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Review Article

Correlation between Oral Premalignant Lesions and Tobacco Use

Raneem MohammedSalahEldin AbdElgadir[1], Abrar Ahmed Alyayeb[1], Afra Siddig Mohammed[1], Alaa Abdallah Abakr[1], Hiba Salah FadlAlseed[1], Ahmed Hashim MohannedSalih Alfaki[1]*.

[1] Napata College, Dentistry, Khartoum, Sudan

***Corresponding author:** Dr. Ahmed Hashim, Assistant professor, dentistry, Napata College, Khartoum, Sudan. Email: ahmedsalihcancerregistry@gmail.com

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Abstract

Background: Tobacco use is a major public health problem globally. According to the WHO, tobacco is the second most significant cause of death in the world. Tobacco is used in different forms: smoke and smokeless. The use of tobacco and smokeless tobacco has increased and has associated with oral leukoplakia and other precancerous oral lesions. The presence of leukoplakia in adolescent users of smokeless tobacco is related to years of use, frequency of use, and the amount used. Malignant transformation may occur in 0.5% to 6.2% of individuals and is expected to increase with years of use. Objectives: To identify the correlation between oral premalignant lesions and tobacco use. To study the prevalence of oral premalignant lesions among tobacco using patients. To determine the correlation between tobacco and oral premalignant lesions and the risk of tobacco using and to find out the relation between oral premalignant lesions in tobacco users and gender.

Methods: This is an analytical, quantitative systematic review study (known to some as a review article) that was conducted in the Republic of the Sudan by students at the school of dentistry at Napata College. This review is meant to discuss the prevalence of oral premalignant lesions among tobacco users, to assess the association between them and to determine the most found types of oral lesions in tobacco users. To write this paper, we inserted a plethora of keywords associated with the topic at hand. A number of researches were excluded as they were inaccessible to us; unrelated to the topic or because they were relatively anachronistic. Following this, we were left with a total of 13 papers, the findings of which are illustrated here.

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Results: As an overall, and from the studies mentioned, all studies agreed that thereis a correlation between oral premalignant lesions and tobacco use, in which the prevalenceof oral premalignant lesions found in tobacco using patients was between 48% and 60%. Regarding the most seen types of oral lesions related to tobacco use, the commonest lesions in all studies were found to be leukoplakia, keratosis and oral sub-mucous fibrosis. There was a degree of association found between male tobacco users and oral premalignant lesions in some studies.

Conclusion: This study concluded that there is a clear association between oral premalignant lesions and tobacco use, with leukoplakia, keratosis and oral sub-mucous fibrosis being the most common types of lesions seen. Some studies also stated that there is an association between male tobacco users and oral premalignant lesions.

Keywords: Oral, Premalignant Lesions, Tobacco, keratosis, oral sub-mucous fibrosis.

Introduction

The WHO defined the precancerous lesions as "a morphologically altered tissue in which cancer is more likely to occur than in its apparently normal counterpart". In May 2005 at a workshop that has been co-oriented by the WHO in London, the use of the term 'Potentially malignant disorder' was recommended. The usage of this terminology indicates a group of morphological alterations. Not all the lesions and conditions described under this term may transform to cancer.

Some studies in the southeast Asian countries showed that most patients that have premalignant lesions and oral cancers came to the health care centers were found to be habitual gutka users (gutka is a form of smokeless tobacco and it is a mixture of powdered tobacco, areca nut, slaked lime and other components) [(1)].

In some countries tobacco chewing is a common habit and there is evidence of cancer occurring due to this habit and for this, tobacco has been established as a risk factor for development of oral mucosa[(2)]. High prevalence of oral premalignant lesions (OL) and cancer were found in communities where tobacco using habit is related to culture, tradition and religious ceremonies [(3)].

