Interplay of lifestyle factors in oral leukoplakia: A translational study in Chhattisgarh, India

Golchha T#, Rajput Y#, Shrivastava S, Sahu M, Chandrakar A, Mungutwar V, Mishra SS, PinakaPani R, Khodiar PK, Banjara H, Gahine R#, Choudhary V, Shammas MA, Patra PK and Jagannath Pal*

1Department of Biochemistry, Pt. J.N.M. Medical College, Raipur, Chhattisgarh, India
2Multi-Disciplinary Research Unit (MRU), Pt. J.N.M. Medical College, Raipur, Chhattisgarh, India
3Department of Pathology, Govt. Medical College, Rajnandgaon, Chhattisgarh, India
4Department of ENT, Dr.B.R.A.M. Hospital and Pt. J.N.M. Medical College, Raipur, Chhattisgarh, India
5Government Dental College, Raipur, Chhattisgarh, India
6Regional Cancer Centre, Dr.B.R.A.M. Hospital, Raipur, Chhattisgarh, India
7Harvard (Dana Farber) Cancer Institute, Boston, MA, USA
8Department of Biochemistry, CIMS, Bilaspur, Chhattisgarh, India
9Dept of Pathology, Pt. J.N.M. Medical College, Raipur, Chhattisgarh, India

# Equally contributed

Abstract

Background: Oral squamous cell carcinoma is one of the leading cancers in India. It is frequently preceded by a potentially malignant disorder called oral leukoplakia (OL), which is linked to widespread high-risk oral habits. In the state of Chhattisgarh, India, tobacco-chewing is one of the most common habits in both males and females. However, the impact of lifestyle factors in etiology of OL in this region has not been investigated, and their evaluation could help develop translational strategies to reduce cancer incidence and improve overall public health.

Materials and methods: Sixty patients with oral patches and clinical diagnosis of OL were enrolled. History and clinical presentation were recorded, brush cytology carried out and the patients followed-up after one year.

Results: Mean age at presentation of OL was 43.4±12.6 years. OL was predominantly associated with chewing tobacco in both genders. The habit was reported in 82.6% (OR=7.07, p<0.0001) male and 62.5% (OR=5.1, p<0.02) female OL patients. Among tobacco chewers, increased risk of developing OL in males was 5.04-fold (p = 0.0006) higher relative to females. The most common site of involvement of OL was buccal mucosa (75%). Patients who chewed tobacco and consumed alcohol for > 10 years had increased incidence of non homogeneous OL. At one-year follow-up, patients with or without any oral habit, who did not show any improvement, were 21% and 60%, respectively. Literacy rates in patients who complied vs. those who did not comply with follow-up surveillance were 100% and 67%, respectively.

Conclusion: Awareness program against habit of chewing tobacco, with special focus on males at 20-year age group, may reduce the occurrence of OL in this region. OL patients with no history of oral habit should be followed-up more frequently. Increase in literacy rate may help in improving patient compliance to follow-up surveillance.

Introduction

Oral squamous cell carcinoma (OSCC) is sixth commonest cancer worldwide [1]. It is also the most common form of oral cancer comprising almost 90% of all oral malignancies [1]. It is one of the leading cancers in India and constitutes 30% of all new cancer cases and most of the cases (60%) present with advanced disease, leaving very limited treatment option [2]. It is often preceded by persistent oral potentially malignant disorders OPMD, a group of oral lesions commonly presented as white patches called oral leukoplakia (OL) [3]. India has the highest prevalence of OL primarily due to several forms of high-risk oral habits. Its prevalence ranges from 0.2 to 8.2% depending on geographic regions [4-7]. Though most of the cases regress spontaneously, some may progress to OSCC with a variable transformation rate from 0.1 to 34% [5,8-10].

