

# Oral Mucosal Lesions Associated with Smokers and Chewers – A Case-Control Study in Chennai Population

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## ABSTRACT

**Aims and Objectives:** To determine the association of oral mucosal lesions in a group of Chennai population aged 15 years and above with smoking and chewing habits. To also determine the dose-response relationship of these habits associated with the risk of oral mucosal lesions.

**Materials and Methods:** The study was undertaken with 450 subjects with smoking and/or chewing habits aged 15 years and over gathered through random selection in Chennai, India. Subjects with alcohol intake were excluded from the study. Based on the habits the study group was categorized into smokers, chewers and mixed (smoking+chewing). One hundred and fifty subjects diagnosed with oral mucosal lesions designated as “cases” and 300 lesion-free “controls”, frequency matched for age, sex, habit and family income were assessed during the study. The study protocol included a visual oral soft tissue examination and a questionnaire-based interview. In addition, those requiring further examination, scalpel biopsies were performed to establish a definitive diagnosis.

**Results:** Irrespective of the type of habit, 78% of cases smoked and/or chewed for more than 10 years as compared to 37.4% of the control group. Similarly, 71.3% of cases smoked and/or chewed more than 5 times per day as compared to 25.6% of the control group. Eleven habits related mucosal lesions of the oral cavity were encountered. Smoker's melanosis was the most common oral mucosal lesion followed by Oral submucous fibrosis and Leukoplakia. Dose-response relationships were observed for both duration and frequency of habits on the risk of oral mucosal lesions.

**Conclusion:** The result of the present study provides information on the association of oral mucosal lesions in smokers, chewers and patients with mixed habits. The mucosal lesions encountered included a few potentially malignant conditions and oral squamous cell carcinoma. Habits were more prevalent in men thus more lesions were encountered in males than in females. Moreover, increase in the duration and frequency of habits was significant predictors of risk in the case population.

**Keywords:** Dose-response relationship, Habits, Tobacco

## INTRODUCTION

Tobacco use including both the smoking and non-smoking forms are common in India [1]. Tobacco in any form, either smoked or smokeless, can cause a wide spectrum of oral mucosal alterations or lesions including oral pre-cancer and oral cancer. The type and location of the alteration/lesion varies with the type of tobacco used, the way it is used, and the frequency and duration of use [2].

Prevalence of tobacco use is about 15% to over 50% among men [1]. Amongst women, smoking is more common in north eastern states, Jammu and Kashmir and Bihar, while most other parts of India have prevalence rates of about 4% or less [3].

Smokeless tobacco products contain a large array of carcinogens although the actual number found is fewer than in cigarette smoke. Benzopyrene and other polycyclic aromatic carcinogens (PAHs) are the most important carcinogenic agents in cigarette smoke but in unburnt tobacco, nitrosamines are the strongest carcinogens [4].

Cross-sectional studies in Chennai regarding prevalence of oral lesions in relation to habits have shown a prevalence rate of 4.1% [5]. To further understand the relation between habits and oral mucosal lesions, a case-control study was designed to evaluate the risk factors and dose-response parameters in the development of oral lesions.

## AIMS AND OBJECTIVES

To determine the association of oral mucosal lesions in a group of Chennai population aged 15 years and above with smoking and chewing habits. To also determine the dose-response relationship in terms of duration and frequency of habits associated with the risk of oral mucosal lesions.

## MATERIALS AND METHODS

It is a population-based Case-Control Study done in Chennai within a period of one year from January 2013 to December 2013. The study was undertaken with 450 subjects with smoking and/or chewing habits aged 15 years and over gathered through random selection in Chennai, India. Subjects with alcohol intake were excluded from the study. Smokers were defined as daily or almost daily smokers, who had smoked at least 100 pieces of cigarettes in their lifetime. Tobacco/betel nut/betel quid chewers were defined as daily or almost daily chewers, who had the habit for at least six months. Based on the habits the study group was categorized into smokers, chewers and mixed (smoking + chewing). One hundred and fifty subjects diagnosed with oral mucosal lesions designated as “cases” and 300 lesion-free “controls”, frequency matched for age, sex, habit and family income were assessed during the study. The 150 “cases” and 300 “controls” were distributed as follows:

**Smokers** group had 55 “cases” and 110 “controls”

**Chewers** group had 55 “cases” and 110 “controls”

**Mixed** group has 40 “cases” and 80 “controls”

The study protocol included a visual oral soft tissue examination and a questionnaire-based interview. Permission was obtained from the Institutional Ethical Committee before starting the study. The nature and purpose of the study were briefly outlined to each participating patient/subject and written consent in the local language was obtained.

