

Prevalence of Oral Precancerous Lesions in Tobacco and Areca Nut Habituated Patients in Barpeta District, Assam, India: A Cross-sectional Study

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ABSTRACT

Introduction: Oral cancer has become one of the leading causes of death and disease globally as well as in India. Tobacco consumption is responsible for nearly half of all cancers in men and nearly one-fourth of cancers in women in India and more than two-third of oral cancers are directly attributable to tobacco use. Early detection of precancerous lesions and tobacco cessation activities, if conducted together can have high impact on reducing incidence of oral cancer.

Aim: To study prevalence of oral precancerous lesions in tobacco and areca nut habituated patients in Barpeta district, Assam, India.

Materials and Methods: The present observational, cross-sectional, hospital-based study was conducted on Outpatient Department (OPD) patients of Dentistry Department of Fakhruddin Ali Ahmed Government Medical College, College, Barpeta, Assam, India, from June 2021 to June 2022. Patients with tobacco and areca nut chewing habits were selected as study participants. Total number of study participants were 404. Oral cavity screening was done to detect oral precancerous

lesion. History of tobacco and areca nut chewing habits were recorded in terms of gender, age, form of tobacco, duration and frequency. Chi-square test was used for statistical analysis.

Results: Prevalence of oral precancerous lesions in tobacco consuming patients was 3.46% in smoke form and 9.9% in smokeless form. Premalignant lesions had been seen predominantly in male. Among the premalignant lesions prevalence of oral leukoplakia was highest (22.27%) followed by erythroplakia (4.46%). Overall, prevalence of precancerous lesions in tobacco and areca nut habituated patient in the present study was 37.62%. The association between prevalence of oral precancerous lesion with frequency and duration of habits was statistically insignificant ($\chi^2=7.167$, p-value=1.000).

Conclusion: In the present study, prevalence of oral precancerous lesion in tobacco and areca nut consuming patients in Barpeta district was quite high. The findings from this present study can be used to design cohort study to further understand the relation between precancerous lesions in tobacco and areca nut habituated patients.

Keywords: Oral cancer, Oral leukoplakia, Smokeless tobacco

INTRODUCTION

Oral cancer is a significant global health issue and according to global health statistics 2020, total number of new cases were 377,713 and, 177,757 deaths occurred due to oral cancer [1]. More than two-third of the oral cancer cases are reported from Asia [2]. India alone accounts for one-third of the world's oral cancer and according to latest Indian Council of Medical Research (ICMR) cancer statistics and Globocan 2020 data, 135,929 people registered with new cancer and mortality due to tobacco use in India is estimated at 75,290 person in 2020 [3].

The concept of certain precancerous lesions proceeding into oral cancer has long been accepted. According to a workshop coordinated by World Health Organisation (WHO) in May 2005 at London the use of the term potentially malignant disorders was recommended. The usage of this terminology conveys that not all lesions and conditions described under this term may transform to cancer, instead there is a family of morphological alterations amongst which some may have an increased potential for malignant transformation [4]. There are many factors causing precancerous lesions among which tobacco, snuff, gutkha, betel nut in quid form (pan), alcohol, spicy food, malnutrition, poor oral hygiene, malocclusion, sharply broken tooth, ill-fitting dentures etc., are common predisposing factors. Also, we know that the most common oral precancerous lesions are oral leukoplakia, erythroplakia, nicotina palati and oral sub mucous fibrosis. Other oral

precancerous lesions include candidiasis, recurrent herpes labialis, hairy tongue, lichen planus etc. Tobacco has become a global epidemic and the abuse of tobacco is a worldwide health problem. The Indian situation as far as tobacco consumption is concerned is far worse because of the prevalence of the tobacco chewing habit, which covers a spectrum of socio-economic and ethnic groups and is spread over urbanised areas as well as remote villages. In case of north eastern states tobacco use remains a challenge as the prevalence rate is still quite high [5]. In India, tobacco consumption is one of the common causes of oral cancers. It has been reported that 28.6% of Indian population use tobacco and 800,000 people die every year in India due to tobacco related diseases [6]. The WHO predicted that tobacco deaths in India may exceed 1.5 million annually by 2020 [7]. Tobacco use in India differs from the globe.