The common risk factors for OL are high risk oral habits which include chewing tobacco, betel nut, smoking tobacco and alcohol consumption with variable contribution in different populations [11]. There is a significant difference in the pattern of high-risk oral habits in western countries and India. While in western countries, smoking tobacco and alcohol are dominant high-risk oral habits, in India, smokeless form of tobacco chewing is a widespread oral habit. This includes khaini, gutkha, and snuff, either used separately or as an ingredient of pan masala or betel quid [12].Unlike diffuse effect of tobacco smoking, soluble form of tobacco causes localized exposure with high concentration of tobacco leading to more penetrating and injurious impact on oral mucosa. The differences in potentially risky...
oral habits in different geographical regions within India provide a natural opportunity to study their impact on etiology of OL in light of specific environmental and lifestyle factors and/or gender of consumers. This will allow formulation of an overall preventive health policy as well as policies suited for specific regions.

Though there are several studies on premalignant lesions from various regions of India [13,14], most of them lack inappropriate number of hospital-based control population and thus may not represent the background risk factor exposure within general population. Moreover, most of these studies fail to provide any assessment with translational implication which may help to undertake community based preventive strategy.

It has been proposed that oral cancer and premalignant lesions mostly affect males suggesting that the high risk associated with these habits is gender-specific [15]. However, contradictory reports from different parts of the world regarding gender specific vulnerability to oral cancer also exist. In fact, several recent reports suggest that compared to men, there is increased risk among women with the habit of smoking and alcohol intake for developing oral cancer [15-17]. There are other studies which claim that estrogen, a gender specific hormone may have protective role contributing to low occurrence of oral cancer in young females compared to males [18,19]. Therefore, it remains to be determined if and how the high-risk oral habits differentially impact males and females with relevance to development of precancerous oral conditions.

A thorough investigation of oral habits and their consequence in light of differences in gender, geographical location, environment and lifestyle factors will not only identify specific risk factors but also the populations which could be at risk. This in turn will allow development of strategies for prevention, identification and regular follow-up of vulnerable groups as well as early diagnosis of oral cancer, improving the clinical outcome of disease.

In state of Chhattisgarh, located in central India, the use of soluble forms of tobacco and alcohol consumption is very high in the general population. This region is also unique from rest of the country in having a high percentage of tribal population. Many residents are below poverty line. As per National Family Health Survey (NFHS-4) 2015, unlike other parts of India, the high-risk oral habits in this region are prevalent in both male and female population [20]. So, this provides a natural opportunity to study the impact of oral habits and gender on various characteristics of OL relative to control population. Moreover, there is no report from this region, evaluating the impact of the prevalent risk factors in occurrence of OL and oral cancer. It is, therefore, extremely important to formulate an evidence-based preventive strategy against OL and oral cancer in this region which is unique with respect to prevalence of oral habits as well as socioeconomic features.

In this hospital-based pilot study, we evaluated the impact of major contributing risk factors in occurrence of OL in this region to identify the high risk individuals/groups for implementing effective awareness and surveillance programs for them. This is the first pilot study in this region designed with clear translational goals which include: (1) Identifying target population on whom awareness program should be focused for effective prevention of OL; (2) Impact of educational background on patients’ compliance on follow-up surveillance; (3) Impact of gender on vulnerability; and (4) Comparison of the impact of high risk oral habits in causation of OL with other parts of the world.

Materials and methods

Study was carried out at Multidisciplinary Research Unit (MRU), Pt. Jawaharlal Nehru Memorial Medical College, Raipur, Chhattisgarh, India, following approval by institutional ethical committee. Patients who attended ENT and dental clinic with oral lesion and clinically diagnosed as leukoplakia and willing to participate in the study were referred to MRU for enrollment. After taking informed consent from the patients, the history was taken, and brush biopsy conducted for cytological assessment. In suspected cases, punch biopsy was carried out in ENT OPD. Patients having history of chronic illness and use of steroid treatment were excluded from the study.