A study was conducted by *D.L. Francis*in India in the year 2020 to assess the tobacco use and prevalence of premalignant lesions and oral cancer among tea plantation workers, Nilgiri Hills, Tamil Nadu, India. The study showed that among a 400 study population from 5 tea estates, 46% had no formal education and 65% had indigenous brushing habits. A percentage of 52% of oral mucosal lesions were detected, out of which the commonest was leukoplakia 34%, 42% tobacco pouch keratosis and 6% malignant oral tumors. Prevalence of oral mucosal lesions in the study population was due to tobacco usage and lack of awareness regarding the deleterious effects of the products used[(4)].
Another study was done by *Chinmay T. Jani*in India in the year 2019 to determine prevalence of tobacco use in industrial workers and associated it with the prevalence of oral premalignant lesions. Of 909 subjects, 537 (59.1%) had a history of consuming tobacco; of which, 360 (39.6%) were consumers of smokeless tobacco (SLT) and 141 (15.5%) were smokers. Oral premalignant lesions were present in around 52% of the study population that was exposed to tobacco, amongst which tobacco quid lesion was the most common (10.9%) followed by oral sub-mucous fibrosis (OSMF) (9.8%). OSMF was seen more in beetle nut chewers. The odds of developing an

oral premalignant lesion as a result of exposure to tobacco are 43.62 times more than the odds of acquiring a lesion without exposure [5].

Again in India, a study was conducted by *Punith Shetty* in the year 2017 to assess the determinants of tobacco use and the prevalence of oral precancerous lesions in cab drivers. Nearly 70.88% of cab drivers were consuming tobacco in any form. Long working hours, working at night, and family members consuming tobacco were significant risk factors for tobacco use among cab drivers. Forty-eight drivers were detected to have oral precancerous lesions [6].

Mohammed Junaid carried out another study in the year 2017 to determine the patterns of tobacco usage among subjects with potentially malignant oral lesions or conditions through a comparative study design. Cases with leukoplakia had a higher mean FNTD score when compared to the control group (P = 0.0001). The most common form of smokeless tobacco used by case (OSMF) subjects was found to be mawa (53%) significantly higher than the control group (P = 0.05). Mean FNTD scores of mawa users were higher than other tobacco users in both case and control group [7].

Also, *Kavita Nitish Garg* conducted a study retrospectively analyzing 191 cases of potentially malignant oral lesions, which had been biopsied in order to assess their relationship with tobacco usage. Out of 191 cases, 122 patients reported with tobacco habit (chewers, smokers, and both) and frequency (<5 and >5 packets/day) was seen in 109 cases and duration (<5 and >5 years) seen in 99 cases. These parameters were correlated with histopathological diagnosis and results showed that both the groups came under the high-risk category. Further analysis of decategorized group (age and gender) was also done [8].

Another study was done by *Sunil Surendraprasad Mishra*to determine, through a questionnaire, the prevalence of oral premalignant lesions and conditions in the population of Aurangabad city having adverse oral habits of using tobacco and tobacco-related products in various forms, to analyze the adverse health effects of these habits with respect to the duration and frequency of consumption, and to analyze the patients' motivation towards the cessation of this habit. The results showed that areca nut was the most popular product among young adults.

The survey data suggested that only few of the patients had tried to stop these adverse habits at some point in their lives. The most common reason for this was, advice given by the dentist after the patients were made aware of these lesions [9].

Meanwhile in Iran, *Fatemeh Ahmadi* carried out a study to evaluate oral lesions in male smokers compared with nonsmokers in Hamadan. A total of 516 male participants were assessed, 258 of whom were smokers and 258 of whom were healthy nonsmokers. The prevalence of lesions was evaluated by clinical observation and biopsy. The authors found that the most prevalent lesions among smokers were gingival problems and coated tongue; smokers had significantly more lesions than did nonsmokers. Malignant and premalignant lesions were found in a higher age range. Among all participants in our study, we found a large number of oral mucosal lesions in smokers that had a strong correlation with smoking. Dental services need to implement care and health education for smokers to promote health [(10)].

Sujatha, D. conducted a study on the same topic. Results showed that males had a higher prevalence and comprised 87.9% of the sample. The commonest habit in this study sample was smoking (39.2%) followed by smokeless tobacco use (28.1%). Out of the 1028 patients with habits 40% had no clinically detectable changes in their mucosa. Of the mucosal changes leukoplakia (14%) was the commonest [(11)].