The clinical diagnosis was established based on the criteria as provided by the epidemiology guide for the diagnosis of oral mucosal diseases (WHO). In addition, those requiring further examination, scalpel biopsies were performed to establish a definitive histopathological diagnosis.

## STATISTICAL ANALYSIS

Data was entered into a spread sheet and analysed using SPSS (Statistical Package for Social Science) version 11.5. Differences of qualitative data between case and control group was assessed using Pearson's chi-square test ( $\chi^2$ -Test). Risk was assessed using univariate odds ratio (OR) with 95% confidence interval and adjusted odds ratio was obtained using multivariate logistic regression. All statistical tests were two tailed test. Independent t-test was also done to calculate the weighted mean of duration and frequency of habits between case and control group. P-value  $\leq 0.05$  was taken as statistically significant. The test was considered "significant" if  $p \leq 0.05$ , "highly significant" if  $p \leq 0.01$  and "very highly significant" if  $p \leq 0.001$ .

## RESULTS

In the present study, 84.0% of males and 16.0% of females in the case category and an equal percentage in the control group constituted the study population. [Table/Fig-1] shows the distribution of entire subjects by basic characteristics.

In our study, Smoker's melanosis was the most common oral mucosal lesion encountered in the entire case group followed by Oral submucous fibrosis (OSMF) and Leukoplakia. Other than Smoker's palate and Paan-chewer's lesion which exclusively occurred in smokers and chewers respectively, rest were seen in at least two habits [Table/Fig-2].

Weighted mean  $\pm$  Standard Deviation of duration and frequency of habits between case and control group was calculated. The difference between the means was found to be highly significant [Table/Fig-3].

### Smoker's Group

As 98.2% of the subjects were males and only 1.8% females, comparison has been done taking only males into consideration.

Considering the duration of smoking habits, [Table/Fig-4] shows significant OR of 54.1 (95% CI = 3.01 - 102.1) for men who had been smoking for more than 30 years ( $p=0.001$ ) suggesting a 54.1 times more risk of getting a lesion in men of case population as compared to controls.

| Characteristics |                 | Study Group |       |      |       | Pearson's<br>chi square<br>test    |
|-----------------|-----------------|-------------|-------|------|-------|------------------------------------|
|                 |                 | Control     |       | Case |       |                                    |
|                 |                 | n           | Col % | n    | Col % |                                    |
| Age Group       | 15 - 24 years   | 26          | 8.7%  | 13   | 8.7%  | $\chi^2=0.00$<br>p=1.00<br><br>NS  |
|                 | 25 - 34 years   | 48          | 16.0% | 24   | 16.0% |                                    |
|                 | 35 - 44 years   | 64          | 21.3% | 32   | 21.3% |                                    |
|                 | 45 - 54 years   | 52          | 17.3% | 26   | 17.3% |                                    |
|                 | 55 - 64 years   | 66          | 22.0% | 33   | 22.0% |                                    |
|                 | 65 - 74 years   | 28          | 9.3%  | 14   | 9.3%  |                                    |
|                 | > 74 years      | 16          | 5.3%  | 8    | 5.3%  |                                    |
| Sex             | Male            | 252         | 84.0% | 126  | 84.0% | $\chi^2=0.00$<br>p=1.00<br>NS      |
|                 | Female          | 48          | 16.0% | 24   | 16.0% |                                    |
| Education       | No education    | 35          | 11.7% | 22   | 14.7% | $\chi^2=12.5$<br>p=0.006<br><br>HS |
|                 | Basic education | 136         | 45.3% | 85   | 56.7% |                                    |
|                 | High school     | 86          | 28.7% | 36   | 24.0% |                                    |
|                 | UG/PG           | 43          | 14.3% | 7    | 4.7%  |                                    |
| Monthly Income  | <Rs. 5000       | 146         | 48.7% | 73   | 48.7% | $\chi^2=0.00$<br>p=1.00<br><br>NS  |
|                 | Rs. 5001 -10000 | 142         | 47.3% | 71   | 47.3% |                                    |
|                 | > Rs.10000      | 12          | 4.0%  | 6    | 4.0%  |                                    |