Background control population: As the exposure happened much earlier than the start date of the study, we used the data for the general background population to compare the high-risk lifestyle factor from the published fact sheet of Annual Health Survey Chhattisgarh 2010-2011, conducted on 1220077 population of Chhattisgarh [21].

Statistical analyses: The data were analyzed using following software: https://www.medcalc.org/calc/odds_ratio.php

Association between gender predisposition, tobacco use, oral lesions and clinical characteristics were expressed as odds ratio with 95% confidence intervals.

Results

The present study was conducted over a period from June 2016 to September 2018. Total 60 patients of OL were examined during this period. Out of 60 patients, 56 were from different parts within Chhattisgarh state, whereas 4 patients were from adjacent areas outside the state. For comparing the exposure with the background control population, we used Annual Health Survey 2010-11 fact sheet Chhattisgarh, which was conducted on 1220077 population over the 16 districts of Chhattisgarh [21].

Patient profile

Out of 60 OL patients, majority (31.66%) belonged to the age group of 31 to 40 years. Mean age of the overall OL patients were 43.4±12.6 years. Although the mean age of male OL patients (43.25±12.6) was slightly less than that of female OL patients (44.37±13.29), this difference was not statistically significant (p=0.8) (Table 1). In OL patients, the proportion of males was significantly higher than the females(86.66% vs.13.33%) as compared to this ratio in general population (50.81% males vs. 49.19%females) (p<0.0001). Literacy rate in the OL patients (83.34%) was not statistically different as compared to that in general population (74.75%; p=0.12). Complete educational profile of OL patients is shown in Table 2.

Distribution of high-risk oral habits in OL

Out of 60 patients, frequency of no oral habit, smoking, tobacco chewing, alcohol, pan and areca nut were 13.3, 30%, 80%, 41.66%, 10% and 6.66% respectively (Table 3). Out of 52 males in OL patients, 49 (94.3%) had at least one of the high-risk oral habits, whereas in 8 females, 5 (62.5%) had similar oral habits (Table 4).

Table 1. Age distribution of oral leukoplakia patients

| Age (Y) | % of OL patients (n) | Mean age (Mean±SD) |
|---------|----------------------|--------------------|
| 21-30   | 16.66(10)            | 43.4±12.6          |
| 31-40   | 31.66(9)             | Male               |
| 41-50   | 23.33(14)            | Female             |
| >50     | 28.33(7)             | 43.25±12.6         |

Table 2. Association between gender predisposition, tobacco use, oral lesions and clinical characteristics

| Age (Y) | % of OL patients (n) | Mean age (Mean±SD) |
|---------|----------------------|--------------------|
| 21-30   | 16.66(10)            | 43.4±12.6          |
| 31-40   | 31.66(9)             | Male               |
| 41-50   | 23.33(14)            | Female             |
| >50     | 28.33(7)             | 43.25±12.6         |

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Frequency of oral habits in OL patients were compared with the corresponding habit in general local population of Chhattisgarh from the annual fact sheet data [21]. Among the male OL patients, frequency of smoking was 34.61% compared to 12.29% in general male population, indicating that smoking is associated with a significant 3.77-fold increase in the risk for development of OL (OR=3.77; 95%CI: 2.13-6.68, p<0.0001). Frequency of chewing tobacco among the male OL patients was 82.6% compared to 40.29% in general male population thus suggesting that chewing tobacco is associated with statistically significant 7.07-fold increase in the risk of OL (OR=7.07; 95%CI: 3.45-14.52, p<0.0001). Habit of drinking alcohol among male OL population was 48.07% compared to 31.59% in general male population with statistically significant risk association (OR=2, 95%CI: 1.16-3.45, p=0.0123; Table 4). In our study female OL patients did not smoke or consumed alcohol. However, the frequency of chewing tobacco among the female OL patients was 62.5% compared to 24.4% in general female population indicating a statistically significant risk association (OR=5.16 95%CI: 1.23-21.60, p<0.02; Table 4).