Another study was done by *Joelma Sousa Lima*, to describe the clinical features observed in dysplastic and non-dysplastic OL in both smokers and non-smokers. The results demonstrated that 131 cases of OL were dysplastic (74 smokers and 57 non-smokers), and 184 were non dysplastic (96 smokers and 88 non-smokers). For OL cases in smokers for which information about alcohol consumption was also available (84 cases), the results revealed no significant difference in the amount of dysplastic and non-dysplastic lesions. Dysplastic lesions were more frequent in male smokers and in non-smoking females. The median age of smokers with cases of OL was significantly lower than in non-smokers; the lowest median ages were observed in female smokers with dysplastic OL. The most frequent anatomical sites of dysplastic lesions were the floor of the mouth in smokers and the tongue in non-smokers.

Dysplastic lesions in smokers were significantly smaller than non-dysplastic lesions in non-smokers. Being a male smoker, being female, being younger, and having smaller lesions were associated with dysplastic features in OL. This clinical data may be important for predicting OL malignant transformation [(12)].

Finally, El Mustafa conducted a study in UK in the year 2021 where he stated that some lesions were relatively common, affecting between 1 to 5% of the population (leukoplakia) and may resemble benign and

prevalent mucosal disease. These lesions pose a risk for malignancy that is independent of tobacco or alcohol, with a wide range of transformation rates between 13 and 70%. The commonest types are white patches (leukoplakia), red patches (erythroplakia) and sub mucous fibrosis [13].

Methodology

Study Design:

This study is an analytical quantitative systematic review study.

Study Area and Population:

An online search was conducted in which all the relevant keywords were entered into a plethora of reliable scientific sources (e.g.: Google Scholar, PubMed, etc.). Inclusion and exclusion criteria are manifested in this study.

Study subject: selection and definitions:

As aforementioned, inclusion/exclusion criterions were used in regards to the findings. The inclusion criteria were as follows: open access articles, published between the years 2010 and 2020, the literature published in an internationally credited, peer-reviewed journal and researches related to the title (13 articles). As for our exclusion criteria, the following applies: no closed access publications were included, no unpublished data were considered and researches about specific oral premalignant lesions or specific tobacco types (7 articles).

Data collection and Analysis:

Online searches of relevant keywords were carried out. Our inclusion and exclusion criteria were applied. The remainders were analyzed using SPSS v. 21. The downloaded articles were summarized and presented, and the collected data was compared.

Data management and statistical analysis:

The data analysis statements were provided for each specific objective. The literature in regards to the indications of all the aforementioned drugs was illustrated in this study. These indications will be a combination of all the illustrated uses in the respective articles. We will be discussing the proper citation will be used.

Ethical Considerations:

From an ethical perspective, we announce no conflicts of interest essential emergency drugs mentioned in Haas' 2006 paper [1].

Results and Discussion

All studies agreed that there is a correlation between oral premalignant lesions and tobacco use, in which the prevalence of oral premalignant lesions found in tobacco using patients was between 48% and 60%.

In *D.L. Francis's* study, the prevalence of premalignant lesions in smokers was 52%.

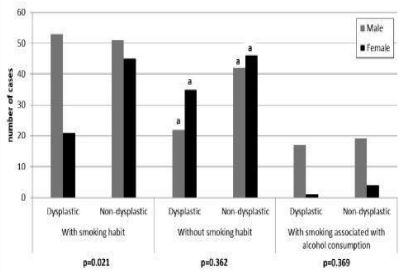

Figure 2 - Frequency of dysplastic and non-dysplastic lesions according to smoking habit, alcohol consumption and gender. (Chi-Square test; statistically significant when $p < 0.05$; a = statistically significant when compared with smoking habit/dysplastic lesions.)

Figure (1): Percentage of oral premalignant lesions in tobacco users was found in *D.L.Francis's* study.

The same exact percentage of oral premalignant lesions in tobacco users was found in *Sunil Surendraprasad Mishra's* study, which was 52%. Regarding the most seen types of oral lesions, keratosis (67.6%) and leukoplakia (31.4%) were the commonest. *Punith Shetty's* study revealed that 48% of tobacco using participants had premalignant oral lesions. The highest percentage of oral lesions related to tobacco use was found in *Sujatha, D.'s* study with 60%.