The documented form of tobacco used globally is the cigarette, however in India, only 20% of tobacco is consumed as cigarette, 40% is consumed as bidi and rest in the form of smokeless tobacco such as khaini, zarda which are mixtures of powdered tobacco and slaked lime and mishri, a powdered form of tobacco which is rubbed on the gums [8]. Tobacco in smoke and smokeless forms used in chewing/snuff contain hydrocarbons and several potent nitrosamines which are DNA toxic carcinogens and play a key role in initiation and promotion of oral cancers [9]. On the other hand, areca nut is a major concern in India and many South East Asian countries. Chewing of betel nut, which comes from the *Areca*

catechu palm tree that contains alkaloids (particularly arecoline) and tannins is practiced by 10-20% of the world's population [10]. Betel nut chewing is considered the fourth most commonly used addictive substance in the world after tobacco, alcohol and caffeine [11].

Since the number of studies on prevalence of precancerous lesion in lower region of Assam is inadequate, such type of regional databases will be helpful in understanding the severity of the problem at state level as well as at national level [12]. Oral screening for precancerous lesions and tobacco cessation activities, if conducted together can have high impact on reducing incidence of oral cancer. The aim of the present study was to find out the prevalence of oral precancerous lesions in tobacco and areca nut habituated patients in Barpeta district in Assam, India.

MATERIALS AND METHODS

The present observational, cross-sectional, hospital-based study was conducted in the Department of Dentistry, Fakhruddin Ali Ahmed (FAA) Government Medical College and Hospital, Barpeta district, Assam, India, from June 2021 to June 2022. An ethical clearance (FAAMC&H/IEC/498/2019/4656) was obtained from Institutional Ethical Committee (dated 26-07-2019) and written informed consent was obtained from each participants. A total of 404 subjects were selected for the study. The study subjects were selected from the Outpatient Department (OPD) of Dentistry.

Inclusion criteria: Tobacco and areca nut in smoke and smoke free form habit history patients, consuming for at least six months with frequency of consuming tobacco and areca nut atleast once a day were included in the study.

Exclusion criteria: Participants with the previous history of hospitalisation for any systemic illness, immunocompromised patients, patients with recurrence of the primary lesion, patients suffering from dental pain, patient having orofacial injury and patients having ill-fitting dentures were excluded from the study.

Study Procedure

Simple random sampling technique was used in this study. The total number of 404 participants were selected as per availability of tobacco and areca nut habituated patients attending Dental OPD of FAA Medical College between June 2021 and June 2022. Standardised interviewer administered questionnaire based on Global Adult Tobacco Survey-2 was used to collect data on tobacco and areca nut habituation which is depicted in [Table/Fig-1] [13]. Total number of questions in questionnaire were seven.

All 404 subjects were divided into four groups:

Group 1: Smoke form tobacco habit subjects

Group 2: Smokeless form tobacco habit subjects

Group 3: Areca nut consuming subjects

Group 4: Mixed subjects with more than one if the above habits.

All study subjects were informed about the study and a detailed case history proforma was duly filled. Data was collected using a combination of clinical oral examination and standardised interviewer based questionnaire. Patients were asked to rinse mouth thoroughly with water and then examination was done under an incandescent light. All oral examinations were done by specialist examiners who are familiar with oral mucosal lesions. A sterile mouth mirror was used for retraction of tissues and examination was done using a gloves. In clinical examination the features of the lesion, anatomical location, extension, aetiological factors if any, related factors etc., were recorded. The clinical diagnosis was done as per WHO (1997 and 2017) criteria [14,15]. In case of suspected cancer lesion biopsy was done to confirm histopathologically [16].

STATISTICAL ANALYSIS

Statistical analysis was performed using Statistical Package for Social Science (SPSS) software version 22.0. The association

Questionnaire	
1. What is the person's age/How old are you?	
2. Is this person male or female?	
Male	
Female	
3. Does this person currently have tobacco/areca nut smoking/chewing habit?	
Yes	
No	
4. What type of habits do you have?	
Smoking	
Using tobacco in smokeless form	
Areca nut habits	
Mixed habits	
5. On an average how many times do you have habits per day?	
1-5 times	
6-10 times	
11-15 times	
>15 times	
6. How long has it been since you have use tobacco/areca nut?	
6 months-5 years	
6-10 years	
11-15 years	
>15 years	
7. Presence of oral precancerous lesion	
Leukoplakia	
Oral squamous cell carcinoma	
Erythroplakia	
Oral lichen planus	
Smoker's palate	
Oral carcinoma	
No lesion	

[Table/Fig-1]: Standardised interviewer based questionnaire.

of oral precancerous lesions in relation to age, gender, use of various tobacco habits, frequency and duration of various tobacco habits was studied by Chi-square test. For graph Microsoft Excel software version 2019 was used. A p-value <0.05 was considered statistically significant.

