlation between serum cortisol levels and anxiety and depression (Table 4)**

A very high statistically significant strong positive correlation was found between anxiety, depression and serum cortisol levels The Mean anxiety score was found to be significantly higher among patients with OSMF (18.30 ± 3.31) and Leukoplakia (17.73 ± 3.38) when compared to control group (7.60 ± 4.56). Similarly mean depression score significantly higher among patients with OSMF (11.47 ± 5.34) and Leukoplakia (12.17 ± 3.72) when compared to control group (3.90 ± 2.16) Comparison of mean serum cortisol level between three groups showed significantly high mean serum cortisol levels in patients with OSMF (467.11 ±93.89) followed by in patients with Leukoplakia (369.07 ±81.24) and in controls (187.54 ±43.33).

**Table 1: Comparison of Anxiety levels among study subjects of all the groups.**

| Group | Anxiety Level | | | Chi-Square | |
|---|---|---|---|---|---|
| | Normal N (%) | Mild N (%) | Moderate N (%) | p-value | Significance |
| GROUP I (OSMF) | 00 (0.0) | 15 (34.9) | 15(60.0) | 0.001 | Significant |
| GROUP II (Leukoplakia) | 00 (0.0) | 20 (46.5) | 10 (40.0) | | |
| GROUP III (Control) | 22 (100.0) | 08 (18.6) | 00 (0.0) | | |
| Total | 22 (100.0) | 43 (100) | 25 (100.0) | | |

**Table 2: Comparison of depression levels among study subjects of all the groups.**

| Group | Depression Level | | | | | Fisher Freeman Halton Exact Test | |
|---|---|---|---|---|---|---|---|
| | NormalN (%) | Mild N (%) | Moderate N (%) | SevereN (%) | Very Severe N (%) | p- value | Significance |
| GROUP I (OSMF) | 08(21.0) | 09 (36.0) | 11(50.0) | 01 (33.3) | 01 (50.0) | 0.001 | Significant |
| GROUP II (Leukoplakia) | 03 (7.9) | 13 (52.0) | 11 (50.0) | 02 (66.7) | 01 (50.0) | | |
| GROUP III (Control) | 27 (71.1) | 03 (12.0) | 00 (0.0) | 00 (0.0) | 00 (0.0) | | |

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| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Total** | **38 (100.0)** | **25 (100.0)** | **22 (100.0)** | **03 (100.0)** | **02 (100.0)** | | |

**Table 3: Comparison of serum cortisol level among the study subjects of all the groups.**

| Pre-malignant lesions/conditions | N | Mean serumcortisol levelMean ± SD (nmol/L) | One-way ANOVA | |
|---|---|---|---|---|
| | | | p-value | Significance |
| **GROUP I (OSMF)** | 30 | 467.11 ± 93.89 | 0.0001 | Significant |
| **GROUP II (Leukoplakia)** | 30 30 | 369.07 ± 81.24 | | |
| **GROUP III (Control)** | 30 | 187.54 ± 43.33 | | |

**Table 4: Correlation between serum cortisol levels and anxiety and depression**

| Variables | N | Serum Cortisol |
|---|---|---|
| **Anxiety** | **CorrelationCoefficient** | 0.837* |
| | **Sig (2-tailed)** | 0.0001 |
| | **N** | 90 |
| **Depression** | **CorrelationCoefficient** | 0.784* |
| | **Sig (2-tailed)** | 0.0001 |
| | **N** | 90 |

*Correlation is significant at 0.01 level

A very high statistically significant strong positive correlation was found between anxiety, depression and serum cortisol levels (p=0.0001).

## DISCUSSION

Cortisol is a key player in the stress response. In the presence of a physical or psychological threat, cortisol levels surge to provide the energy and substrate necessary to cope with stress provoking stimuli or escape from danger. However, although a stress-induced increase in cortisol secretion is adaptive in the short term, excessive or prolonged cortisol secretion may have crippling effects, both physically and psychologically.33 Stress is one of the main etiology and predisposing factor in many diseases. In course of time people fall in prey to deleterious habits such as gutka, tobacco and betel nut chewing, pan chewing, smoking etc, leading to harmful effects on oral mucosa.[2]

In many studies it was found that both physical and mental stress were related to increase in cortisol level (Schommer et al. 2003, Arjun et al 2014).[10] There is good evidence of many studies where stress and anxiety are related to increased resting levels of cortisol (Schommer et al. 2003; Wirtz et al. 2007). According to Gupta et al 2014[9] The interrelationship between chronic physical illness and psychiatric morbidity is also well established.2. Hence the following study was conducted to determine the Anxiety, Depression and serum cortisol level in OSMF and Leukoplakia patients and co-relate the serum cortisol level with Anxiety and Depression in OSMF and Leukoplakia patients.[6,7]

In the present study, assessment of Depression by HAM-D scale given in the year (1960)[3, 2], had been recorded which revealed 38(42.3%) subjects had normal depression, 25(27.8%) patients had mild depression, 22(24.4%) patients had moderate depression, 3(3.3%) had

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severe depression, 2(2.2%) patients had very severe depression. Very few patients had severe and very severe depression which is in accordance with study conducted by Kanodia et al.[3]
The mean Depression Score in present study was 11.47 ± 5.34 in GROUP I, 12.17 ± 3.72 in GROUP II and 3.90 ± 2.16 in GROUP III and was statistically significant with a P value of 0.0001. GROUP I(OSMF) had increased mean depression score compared to the control group, similar results were seen in a study conducted by Kanodia et al.[3]
There are no studies regarding Depression level in Leukoplakia. In the present study GROUP II(Leukoplakia) showed maximum mean depression score compared to all the groups. The mean serum cortisol level among tobacco users was 418.09 ± 100.11 nmol/L and 187.54 ± 43.32 nmol/L in nonusers, and was statistically significant with a P value of 0.0001. The mean cortisol level of GROUP I (OSMF) showed a highly significant difference from the control group which is in accordance with the study by Kanodia et al.[3] In the present study the mean cortisol level of GROUP II (Leukoplakia) also showed a highly significant difference from the control group. In a study conducted by Kanodia et al majority of OSMF patients had mild depression and in the present study 11(50%) GROUP I(OSMF) patients had moderate depression and 9(36%) GROUP I(OSMF) had mild depression. Only one patient had severe and very severe depression which is in accordance with study conducted by Kanodia et al.[3]
In the present study, similarly mean depression score significantly higher among patients with OSMF, Leukoplakia when compared to control group. Comparison of mean serum cortisol level between three groups showed significantly high mean serum cortisol levels in patients with OSMF followed by in patients with Leukoplakia and in controls (187.54±43.33) as conducted by Mubeen et al and Raja et al psychiatric morbidity was increased in patients with advance OSMF stages, which is co-related in the current study positively.[7,8]

## CONCLUSION

A significant increase in serum cortisol levels were seen in patients with anxiety and depression when compared to that of normal patients. Serum cortisol levels were also raised in patients with advance stage of OSMF and leukoplakia. It can be concluded that there is strong positive co-relation between serum cortisol level, anxiety level and depression level in patients with habit oriented diseases like OSMF and Leukoplakia. Proper psychological counseling should be given to patients so that they can cope with stress avoiding ill effects of the habit.

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