Among the OL group having habit of chewing tobacco, 89.6% were males and 10.4% females, whereas individuals with this habit in general population were 63% males and 37% females. This suggests that among tobacco chewers, risk of developing OL was 5.04-fold higher (OR=5.04, 95% CI: 1.99-12.72, p = 0.0006) in males relative to females (Table 5).

### Duration of oral habit

Mean duration of exposure (in years) to smoking, chewing tobacco and alcohol was 21.27±13.54, 11.05±9.27 and 12.62±8.09, respectively (Table 6).

### Clinical Profile of OL lesion

**Anatomical Site distribution:** The most common site of involvement of OL was buccal mucosa (75%), followed by dorsum of tongue (13.33%) and lips (11.66%) (Table 7). Tongue which is one of the common sites for malignant transformation [22,23], was the predominant site of OL in patients who did not have any high risk oral habit, whereas it was buccal mucosa in the group which had these habits; the association of presence or absence of high risk habits with the specific location was statistically significant (p≤0.0007, Table 8). Interestingly malignant transformation rate of OL in patients having no high-risk oral habit is also reported to be high [38-40].

**Clinical appearance:** Out of 60 OL patients, 44 (73.33%) cases had homogeneous OL patch and only 16 (26.67%) had non-homogeneous OL patch (Figure 1). Among the anatomical sites, the proportion of homogeneous leukoplakia were as follows: buccal mucosa 75.55%, lips 42.85% and tongue 37.5% (Table 9). Homogeneous appearance of
OL lesion was slightly higher in non-addiction group compared to the addiction group, however this difference was not statistically significant (p=0.5; Table 10).

**Association of occurrence of non-homogeneous OL with duration of habits:** As non-homogeneous OL have more potential for malignant transformation, we determined the proportion of non-homogeneous OL with relation to different habit and duration (Table 11). Duration of habits is segregated into less than and more than 10 years. Occurrence of non-homogeneous OL was significantly higher in patients exposed to risky behavior (of chewing raw tobacco and alcohol consumption) for >10 years than those exposed for <10 years p 0.02 and 0.04 respectively. However, corresponding mean age differences were not statistically significant excluding the possibility of contribution of age difference in the two groups. Surprisingly, in patients having habits of Gutkha (a processed form of tobacco) chewing and smoking tobacco, no statistical associations were observed with duration of habit and occurrence of non-homogeneous OL (Table 11).

**Patient follow-up and compliance:** During the study period, only 36 patients were qualified for one-year follow-up. We categorized the patients in 3 groups based on compliance to follow up: (1) Patients visited physically for follow up; (2) Patients responded to the questions over the phone but were not willing to visit for follow up; (3) No response or contact could be made. We observed that out of 36 OL patients, 11 patients complied through follow-up visits, 13 complied through phone conversations and 12 did not comply (Table 12).

Illiteracy rates in OL patients complying through follow-up visits, complying through phone and non-complying were 0%, 15.3% and 33.3%, respectively. In OL patients, educated up to 10th standard, the compliance rates for physical follow-up, over the phone and non-complying were 54.5%, 38.5% and 41.6%, respectively, whereas for higher education (>10th class) group these rates were 45.5%, 46.1% and 25%, respectively. Out of 24 follow-up patients, 70.83% (17/24) reported improvement in OL patch while 29.16% (7/24) reported no improvement (Table 13). Interestingly, when we analyzed response rate in habit and no habit group, at 1 year follow up, 60% (3/5) of no habit patients reported no improvement in contrast to 21% (4/19) in oral habit group (Table 13) (Figure 2). However, the difference was not statistically significant (p=0.09).