Regarding the most seen types of oral lesions related to tobacco use, the commonest lesions in all studies were found to be leukoplakia, keratosis and oral sub mucous fibrosis. In *Sunil Surendraprasad Mishra's* study, the most seen types of oral lesions were keratosis (67.6%) and leukoplakia (31.4%).

Table (1): Types of oral lesions found in *Sunil Surendraprasad Mishra's* study.

Oral Lesion Substance	*LkP (%)	Keratosis (%)	**OSMF (%)	Keratosis + OSMF (%)	Keratosis + LKP (%)	LKP + OSMF (%)	Total (%)
Duration (yrs)							
Tobacco chewers (n=586)							
≥1 to <5	16 (11.94)	116 (86.57)	2 (1.49)	0	0	0	134 (100)
≥5 to <10	38 (31.66)	80 (66.67)	2 (1.67)	0	0	0	120 (100)
≥10 to <15	24 (19.67)	98 (80.33)	0	0	0	0	122 (100)
≥15 to <20	26 (39.39)	40 (60.61)	0	0	0	0	66 (100)
≥20	80 (55.55)	62 (43.05)	2 (1.40)	0	0	0	144 (100)
Total	184 (31.40)	396 (67.58)	6 (1.02)	0	0	0	586 (100)

Profile of oral lesions among study participants. In *D.L. Francis's* study, the commonest lesions were also keratosis (42%) and leukoplakia (34%).

Table (2): Types of oral lesions found in *D.L. Francis's* study.

	Smoker			Non-smoker		
	Dysplastic (%)	Non-dysplastic (%)	p value	Dysplastic (%)	Non-dysplastic (%)	p value
Floor of mouth	18 (24.3)	2 (2.1)	< 0.001	8 (14.0)	6 (6.8)	0.104
Tongue	14 (18.9)	9 (9.4)		22 (38.6)	21 (23.9)	
Gingiva	6 (8.1)	38 (39.6)		12 (21.1)	33 (37.5)	
Buccal mucosa	17 (23.0)	27 (28.1)		8 (14.0)	18 (20.5)	
Palate	15 (20.3)	12 (12.5)		2 (3.5)	1 (1.1)	
Multiple sites	4 (5.4)	3 (3.1)		3 (5.3)	4 (4.5)	
WI	0 (0.0)	5 (5.2)		2 (3.5)	5 (5.7)	
Total	74 (100.0)	96 (100.0)		57 (100.0)	88 (100.0)	

WI – without information. Chi-square test. Statistically significant when $p < 0.05$.

Frequency of dysplastic and non-dysplastic lesions according to smoking habit and

anatomical site. In *Sujatha, D.'s* study, the commonest oral lesion was found to be leukoplakia (14%).

Table (3): Types of oral lesions found in Sujatha, D.'s study.

Variables	Cases (N=258)		Controls (N=258)		Odds ratio		p value
	Yes	No	Yes	No	Statistics	95% CI	
Gingivitis	148	110	83	175	2.83	1.94, 4.13	0.001
Periodontitis	110	148	15	243	12.04	6.65, 23.00	0.001
Melanosis	120	138	25	233	8.10	4.93, 13.64	0.001
Friction keratosis	19	239	2	256	10.17	2.41, 90.71	0.001
Leukoplakia	7	251	2	256	3.57	0.67, 35.45	0.092
Nicotinic stomatitis	6	252	0	258	ND	-	-
Squamous cell carcinoma	3	255	0	258	ND	-	-
Coated tongue	258	0	91	167	ND	-	-

Fatemeh Ahmadi's study also agreed that the commonest oral lesion found in tobacco using patients was leukoplakia (41.6%), followed by keratosis (24.8%).

Table (4): Types of oral lesions found in *Fatemeh Ahmadi's* study.

Oral lesion	Number	Percentage (%)
Keratosis	182	24.8
Leukoplakia	306	41.6
Lichen planus	68	9.3
OSMF	179	24.4
Total	735	100.0

Regarding *Punith Shetty's* study, the commonest oral lesion was also leukoplakia (10%), followed by oral sub mucous fibrosis (6.6%) and then leukoplakia (2.5%).