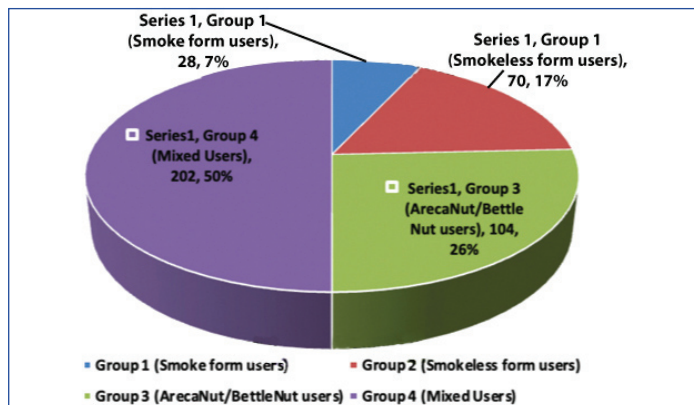
RESULTS

The age group of total 404 subjects was in the range of 20-90 years, of which 261 (64.6%) were males and 143 (35.4%) were females. Regarding distribution of study population by age, majority of male population was seen in the age group of 41-50 years. On the other hand, majority of female population was also seen in age group 41-50 years. There was significant association of habit with age group of study population (p-value <0.000) [Table/Fig-2].

Age group (years)	Males (n)	Females (n)
20-30	56	20
31-40	42	38
41-50	60	54
51-60	56	21
61-70	37	10
71-80	8	0
81-90	2	0
Total	261	143

[Table/Fig-2]: Distribution of study population according to age and gender. $\chi^2=33.898$; p-value <0.000 (Chi-square test)

Out of total 404 tobacco consuming population, 28 (6.93%) were using tobacco in smoke form, 70 (17.32%) were using smokeless forms of tobacco, 104 (25.74%) were areca nut consuming patients and 202 (50%) were mixed users which is shown in [Table/Fig-3].



[Table/Fig-3]: Distribution of study participants in relation to various tobacco habits.

In the present study, the total numbers of leukoplakia subjects were 90, so the prevalence rate of leukoplakia was 22.27%. The incidence of leukoplakia was highest in group 4 followed by group 2. The prevalence rate of erythroplakia was 4.46%. The incidence was highest in mixed user (group 4). In case of Oral Submucous Fibrosis (OSMF), prevalence was 3.47% and the incidence being highest in group 4. In case of OSMF along with leukoplakia, the prevalence rate was 0.49%. Out of 404 subjects, 230 (56.93%) tobacco and areca nut users showed no lesions [Table/Fig-4].

Precancerous lesion	Group 1 (n)	Group 2 (n)	Group 3 (n)	Group 4 (n)	Total n (%)
Leukoplakia	2	36	6	46	90 (22.27)
Oral submucous fibrosis	0	0	2	12	14 (3.47)
Erythroplakia	2	2	2	12	18 (4.46)
Oral lichen planus	0	0	0	0	0
Oral submucous fibrosis+ Leukoplakia	0	0	0	2	2 (0.49)
Leukoplakia+Erythroplakia	0	2	2	4	8 (1.98)
Smoker's palate	10	0	0	8	18 (4.46)
Smoker's palate+Leukoplakia	0	0	0	2	2 (0.49)
Total	14	40	12	86	152 (37.62)
No lesion	8	26	90	106	230 (56.93)
Presence of carcinoma	6	4	2	10	22 (5.45)

[Table/Fig-4]: Distribution of precancerous lesions in all the four groups (N=404). $\chi^2=160.073$; p-value <0.0001 (Chi-square test)

Group 1 showing frequency of 14 and prevalence of precancerous lesion as 3.46%. Group 2 showing frequency of 40 and prevalence of precancerous lesion as 9.90%. Group 3 showing frequency of 12 and prevalence of precancerous lesion as 2.97%. Group 4