**Table 6. Duration of exposure of high-risk oral habits in OL patients**

| Habit                  | Duration of Exposure (n=54) | Mean±SD (Range) | Median(Y) |
|------------------------|----------------------------|-----------------|-----------|
|                        | 1-5(Y)         | 6-10(Y)        | 11-20(Y) | >20(Y) |
|                        | % (n)          |                 |          |      |
| Smoker                 | 2 (1)          | 7 (4)          | 11(6)    | 13(7) |
| Burning Tobacco        | 31(17)         | 22(12)         | 28(15)   | 7(4)  |
| Alcohol                | 9 (5)          | 17 (9)         | 15 (8)   | 6 (3) | 12.62±8.09(2-38) | 10 |

**Table 7. Anatomical site distribution of oral lesions (B=Buccal Mucosa which includes buccal mucosa only, buccal and gingiva, and buccal and lip; L=lip; T=Tongue)**

| Anatomical site | With habit % (n) | Without habit % (n) | p-value |
|-----------------|------------------|---------------------|---------|
| B               | 75 (45)          |                     |         |
| L               | 11.66(07)        |                     |         |
| T               | 13.33(8)         |                     |         |
| Total           | 100(60)          |                     |         |

**Table 8. Anatomical site distribution according to oral habit (B=Buccal Mucosa which includes buccal mucosa only, buccal and gingiva, and buccal and lip; L=lip; T=Tongue)**

**Table 9. Appearance of oral leukoplakia lesion in patients with and without high risk habits**

| Appearance of patch Total % (n) | B % (45) | L % (7) | T % (8) |
|---------------------------------|----------|---------|---------|
| Homogeneous                     | 73.33(44)| 57.14(4)| 62.5(5) |
| Non-Homogeneous                 | 26.67(16)| 42.85(3)| 37.5(3) |
| Total                           | 100(60)  | 100(45) | 100(8)  |

**Table 10. Proportion of homogeneous and non-homogeneous patches in OL patients at different anatomical sites. (B=Buccal Mucosa which includes buccal mucosa only, buccal and gingiva, and buccal and lip; L=lip; T=Tongue)**

| Appearance of lesion Total % (n) | With habit % (n) | Without habit % (n) | p-value |
|----------------------------------|------------------|---------------------|---------|
| Homogeneous                      | 72(40)           | 83(65)              |         |
| Non-Homogeneous                  | 28(15)           | 17(10)              |         |
| Total                            | 100(54)          | 100(60)             |         |

**Table 11. Distribution of non-homogeneous OL and age among different oral habit groups according to duration of the habit (* statistically significant)**

| Oral habit | Duration <10 Year | Duration >10 Year | P value |
|------------|-------------------|------------------|---------|
| Raw Tobacco Chewing | NH (%) | 18% | 47% | 0.02*|
| Age Mean±SD | 44±14 | 46±9 | 0.57 |
| Gutkha Chewing | NH (%) | 24% | 36% | 0.39 |
| Age Mean±SD | 45±13.6 | 42±8 | 0.44 |
| Smoking tobacco | NH (%) | 25% | 33% | 0.56 |
| Age Mean±SD | 41±11.7 | 52±46±11 | 0.003 |
| Alcohol Drinking | NH (%) | 20% | 47% | 0.04* |
| Age Mean±SD | 44±14 | 45±8 | 0.69 |
| No habit | NH (%) | 22% |         |         |
| Age Mean±SD | 37±13 |         |         |

**Figure 1. Homogeneous (a) and non-homogeneous oral leukoplakia**

OL lesion was slightly higher in non-addiction group compared to the addiction group, however this difference was not statistically significant (p=0.5; Table 10).
Table 13. Clinical outcome at one-year follow-up

| Clinical outcome | Total (%) | Without habit (%) | With habit (%) | P value |
|------------------|-----------|------------------|---------------|---------|
| Improvement      | 70.8(17)  | 40 (2)           | 79(15)        | 0.09    |
| No improvement   | 29.2(7)   | 60(3)            | 21(4)         |         |
| Total            | 100(24)   | 100(5)           | 100(19)       |         |

Figure 2. One year follow up change in oral leukoplakia with (Panel-1) or without (panel 2) improvement. Panel-1 : OL with oral high-risk habit; (a)1st visit; (b)2nd visit showing improvement; Panel-2 : OL without oral high-risk habit; (a)1st visit; (b)2nd visit showing no improvement

Discussion

We conducted the hospital-based pilot study on OL patients in a local population in India. As it is the oldest and apex medical college, it has a wide catchment area of patients over the state of Chhattisgarh. We evaluated various clinical, etiological as well as socio-demographical parameters among OL patients and compared those with the background general population of Chhattisgarh to understand how those factors may influence the pathogenesis of OL and disease outcome.