[Table/Fig-1]: Distribution of entire study subjects by basic characteristics

NS: Not Significant; S: Significant; HS: Highly Significant

[Table/Fig-5] shows frequencies of '11 - 15' and '> 15' cigarette/bidi/chutta per day had significant ORs of 4.68 (95% CI = 1.36 - 16.9) and 22.9 (95% CI = 7.91 - 68.9) respectively ( $p=0.004$  and  $p=0.001$  respectively in each instance).

### Chewer's Group

[Table/Fig-6] shows significant OR of 4.67 (95% CI = 1.10 - 25.4) for men who had been chewing for 21 - 30 years ( $p=0.03$ ) suggesting a 4.67 times more risk of getting a lesion. For females, [Table/Fig-7] shows significant OR of 9.41 (95% CI = 1.91 - 52.1) who had been chewing for more than 30 years ( $p=0.001$ ) suggesting a 9.41 times more risk of a soft tissue lesion in the case group.

In terms of frequency of chewing habits, '11-15' betel quid/gutkha/mawa/khaini/paan masala per day had significant OR of 8.97 (95% CI = 1.01 - 220.1) ( $p=0.02$ ) in men and a frequency of '6 - 10' betel

| Oral Mucosal Lesions                 | Habit  |        |        |        |       |       | Total |
|--------------------------------------|--------|--------|--------|--------|-------|-------|-------|
|                                      | Smoker |        | Chewer |        | Mixed |       |       |
|                                      | n      | %      | n      | %      | n     | %     |       |
| Leukoedema                           | 4      | 66.7%  | -      | -      | 2     | 33.3% | 6     |
| Leukoplakia                          | 5      | 26.3%  | 5      | 26.3%  | 9     | 47.4% | 19    |
| Median Rhomboid Glossitis            | 4      | 66.7%  | 1      | 16.7%  | 1     | 16.7% | 6     |
| Oral Lichen planus like lesion (OLP) | -      | -      | 5      | 83.3%  | 1     | 16.7% | 6     |
| Oral Squamous cell Carcinoma (OSMF)  | 1      | 7.1%   | 8      | 57.1%  | 5     | 35.7% | 14    |
| Oral Submucous Fibrosis              | -      | -      | 15     | 75.0%  | 5     | 25.0% | 20    |
| Pan-Chewer's lesion                  | -      | -      | 12     | 100.0% | -     | -     | 12    |
| Palatal Erythema                     | 3      | 42.9%  | -      | -      | 4     | 57.1% | 7     |
| Smoker's Melanosis                   | 32     | 72.7%  | -      | -      | 12    | 27.3% | 44    |
| Smoker's Palate                      | 6      | 100.0% | -      | -      | -     | -     | 6     |
| Tobacco Pouch Keratosis              | -      | -      | 9      | 90.0%  | 1     | 10.0% | 10    |
| Total                                | 55     | 100%   | 55     | 100%   | 40    | 100%  | 150   |

[Table/Fig-2]: Distribution of oral mucosal lesions based on habits

|         | Weighted Mean of Duration of Habit (W. Mean $\pm$ S.D.) | t-test (Independent t-test)                  | Weighted mean of Frequency of habit | Probability of unpaired t-test               |
|---------|---------------------------------------------------------|----------------------------------------------|-------------------------------------|----------------------------------------------|
| Case    | 23.92 $\pm$ 11.67                                       | t-value = 29.87<br>df= 3419<br>p =0.00<br>HS | 23.79 $\pm$ 19.73                   | t-value = 27.97<br>df= 3419<br>p =0.00<br>HS |
| Control | 12.48 $\pm$ 10.28                                       |                                              | 8.75 $\pm$ 6.56                     |                                              |

[Table/Fig-3]: Weighted mean of duration and frequency of habits and determination of dose - response relationship