Types of lesion	20-30 years	31-40 years	41-50 years	51-60 years	61-70 years	71-80 years	81-90 years	Total (n)
Leukoplakia {n (%)}	14 (20)	17 (21.25)	27 (23.69)	16 (20.78)	10 (30.30)	4 (66.67%)	2 (100%)	90
Oral submucous fibrosis {n (%)}	2 (2.86)	3 (3.75)	3 (2.63)	6 (7.79)	0	0	0	14
Smoker's palate {n (%)}	2 (2.86)	0	4 (3.51)	8 (10.39)	4 (12.12)	0	0	18
Erythroplakia {n (%)}	2 (2.86)	2 (2.5)	4 (3.51)	10 (12.99)	0	0	0	18
Oral lichen planus {n (%)}	0	0	0	0	0	0	0	0
Oral submucous fibrosis+Leukoplakia {n (%)}	0	0	2 (1.76)	0	0	0	0	2
Smoker's palate+Leukoplakia {n (%)}	0	0	0	1 (1.3)	1 (3.03)	0	0	2
Leukoplakia+Erythroplakia {n (%)}	0	0	2 (1.76)	4 (5.19)	2 (6.06)	0	0	8
No lesion {n (%)}	50 (71.43)	58 (72.5)	72 (63.16)	32 (41.56)	16 (48.49)	2 (33.33)	0	230
Total (n)	70	80	114	77	33	6	2	382

[Table/Fig-5]: Prevalence of oral precancerous lesions in relation to age. $\chi^2=76.731$; p-value=0.001 (Chi-square test)

showing frequency of 86 and prevalence of precancerous lesion as 21.28%.

In relation to age, leukoplakia was predominating in the age group of 41-50 years and in case of OSMF maximum number of cases were found in the age group of 51-60 years. Therefore, strong association was present between age group and different types of lesion (p-value=0.001) [Table/Fig-5]. In relation to gender, leukoplakia was predominantly seen in male patients while OSMF and erythroplakia was predominantly found in female patients. Over all the precancerous lesions were predominantly found in male patients (47.50%). Correlation of gender with prevalence of oral precancerous lesions is depicted in [Table/Fig-6].

Regarding relation of precancerous lesion with duration of habits, in the present study it was found that majority of precancerous lesions were found in subjects with habit history for >15 years group followed by 11-15 years age group. Most of the cases of leukoplakia (n=30) were found in >15 years age group [Table/Fig-7].

Regarding relation of precancerous lesion with frequency of habits, in this study, it was found that majority of the patients had a habit frequency of >15 times per day (n=66) followed by 10-15 times per day (n=39) which is depicted in [Table/Fig-8].

DISCUSSION

As per Global Adult Tobacco Survey (2017), more than one-fourth (28.6%) of adults in India are tobacco users [17]. As per WHO report, the most significant risk factor of cancer is tobacco use, which alone is responsible for death of >9.5% mortality rate in India [18]. According to National Oral Cancer Registry India, oral cancer is the most common cancer in India amongst men (11.28% of all cancers) and fifth most frequently occurring cancer amongst women (4.3% of all cancers) and about 80% of oral cancers are directly attributed to tobacco use [19,20]. On the other hand, areca nut is used by an estimated 600 million people globally, is of major concern in India and many South East Asia countries and is the fourth most commonly used addictive substance after tobacco, alcohol and caffeine [21]. In Assam, areca nut (Tamul) plays an important, ceremonial and cultural role. It is common practice to offer these products to guest at important social gatherings, weddings and other religious events. Due to this cultural tradition, the use of the areca nut is widespread and considered as a part of daily life [22].

In the present study it was found that out of 404 patients, 114 male patients have precancerous lesions and 38 female patients have precancerous lesions, therefore the prevalence in males (47.50%) was higher than prevalence in females (26.76%). The present study was similar to the study done by Srivastava R et al., in population of Kanpur city in which premalignant lesions and malignant lesions were predominantly seen in males (76.3%) [23]. Saraswati TR et al., Sujatha D et al., and Behura SS et al., also similarly reported the male

Types of lesion	Male	Female
Leukoplakia (n)	82	8
Oral submucous fibrosis (n)	4	10
Erythroplakia (n)	8	10
Oral lichen planus (n)	0	0
Smoker's palate (n)	14	4
Oral submucous fibrosis+Leukoplakia (n)	0	2
Leukoplakia+Erythroplakia (n)	4	4
Smoker's palate +Leukoplakia (n)	2	0
Total lesion {n (%)}	114 (47.5)	38 (26.76)
No lesion {n (%)}	126 (52.5)	104 (73.24)
Total (n)	240	142