In the current study, among 60 newly diagnosed OL patients, majority of patients had the age group of 31–40yrs. Although, this result is in contrast to a report from UP by Sharma et al. in which they found greater proportion of cases in the older age group of > 41yrs [24], it is similar to other reports from UP and Kerala [25,26]. In our study, the difference of mean age of presentation of OL in male and female patients were not statistically significant. However earlier study showed that females had more age of incidence [27].

In our study, the occurrence of OL was observed higher in male than female (6:5:1). The similar observation was also reported earlier from other parts of the country like Karnataka, Uttar Pradesh where male female ratio was 7:2:1 and 8:1:1, respectively [24,27]. In contrast reports from western countries like Croatia and Netherland showed a small female preponderance [28,29]. This difference may be due to differential oral habits, lifestyle and/or socio-cultural differences between different geographical areas. Additionally, there might be gender-specific susceptibility and/or protection which may operate along with the lifestyle factors.

In the present study most common high-risk oral habits in OL patients were, chewing tobacco, alcohol, smoking, pan and areca nut. Out of all high-risk habits in OL, tobacco chewing was the most common addiction (80%) in our study. However, in other parts of India, smoking was found to be predominant habit followed by tobacco chewing [24,27]. In our study, we observed that only 6.6% of the patients have the habit of areca nut chewing. This is also similar to the earlier report from Bangalore by Sujata et al. [27]. However, it varied from region to region in India. The earlier study showed high percentage of areca nut among the OL patients in UP (69.6%) [23] and Maharashtra [30].

As previously reported [31-33], we also observed that high risk habits were more common in male (94.3%) as compared to female (62.5%) OL patients. Habit of smoking, chewing tobacco and alcohol significantly increased the risk of male OL patients but within the female OL group, only chewing tobacco showed the significant risk association (Table 4). However, in a meta-analysis, Rodriguez-Archilla et al. observed that overall tobacco consumption increased much lower risk (OR=3.49, p<0.001) of OL and could not find any association with alcohol consumption [34]. Interestingly, among the OL group having the habit of chewing tobacco the male factor over female was 5-fold higher (P = 0.0006). This observation is also much higher than previously calculated (P<0.001) “male factor” as a risk for OL [24]. However, in our analysis we only considered impact of male factor within the tobacco-chewing group. This suggests that even though there is increased percentage of chewing tobacco habit in female population in this region, the incidence of OL in female population is low. This supports the hypothesis that there might be gender-specific protection in female population and/or males might be more susceptible to high risk habits, at least in this region. There is a report suggesting that estrogen may have protective role in occurrence of OL and oral cancer in young females [18,35]. However, we did not observe any statistically significant difference in mean age of occurrence of OL in female versus male patients.

Interestingly, in the group with no risky habit, the male to female ratio was similar to that in general population. This strengthens the hypothesis that differential chewing habit and gender-specific susceptibility to the high-risk habit may interplay in out-numbering male over female patients.

As the mean age of OL patients was 43.4±12y and average addiction period of tobacco-chewing was 11.05±9.27 years in OL patients, the awareness program should start as early as 20 year of age. This age group is the most vulnerable for catching new addiction habit in India. Moreover, this may provide enough opportunity to spread awareness and required information within general population.
Literacy rate among the OL patients was only slightly higher as compared to general population. Only 31.7% of OL patients had education level more than 10\textsuperscript{th} class. Faize et al. [25] noticed that overall 57.1% OPMD patients were illiterate/educated up to primary level. Similarly, Sujatha et al. [27] observed overall 45.8% educated till high school level and only 18% had higher educated (degree or diploma holder).