HS: Highly Significant; S.D: Standard Deviation; df: degrees of freedom

| Duration      | Ca/Co | OR(95%CI)          | p-value       | Add OR(95%CI)     | p-value      |
|---------------|-------|--------------------|---------------|-------------------|--------------|
| <5 years      | 0/10  | -                  | p=0.02<br>S   | -                 | p=0.06<br>NS |
| 5 - 10 years  | 7/56  | 0.14(0.05 - 0.35)  | p=0.001<br>HS | 0.31(0.12 - 0.88) | p=0.03<br>S  |
| 11 - 20 years | 19/32 | 1.29(0.61 - 2.73)  | p=0.47<br>NS  | 2.10(0.87 - 5.14) | p=0.10<br>NS |
| 21 - 30 years | 16/8  | 5.26(1.9 - 14.7)   | p=0.03<br>S   | 4.6(1.09 - 20.4)  | p=0.04<br>S  |
| >30 years     | 12/2  | 54.1(3.01 - 102.1) | p=0.001<br>HS | 4.4(0.63 - 36.8)  | p=0.06<br>NS |

[Table/Fig-4]: Risk estimates of smoking habits and dose-response parameter (duration) in male subjects

NS: Not Significant; S: Significant; HS: Highly Significant

Ca = Case; Co = Control; OR = Odds ratio; Add OR = Adjusted odds ratio  
95%CI = 95% confidence interval

| Frequency | Ca/Co | OR(95%CI)         | p-value       | Add OR(95%CI)    | p-value       |
|-----------|-------|-------------------|---------------|------------------|---------------|
| 1         | 0/1   | -                 | p=0.47<br>NS  | -                | p=0.21<br>NS  |
| 2 - 5     | 6/54  | 0.13(0.04 - 0.34) | p=0.001<br>HS | 0.10(0.1 - 0.36) | p=0.001<br>HS |
| 6 - 10    | 12/37 | 0.13(0.04 - 0.34) | p=0.01<br>HS  | 0.4(0.25 - 1.17) | p=0.12<br>NS  |
| 11 - 15   | 5/10  | 4.68(1.36 - 16.9) | p=0.004<br>HS | 3.9(1.1 - 15.9)  | p=0.01<br>HS  |
| >15       | 31/6  | 22.9(7.91 - 68.9) | p=0.001<br>HS | 20.8(8.6 - 61.3) | p=0.01<br>HS  |

**[Table/Fig-5]:** Risk estimates of smoking habits and dose-response parameter (frequency) in male subjects

NS: Not Significant; S: Significant; HS: Highly Significant

Ca = Case; Co = Control; OR = Odds ratio; Add OR = Adjusted odds ratio  
95%CI = 95% confidence interval

quid/gutkha/mawa/khaini/paan masala per day had significant OR of 24.6 (95% CI = 2.7 - 111.4) (p=0.05) in females [Table/Fig-8,9].

## Mixed Group

As 97.5% of the subjects were males and only 2.5% females, comparison has been done taking only males into consideration in the mixed group. [Table/Fig-10] shows significant risk for men who had been smoking and chewing for more than 30 years (p=0.001). [Table/Fig-11] shows frequencies of '> 15' times per day had significant OR of 10.2 (95% CI = 3.21 - 33.6) (p=0.001).

## DISCUSSION

### Smoker's Group

In the present study, the prevalence of smoking as well as occurrence of oral mucosal lesions in the case group was high among men

| Duration     | Ca/Co | OR(95%CI)          | p-value      | Add OR(95%CI)      | p-value      |
|--------------|-------|--------------------|--------------|--------------------|--------------|
| <5 years     | 3/17  | 0.29 (0.06 - 1.17) | p=0.06<br>NS | 0.28 (0.08 - 1.07) | p=0.06<br>NS |
| 5 - 10 years | 6/27  | 0.32(0.10 - 0.96)  | p=0.02<br>S  | 0.31(0.12 - 0.88)  | p=0.03<br>S  |
| 11 - 20years | 14/17 | 2.12(0.80 - 5.95)  | p=0.09<br>NS | 2.10(0.87 - 5.14)  | p=0.10<br>NS |
| 21 - 30years | 6/3   | 4.67(1.10 - 25.4)  | p=0.03<br>S  | 4.6(1.09 - 20.4)   | p=0.04<br>S  |
| >30years     | 4/2   | 4.41(0.64 - 37.1)  | p=0.07<br>NS | 4.4(0.63 - 36.8)   | p=0.06<br>NS |