[Table/Fig-6]: Prevalence of oral precancerous lesions in relation to gender.
 $\chi^2=53.690$; p-value <0.0001 (Chi-square test)

Precancerous lesion	6 months-5 years	6-10 years	11-15 years	>15 years
Leukoplakia {n (%)}	14 (73.68)	20	26 (56.52%)	30 (52.63%)
Oral submucous fibrosis {n (%)}	1 (5.26)	2 (6.67%)	4 (8.7%)	7 (12.28%)
Erythroplakia {n (%)}	2 (10.53)	3 (10%)	5 (10.87%)	8 (14.04%)
Oral lichen planus {n (%)}	0	0 (0%)	0 (0%)	0 (0%)
Smokers palate {n (%)}	2 (10.53)	3 (10%)	6 (13.04%)	7 (12.28%)
Leukoplakia+Oral submucous fibrosis {n (%)}	0	0 (0%)	1 (2.17%)	1 (1.75%)
Leukoplakia+Erythroplakia {n (%)}	0	2 (6.67%)	3 (6.62%)	3 (5.26%)
Smoker's palate+Leukoplakia {n (%)}	0	0	1(2.17%)	1 (1.75%)
Total (n)	19	30	46	57
No lesion (n)	34	46	65	85
Presence of carcinoma	2	5	6	9

[Table/Fig-7]: Depicting relation of oral precancerous lesion with duration of habits.
 $\chi^2=7.167$; p-value=1.000 (Chi-square test)

Precancerous lesion	1-5 times	6-10 times	11-15 times	>15 times
Leukoplakia	9 (64.29)	23	22 (56.41)	36 (54.55)
Oral submucous fibrosis	2 (14.29)	2 (6.06)	4 (10.26)	6 (9.09)
Erythroplakia	2 (14.29)	3 (9.09)	5 (12.82)	8 (12.12)
Oral lichen planus	0	0	0	0
Smoker's palate	1 (7.14)	4 (12.12)	3 (5.13)	10 (15.15)
Oral submucous fibrosis+Leukoplakia	0	0	1 (2.56)	1 (1.52)
Leukoplakia+Erythroplakia	0	1 (3.03)	3 (5.13)	4 (6.06)
Leukoplakia+Smoker's palate	0	0	1 (2.56)	1 (1.52)
Total	14	33	39	66
No lesion	24	37	66	103
Presence of carcinoma	9	3	2	8

[Table/Fig-8]: Depicting the relation of oral precancerous lesion with frequency of habit per day.
 $\chi^2=29.721$; p-value=0.194 (Chi-square test)

predominance in deleterious oral habits [24-26]. The prevalence of precancerous lesion in present study was 37.62%, which was less than the study done by Narasannavar A and Wantamutte AS et al., which reported prevalence of 51.12% and study done by Jacob LB et al., in which prevalence of oral mucosal lesion was found as 60.1% [27,28].

In the indexed study, the most frequently occurring precancerous lesion associated with tobacco and areca nut consuming patients was oral leukoplakia (22.27%) followed by smoker's palate (4.46%)

and erythroplakia (4.46%). In the present study it was found that the prevalence of leukoplakia was 22.3% which was higher than the study conducted by study conducted by Jacob LB et al., which reported prevalence of leukoplakia as 15.9% [28]. Also, the prevalence of leukoplakia of the present study was higher than the study conducted by Krishna Priya M et al., and Balsaraf S et al., in Bhopal India in which prevalence of oral leukoplakia was 5.3% and 9.75%, respectively [29,30]. Also, the present study was similar to the study done by Srivastava R et al., in population of Kanpur city in which the prevalence of leukoplakia was 23.7% [23].

The present study showed prevalence of oral carcinoma in tobacco and areca nut habit history patients as 5.4%. The prevalence of oral cancer in present study was also similar to the study done by Shrivastava R which reported 5.62% of oral cancer in study group, but somewhat different to Mishra G et al., study which reported prevalence of oral cancer in tobacco habituated patients up to 20.3% which was quite high [23,31].

In this study, it was found that the prevalence of oral precancerous lesion was highest (21.28%) in mixed group (Group 4). These findings were different from the study done by Uplap PA et al., and Thomas G et al., in which the prevalence of oral precancerous lesion was highest (65%) in smokeless form group [32,33].