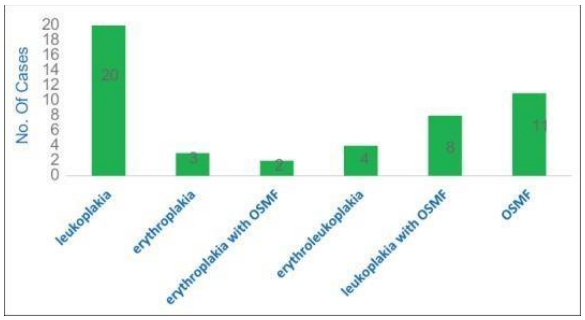

Figure (2): Types of oral lesions found in *Punith Shetty's* study.

Regarding association between oral premalignant lesions in tobacco users and gender:

In *D.L. Francis's* study, considering the group of smokers with dysplastic lesions, women showed a significantly lower median age in comparison with men (p = 0.032). In contrast, women in the group of non-smokers presented a significantly higher median age in comparison with men for both dysplastic (p = 0.001) and non-dysplastic lesions (p = 0.010).

Table (5): Association between gender and oral lesions in *D.L. Francis's* study.

	Smoker	Non-smoker	p value	Smoker		p value	Non-smoker		p value
	General	General		Male	Female		Male	Female	
Dysplastic	56.5 (28–84)	63 (40–83)	0.025	58 (41–84)	53.5 (28–83)	0.032	50.5 (40–83)	67 (42–82)	0.001
Non-dysplastic	55 (28–87)	63 (32–89)	0.004	54 (33–87)	56 (28–79)	0.877	57 (32–86)	64 (34–89)	0.010

Mann-Whitney U-test. Statistically significant when $p < 0.05$.

Median age (minimum and maximum value) of smoking and non-smoking patients with dysplastic and non-dysplastic lesions in general, and in male and female patients. In addition to that, *Kavita Nitish Garg's* study also agreed that males have a bigger risk for oral premalignant lesions compared to women.

Table (6): Association between gender and oral lesions in *Kavita Nitish Garg's* study.

Category	LRL	HRL	QRL	Total	
H/P					
All patients	55	101	35	191	
Those patients whose tobacco history was documented	39	70	32	141	
Age					
<30 years	16	13	20	49	191
>30 years	43	89	10	142	
Gender					
Female	6	4	7	16	191
Male	49	97	28	175	

Conclusion

We found that there is noticeable correlation between tobacco using habits and oral premalignant lesions (Potentially malignant disorder according to WHO) .All studies that we went through agreed that there is a correlation between oral premalignant lesions and tobacco using whatever the type was. Regarding the most seen type of oral lesions related to tobacco use the commonest lesions were found to be leukoplakia 41.6%, keratosis 24.8%, and oral sub mucous fibrosis 24.4%. The prevalence of oral premalignant lesions was due to tobacco using and lack of awareness regarding the deleterious effects of product used.

Association between gender and oral lesions showed that males have a bigger risk for oral premalignant lesions compared to women. When comparing the value between dis-plastic and non-dis-plastic lesions in relation with gender and smoking and non-smoking tobacco in D.L. Francis's study, dis-plastic lesions in tobacco users was found higher in males and in the non-smoking tobacco users in females, while the non-dis-plastic lesions were found more in females whether in smoking or non-smoking tobacco users.

As an overall conclusion, this study can conclude that there is a clear association between oral premalignant lesions and tobacco use, with leukoplakia, keratosis and oral sub mucous fibrosis being the most common types of lesions seen. Some studies also stated that there is an association between male tobacco users and oral premalignant lesions.

Recommendations

- Regular dental check-ups should be provided to tobacco using patients.
- Awareness regarding the effects of tobacco use on oral health should be

raised so that patients can take care of their oral hygiene.

- Social media should have a bigger role in raising the awareness about the effects of tobacco use on oral health.
- The community should promote attitudinal changes towards a positive health-seeking behavior.

- More studies about this topic should be done to help assess the situation more.

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