**[Table/Fig-6]:** Risk estimates of chewing habits and dose-response parameter (duration) in male subjects

NS: Not Significant; S: Significant; HS: Highly Significant

Ca = Case; Co = Control; OR = Odds ratio; Add OR = Adjusted odds ratio  
95%CI = 95% confidence interval

| Duration      | Ca/Co | OR(95%CI)          | p-value       | Add OR(95%CI)       | p-value      |
|---------------|-------|--------------------|---------------|---------------------|--------------|
| < 5 years     | 2/5   | 0.78 (0.09 - 5.21) | p=0.77<br>NS  | 0.62 (0.08 - 4.97)  | p=0.66<br>NS |
| 5 - 10 years  | 1/16  | 0.08 (0.00 - 0.69) | p=0.005<br>HS | 0.071 (0.00 - 0.61) | p=0.01<br>HS |
| 11 - 20 years | 4/12  | 0.59 (0.14 - 2.41) | p=0.41<br>NS  | 0.52 (0.10 - 2.14)  | p=0.30<br>NS |
| 21 - 30 years | 6/8   | 1.69 (0.43 - 6.62) | p=0.39<br>NS  | 1.61 (0.39 - 6.4)   | p=0.24<br>NS |
| > 30 years    | 9/3   | 9.41 (1.91 - 52.1) | p=0.001<br>HS | 9.34 (1.63 - 46.8)  | p=0.01<br>HS |

**[Table/Fig-7]:** Risk estimates of chewing habits and dose-response parameter (duration) in female subjects

NS: Not Significant; S: Significant; HS: Highly Significant

Ca = Case; Co = Control; OR = Odds ratio; Add OR = Adjusted odds ratio  
95%CI = 95% confidence interval

(98.2%) than women (1.8%) and the finding was consistent with previous studies by Saraswathi et al., and Yang et al., [5,6].

Dose-response relationships were analysed for duration and frequency of tobacco smoking and was found that smoking

| Frequency | Ca/Co | OR(95%CI)           | p-value       | Add OR(95%CI)       | p-value      |
|-----------|-------|---------------------|---------------|---------------------|--------------|
| 1         | 2/13  | 0.26 (0.04 - 1.36)  | p=0.09<br>NS  | 0.20 (0.02 - 1.23)  | p=0.10<br>NS |
| 2 - 5     | 10/43 | 0.23 (0.09 - 0.62)  | p=0.001<br>HS | 0.22 (0.07 - 0.60)  | p=0.01<br>HS |
| 6 - 10    | 15/9  | 5.3 (1.79 - 15.9)   | p=0.001<br>HS | 5.1 (1.7 - 3.6)     | p=0.01<br>HS |
| 11 - 15   | 4/1   | 8.97 (1.01 - 220.1) | p=0.02<br>S   | 8.81 (1.01 - 190.2) | p=0.01<br>HS |

**[Table/Fig-8]:** Risk estimates of chewing habits and dose-response parameter (frequency) in male subjects

NS: Not Significant; S: Significant; HS: Highly Significant

Ca = Case; Co = Control; OR = Odds ratio; Add OR = Adjusted odds ratio  
95%CI = 95% confidence interval

| Frequency | Ca/Co | OR(95%CI)         | p-value      | Add OR(95%CI)        | p-value       |
|-----------|-------|-------------------|--------------|----------------------|---------------|
| 1         | 0/6   | -                 | p=0.07<br>NS | -                    | p=0.99<br>NS  |
| 2 - 5     | 13/37 | 0.56(0.10 - 0.96) | p=0.02<br>S  | 0.52(0.29 - 0.94)    | p=0.03<br>S   |
| 6 - 10    | 8/1   | 24.6(2.7 - 111.4) | p=0.05<br>S  | 22.4(2.82 - 521.034) | p=0.004<br>HS |
| 11 - 15   | 1/0   | -                 | p=0.15<br>NS | -                    | p=0.08<br>NS  |