In our study, buccal mucosa was the most frequent (75\%) site of the leukoplakia patch followed by 13.11\% in dorsum of tongue and only 11.66\% patch found in lip area. In majority of the previous findings worldwide, including India, the most common site for leukoplakia patch was buccal mucosa [3,25,36,37]. Interestingly, when we segregate the OL patients in groups with or without high risk habits, we found that in no habit group, predominant site of OL was tongue, which is also the common site for malignant transformation [22,23]. Similar finding was also observed by Schepman et al. [38]. This clearly signifies the different etiology and pathogenesis in causation of OL in these two groups. Interestingly at 1 year follow up also 60\% of no habit group shows no improvement of the lesion compared to only 21\% of those with high risk habit group. The high rate of improvement in high risk habit group may be combined effect of abstinence of high-risk oral habit along with surgical or non-surgical treatment. The increase rate of OL at high risk site and less proportion of improvement in patients having no oral habit, support the earlier views in the line of increase rate of malignant transformation in no habit OL group [39-41]. Though it needs to be confirmed in larger sample size, we can say that patients with no high-risk habit need more frequent and careful surveillance. It would be reasonable to look at other etiological factors like HPV for OL patients having no history of high-risk oral habits.

Though malignant transformation rate in non-homogeneous OL of tongue is more common [22,23,41], we observed that non-homogeneous OL in lip was more frequent than the non-homogeneous leukoplakia of tongue (Table 9). One of the informative observations from our study was characterization of high-risk oral habit in occurrence of non-homogeneous OL. In our study patients having habit of raw tobacco chewing (Khaini: a form of chewing tobacco used in India, containing slaked lime) and alcohol consumption more than 10 years shows more occurrence of non-homogeneous OL than patients with habit for less than 10 years. As most of the malignancy or pre malignant conditions occur frequently in higher age group, so effect of long duration of oral habit may be affected by higher age. However, difference of mean age between the shorter and longer duration of the habits were not statistically significant. Though Gutkha chewing and smoking are the well-known risk factors for OL and submucous fibrosis in reports from other part of India [42-45], in our study, we did not find any statistically significant increase in the occurrence of non-homogeneous OL in groups having more than 10 years of habits. This may be due to low consumption or lack of multiple interacting habits. However, this finding should be verified in larger sample size.

As management of OL needs patient compliance to long-term follow-up, we evaluated effect of literacy rate on patient compliance. We observed 0\% illiteracy rate in patients who show compliance for physical follow-up, whereas 75\% of non complying patients are either illiterate or have <10\textsuperscript{th} class education. This suggests more attention is required to patients having low educational level (illiterate or <10\textsuperscript{th} class education) during the first visit; multiple steps should be taken to ensure that they adhere to health surveillance system. Higher literacy rate will give the better compliance for physical follow-up. By increasing coverage of literacy and higher education among general population will benefit the people to come into the health surveillance process.

**Conclusion**

OL in state of Chhattisgarh is predominantly associated with habit of chewing tobacco in both males and females, however, within high risk oral habit group the incidence is much higher in males relative to females. Awareness program against habit of tobacco-chewing with special focus on males at 20-year age group will help to reduce occurrence of OL and oral cancer in this region of India. OL patients with no history of oral habit should be followed up more frequently. Increased literacy rate may help in improving patient compliance to follow up health program. For future study, it will be interesting from preventive/therapeutic point to identify any factor/s responsible for gender-related susceptibility or protection to high risk oral habits in the population. For that type of study, population from this region would be a model population. Larger longitudinal study is required to evaluate malignant transformation rate in different forms of OL and to identify preventable etiological factor/s in causation of OL.

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