In this study, no association was found between duration of tobacco use and the occurrence of oral precancerous lesion ($\chi^2=7.167$, p-value=1.000). Although majority of the precancerous lesions were seen in >15 years age group, but p-value is equal to 1. Therefore, this proves that statistically there was no significant association between duration of tobacco use and the occurrence of oral precancerous lesions. The present study findings was different to the study done by Sujatha D et al., Ambedkar DM et al., and Mahawar P et al., where it was reported as the duration of tobacco habits increased there were more chances of development of precancerous lesions [25,34,35].

The present study results showed that most of the precancerous lesions were seen in >15 times group but statistically the association between the frequency of habits and chances of developing precancerous lesion was insignificant ($\chi^2=29.721$, p-value=0.194). This findings of the study was different to the findings observed by Sujatha D et al., Ambedkar DM et al., Mahawar P et al., and Maher R et al., which reported that the risks increases with frequency of habits and patients with habits of 5-10 times had maximum number of precancerous lesions [25,34-36]. However, the present study results were similar to study done by Hallikeri K et al., which reported that association between the frequency and chances of developing precancerous lesion was statistically insignificant where p-value is 0.3310 [37].

This study also revealed that areca nut plays a significant role in developing precancerous lesions which was similar to study done by Shrikishna BH and Jyoti AC which reported significant association between consumption of areca nut and oral submucous fibrosis with prevalence rate of 18.71% [38]. In this present study, it was found that the prevalence of precancerous lesions in group 3 was 2.97% which was less then the study done on areca nut by Mishra SS et al., which reported prevalence of 22.7% [39]. Findings of similar studies have been compared in [Table/Fig-9] [23,25,28,34,40].

Author and year of the study	Place of the study	N	Parameter assessed	Conclusion
Srivastava R et al., 2020 [23]	Kanpur	12795	Prevalence of potentially malignant lesions, oral cancer and associated risk factors.	Tobacco smoking and chewing of betel quid are the major risk factors for premalignant lesion and oral cancer. Prevalence of precancerous lesions was 27.57%

Sujatha D et al., 2012 [25]	Bengaluru	1028	Prevalence and correlation of oral lesions with tobacco, areca nut and alcohol.	Prevalence of oral soft tissue lesions was 59.24%.
Jacob LB et al., 2022 [28]	Vellore	930	Prevalence of oral lesions and nicotine dependency among tobacco users.	Oral lesion and nicotine dependency are highly prevalent among tobacco users (60.10%).
Ambedkar DM et al., 2014 [34]	Mumbai	106	Prevalence of oral premalignant lesions and its correlation with the use of tobacco in tobacco habituated patients.	Tobacco acts as a major risk factors in the development of single or multiple oral precancerous lesions. Prevalence of oral precancerous lesions was 47.16%.
Alshayeb M et al., 2019 [40]	United Arab Emirates	54	Prevalence and distribution of oral mucosal lesions associated with tobacco use	High prevalence of premalignant lesions (40.6%) among tobacco users.
Present study, 2022	Assam	404	Prevalence of oral precancerous lesion in tobacco and areca nut habituated patients.	The prevalence of oral precancerous lesion and oral cancer in tobacco and areca nut consuming is quite high (37.62%).

[Table/Fig-9]: Study findings and the parameters analysed by different authors [23,25,28,34,40].

Limitation(s)

The present study was an observational, cross-sectional, hospital-based study done on a small population group therefore a more detailed cohort study on a large population is required to get a more detailed and accurate picture. Moreover, in this study detailed information was not gathered on other predictors of oral precancerous lesion such as nutritional status, body mass index, lifestyle etc.

CONCLUSION(S)

In the present study, the prevalence of precancerous lesion was 37.62%. Tobacco both in smoke and smokeless form and also areca nut are strong risk factor for developing oral precancerous lesions. Also, in this study premalignant lesions had been seen predominantly in men. The findings of the study emphasise on the need of reviewing the policy governing the contexts, sales and uses of these mixtures and to educate the people about the hazards and adverse effect of these habits. The public should be made aware of the high risk of oral malignancy in oral lesions induced by tobacco, areca nut and different habits. To decrease the burden of this eminently preventable cancer, a multifaceted approach that integrates health education, tobacco and alcohol control, early detection, and early therapy is required. The findings from this present study can be used to design cohort study to further understand the relation between precancerous lesions in tobacco and areca nut habituated patient.

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