**[Table/Fig-9]:** Risk estimates of chewing habits and dose-response parameter (frequency) in female subjects

NS: Not Significant; S: Significant; HS: Highly Significant

Ca = Case; Co = Control; OR = Odds ratio; Add OR = Adjusted odds ratio  
95%CI = 95% confidence interval

| Duration     | Ca/Co | OR(95%CI)         | p-value       | Add OR(95%CI)      | p-value      |
|--------------|-------|-------------------|---------------|--------------------|--------------|
| <5 years     | 4/23  | 0.27(0.07 - 0.93) | p=0.02<br>S   | 0.10(0.03 - 0.89)  | p=0.01<br>HS |
| 5 - 10 years | 10/37 | 0.38(0.15 - 0.96) | p=0.001<br>HS | 0.291(0.12 - 0.85) | p=0.01<br>HS |
| 11 - 20years | 8/12  | 1.42(0.47 - 4.23) | p=0.48<br>NS  | 1.30(0.27 - 5.14)  | p=0.26<br>NS |
| 21 - 30years | 7/6   | 2.63(0.72 - 9.7)  | p=0.10<br>NS  | 2.31(0.09 - 8.4)   | p=0.08<br>NS |
| >30years     | 10/0  | -                 | p=0.001<br>HS | -                  | p=0.01<br>HS |

**[Table/Fig-10]:** Risk estimates of combination of smoking and chewing habits and dose-response parameter (duration) in male subjects

NS: Not Significant; S: Significant; HS: Highly Significant

Ca = Case; Co = Control; OR = Odds ratio; Add OR = Adjusted odds ratio  
95%CI = 95% confidence interval

| Frequency | Ca/Co | OR(95%CI)         | p-value       | Add OR(95%CI)     | p-value       |
|-----------|-------|-------------------|---------------|-------------------|---------------|
| 1         | 1/1   | 2.03(0.0 - 76.3)  | p=0.61<br>NS  | 1.83(0.0 - 66.8)  | p=0.32<br>NS  |
| 2 - 5     | 9/59  | 0.10(0.03 - 0.26) | p=0.001<br>HS | 0.08(0.01 - 0.19) | p=0.001<br>HS |
| 6 - 10    | 10/11 | 0.13(0.04 - 0.34) | p=0.01<br>HS  | 0.4(0.25 - 1.17)  | p=0.12<br>NS  |
| 11 - 15   | 1/1   | 2.03(0.0 - 76.3)  | p=0.61<br>NS  | 1.83(0.0 - 66.8)  | p=0.32<br>NS  |
| >15       | 18/6  | 10.2(3.21 - 33.6) | p=0.001<br>HS | 9.8(2.9 - 31.3)   | p=0.01<br>HS  |

**[Table/Fig-11]:** Risk estimates of combination of smoking and chewing habits and dose-response parameter (frequency) in male subjects

NS: Not Significant; S: Significant; HS: Highly Significant

Ca = Case; Co = Control; OR = Odds ratio; Add OR = Adjusted odds ratio  
95%CI = 95% confidence interval

cigarette/bidi/chutta for more than 30 years ( $p=0.001$ ) in terms of duration and smoking more than 15 cigarette/bidi/chutta per day ( $p=0.001$ ) in terms of frequency were the strongest predictor of risk in the case population (males).

Among the 55 oral mucosal lesions found in smokers, Smoker's melanosis was the most frequently encountered lesion (58.2%) and consistent with the findings of Saraswathi et al., and Hedin et al., [5,7] and Oral squamous cell carcinoma (OSCC) the least. Smoker's palate (10.9%) and Leukoplakia (9.1%) were the second and third most common lesions. In the present study, all lesions occurred in males with palatal erythema being reported in both males and in a female.

### Chewer's Group

Chewing habit was seen more in men (60%) than women (40%) but only 1.5 times more than women and the finding was compatible with previous studies by Saraswathi et al., and Sinha et al., [5,8]. but inconsistent with the finding of Yang et al., who reported a higher female prevalence [6].

Considering men and women separately, dose-response relationship was computed for both duration and frequency of tobacco/betel (areca) nut chewing on the risk of mucosal lesions of the oral cavity. Consumption of tobacco/betel (areca) nut for 21 – 30 years was the duration of highest risk in males. On the other hand, in females, chewing for more than 30 years had the highest risk. The daily frequency of tobacco/betel (areca) nut chewing was a significant predictor of risk in the case population with the highest risk associated with chewing of 11–15 packets/nos. per day in males whereas the highest risk in females was seen in those chewing 6–10 packets/nos. per day.

Among the 55 cases in chewers, OSMF was the most frequently encountered lesion (27.3%) and consistent with the findings of Saraswathi et al., and Yang et al., [5,6] and Median rhomboid glossitis the least. Pan-chewer's lesion (21.8%) and Tobacco pouch keratosis (16.4%) were the second and third most common lesions.

### Mixed Group

In this study, mixed (smoking + chewing) habit was seen more in men (97.5%) than women (2.5%) and the finding was compatible with previous studies by Yang et al., [6]. Dose-response relationship was determined and was found that smoking and chewing for more than 30 years had significant risks. Daily frequency of mixed habit was a strong predictor of risk in the case population with the highest risk associated with smoking and chewing more than 15 times per day.

Considering the 55 oral mucosal lesions found in the mixed group, Smoker's melanosis was the most frequently encountered lesion (25%). The finding was inconsistent with the study of Yang et al., who reported OSMF as the most prevalent lesion [6]. Leukoplakia (22.5%) was the second most common lesion followed by OSMF (12.5%) and OSCC (12.5%) in the third position.

### Oral Mucosal Lesions

Oral mucosal lesions were predominantly seen in males attributing to the higher prevalence of smoking and/or chewing in men. 72.7% of Smoker's melanosis was seen in smokers and the rest 27.3% occurred in cases using the combination of smoking and chewing. This finding makes tobacco smoking to be the main cause of Smoker's melanosis and this was consistent with the observation made by Saraswathi et al., and Hedin et al., [5,7]. The most prevalent form was bidi and filtered cigarette which contributed to 50% of the cases and this was the prime etiologic agent for inducing Smoker's melanosis.

In this study, all the cases of Smoker's palate (Leukokeratosis nicotina

palati) were seen exclusively in smokers and the finding was same as that of Saraswathi et al., [5]. All the lesions were encountered in males as 98.2% of study samples in the smokers group were men. Male predominance was also reported by Saraswathi et al., and NJ Mani [5,9]. The most prevalent form of tobacco responsible for Smoker's palate in our study was bidi and filtered cigarette contributing equally whereas Mehta FS et al., [10] reported 52% of lesions in bidi smokers.

In our study, 47.4% of leukoplakia cases were found in mixed group and 26.3% each in smokers and chewers group suggesting association with both tobacco smoking and tobacco/betel quid/areca nut chewing. This was consistent with the findings of Saraswathi et al., Yang et al., and Rana et al., [5,6,11]. A higher percentage of cases in mixed group suggested probable synergy or additive effects and the finding was consistent with the study of Murti et al., and Lee et al., [12,13] but was not in agreement with the observation of Ikeda et al., and Macigo et al., [14,15] who reported leukoplakia predominantly in smokers. In males, 89.5% of the lesions occurred and 10.5% in females and this was consistent with the findings of Saraswathi et al., NJ Mani et al., Ikeda et al., and Charles et al., [5,9,14,16]. Combinations of filtered cigarette + Gutkha and Bidi + Gutkha were the major contributors of leukoplakia in the mixed group, betel quid in chewers group and bidi and filtered cigarette in smokers group.

In smokers, 66.7% of leukoedema cases were reported and the rest 33.3% in mixed group. The higher occurrence in smokers suggested smoking as the major risk factor and was consistent with the findings of Axell et al., and Rosnah et al., [17,18]. All the lesions were seen in males. NJ Mani et al., and Axell et al., also reported increased prevalence of leukoedema in men [9,17].

Smokers contributed 66.7% of Median Rhomboid Glossitis (Central Papillary Atrophy of Tongue) followed by 16.7% each by chewers and mixed category suggesting higher percentage of cases among smokers and this was consistent with the findings of Mehta et al., [19]. Bidi smoking was the major risk factor for the development of Central papillary atrophy of tongue and was in agreement with the findings of Murti et al., and Mehta et al., [12,19].

In the mixed group, 57.1% of the Palatal Erythema cases were seen and rest 42.9% in smokers which was not consistent with the findings of Murti et al., [12] who reported 87% of lesions in smokers and rest 13% in mixed category. An 85.7% of cases were seen in males and only 14.3% in females. The higher percentage of occurrence in men was in agreement with the findings of Murti et al., [12].

In the present study, chewing habit was the major risk factor for the development of OSCC with 57.1% of cases. This was followed by 35.7% of cases in mixed group and 7.1% in smokers suggesting less marked association with smoking (consistent with the findings of Hirayama [20]). Previous studies by Yang et al., Hirayama, Reichart et al., Thomas et al., van Wyk et al., and Balaram P et al., reported chewing habit as the major risk factor for OSCC [6,20-24]. On the contrary, studies by Murti et al., and Lumukana et al., reported mixed habits as major risk factors for oral cancer [12,25]. 78.6% of OSCC in our study occurred in males and 21.4% in females and the finding was consistent with the studies of Reichart et al., Ahmed et al and Sankaranarayanan R [21,26,27] who also reported higher prevalence in men. Before the age of 55 years, 57.2% of the lesions occurred and rest 42.8% above 55 years whereas Mehta et al., Ahmed et al., and Gupta et al., reported OSCC in older age group (55 years and above) [10,26,28]. In our study, both smoking and chewing were found to be important in males and chewing of betel quid appeared to play a dominant role in females and this was in agreement with the findings of Ahmed et al., [26].

OSMF occurred in 75% of chewers and the rest 25% in patients with mixed habits and the finding was consistent with the results

of Saraswathi et al., Yang et al., Rana et al., Murti et al., Shah N and Sharma PP and Ariyawardana et al., [5,6,11,12,29,30]. Another study by Lee et al., showed mixed habit to have increased risk than chewing habit only [13]. All lesions in our study were found in males suggesting higher prevalence in men. Literature survey shows wide variation in sex distribution. A male predominance in OSMF cases was shown by Shah N and Sharma PP, Sinor et al., Ahmad et al., Wahi et al., and Hazarey et al., [29,31-34] in India whereas Yang et al., have proposed female predominance [6]. Study by Sirsat and Khanolkar have reported male:female ratio of 1:1 [35]. Gutkha usage was the major risk factor in the development of OSMF in our study followed by Mawa and this was in agreement with the findings of Hazarey et al., [34].

Pan-chewer's lesion exclusively occurred in patients with betel quid chewing habit suggesting pan chewing to be the only risk factor involved in the development of the lesion. In females, 83.3% of the lesions were seen attributing to the high use of betel quid among females in our study and the finding was consistent with that reported by Gupta PC et al., [36].

In the chewers group, 90% of Tobacco Pouch Keratosis were seen suggesting betel quid/khaini/mawa/gutkha chewing as the major risk factor. The rest 10% of the cases were seen in the mixed group.

Oral Lichen Planus-like lesions occurred in 83.3% of chewers and rest 16.7% in patients with mixed habits suggesting tobacco chewing habit to be a major risk factor and this was consistent with the findings of Daftary et al., [37] but not in agreement with another study by Murti et al., [12] who reported majority of the cases in patients with mixed habits. There was a marked female predominance with 83.3% of the lesions occurring in women and this was in agreement with the findings of Ikeda et al., and Daftary et al., [14,37].

## CONCLUSION

The result of the present study provides information on the association of oral mucosal lesions in smokers, chewers and patients with mixed habits. This study highlighted 11 habit related mucosal lesions of the oral cavity which also included a few potentially malignant conditions and oral squamous cell carcinoma. Habits were more prevalent in men thus more lesions were encountered in males than in females.

Dose-response relationships were observed for both duration and frequency of habits on the risk of oral mucosal lesions and the increase in these two parameters were significant predictors of risk in the case population.

Tobacco smoking was a major risk factor for the development of Smoker's melanosis, Smoker's palate, Leukoedema and Median Rhomboid glossitis whereas chewing habit was a strong risk factor for Oral submucous fibrosis, Oral squamous cell carcinoma, Tobacco pouch keratosis, Oral lichen planus-like lesion and Pan-Chewer's lesion. Combinations of tobacco smoking and chewing habits were the main risk factors for Leukoplakia and Palatal erythema.

Future case-control or cohort studies for individual lesions and with larger sample size are necessary to evaluate the risk for oral mucosal lesions including potentially malignant conditions and oral cancer resulting from smoking and chewing habits.

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