

PREVALENCE OF ORAL PREMALIGNANT LESIONS AND CONDITIONS AND ITS ASSOCIATED RISK FACTORS IN MANIPUR, NORTH-EAST INDIA

Dr. TANYA NANDKEOLIAR

Assistant Professor, Department of Periodontology, Dental College, Regional Institute of Medical Sciences, Imphal, Manipur, India. Email:tanya.nandkeoliar@gmail.com

Dr. CH. ANUPRIYA *

Research Assistant, Dental College, Regional Institute of Medical Sciences, Imphal, Manipur, India.

*Corresponding Author Email: anupriya3390@gmail.com

Dr. SUMITA BANERJEE

Assistant Professor, Department of Oral Pathology and Microbiology, Dental College, Regional Institute of Medical Sciences, Imphal, Manipur, India. Email:banerjeesumi10@gmail.com

Dr. SUSHMA KHURAIJAM

Professor and Head, Department of General Pathology, Regional Institute of Medical Sciences, Imphal, Manipur, India. Email:drsushmakh@gmail.com

Dr. D. B. NANDINI

Professor and Head, Department of Oral Pathology and Microbiology, Dental College, Regional Institute of Medical Sciences, Imphal, Manipur, India. Email:nannidb29@gmail.com

Dr. KOIJAM SASHIKUMAR SINGH

Associate Professor, Department of Oral Medicine and Radiology. Dental College, Regional institute of Medical Sciences, Imphal, Manipur, India. Email:koijamsas@gmail.com

Dr. PRAGYA PANDEY

Additional Professor, Department of Conservative Dentistry and Endodontics, Faculty of Dental Sciences, King George's Medical University, Lucknow. Email:w.pragya78@gmail.com

Abstract

Background: Oral cancer is one of the most common, life-threatening diseases all over the world. Several challenges are faced by developing countries in identifying and removing the potential risk factors associated with it. Early detection of oral premalignant lesions and conditions will help in the early treatment of the individuals and will downgrade their further progression into invasive oral cancer. **Aims:** To estimate the prevalence of oral premalignant lesions and conditions and to identify the associated risk factors in Manipur, North-East India. **Methods:** 1400 patients were recruited in this study and divided into two groups- With OPML and Without OPML groups. Individuals having signs and symptoms of oral precancerous lesions and conditions were included in the With OPML group while those without signs and symptoms of oral precancerous lesions/conditions were in the Without OPML group. Vital staining using toluidine blue dye was done in the With OPML group and a biopsy of these lesions and conditions was performed followed by histopathology to reach a confirmatory diagnosis. **Statistical analysis:** The chi-square test was applied to find significant differences among the two groups for tobacco habits, denture wear, and other risk factors. The significance level was set at $P \leq 0.05$. **Results:** The study group consisted of 73.2% males and 26.8% females in the With OPML group, and 56.2% males and 43.8% females in the Without OPML group. The overall prevalence of OPML and conditions in our study was found to be 31% out of which 70%

were associated with tobacco pouch keratosis followed by oral leukoplakia (17%), oral submucous fibrosis (6.8%) and oral lichen planus (5.8%). The risk factors associated with oral premalignant lesions and conditions were smoking and tobacco usage habits, alcohol consumption, stress, and diet.

Conclusion: It is extremely crucial and the need of the hour to identify oral premalignant lesions and conditions as the early detection of these will reduce malignant transformation. This study helps us to find the prevalent Oral premalignant lesion or condition and additionally analyze the associated risk factors in the state of Manipur.

Keywords: Oral Premalignant Conditions, Oral Premalignant Disorders, Oral Premalignant Lesions.

INTRODUCTION

Oral cancer constitutes 0.46% in the world, and 10.3% in India (GLOBOCAN 2020).^[1] India accounts for one-third of the world's oral cancer and has a high prevalence of oral premalignant lesions and conditions.^[2] One of the most life-threatening diseases of the oral cavity is oral cancer which has a history of association with oral potentially malignant disorders (OPMD), earlier termed as oral precancerous lesions and oral precancerous conditions. It is an established fact that OPMDs will eventually transform into oral cancers and hence early diagnosis will help in primary treatment, increasing patient survival rates, and subsequently reducing the morbidity related to oral cancer. Any visible clinical changes in the oral mucosa usually in the form of a white or red patch often lead to the transformation of oral cancer. These oral lesions usually resemble each other clinically and thus a mandatory confirmation biopsy is required.^[3] Knowledge about the risk of oral potentially malignant disorder and the ways to avoid this disease is limited among individuals. Early detection is of decisive importance, timely treatment of oral premalignant lesions and conditions will help in preventing its malignant transformation, and survival rates will distinctly improve when identified at an early stage. High incidence of habits such as smoking, drinking alcohol, chewing tobacco/ pan masala, and paan [betel leaf (Piper betel) with areca nut and slaked lime paste], is observed in various parts of the world. Over one-third of the tobacco consumed is in the smokeless form in the South Asian region.^[4]

There is a deficit of data regarding the OPMDs and also oral cancer registries are not readily available in different areas and regions of India. This study was carried out in Manipur, India (North East) to present the current scenario of oral premalignant lesions and conditions that will add to the overall status of OPMDs and oral cancers in our country.

MATERIAL AND METHODS

This study was carried out among individuals reporting to the Department of Oral Medicine and Radiology. Before the conduction of the study, it was ethically cleared by the institutional ethical board and the CTIRI registration was done. Individuals above the age of 18 years of either sex and residents of Manipur for >6 months with or without signs, symptoms, and clinical findings of oral premalignant lesions (OPML) and conditions were included in the study. The total sample size of the study was calculated to be 1400. All the patients were informed regarding the purpose and design of the study and a written informed consent was taken.

The oral cavity of all the individuals included in the study was thoroughly examined and based on the findings were divided into two groups- With OPML and Without OPML groups. Individuals showing clinical signs and symptoms of OPML and conditions such as Oral Leukoplakia, Oral Lichen Planus (OLP), Oral Submucous Fibrosis (OSMF), and Tobacco Pouch Keratosis were included in the With OPML group. Those having no clinical signs or symptoms of OPML and conditions were part of the

Without OPML group. The With OPML group constituted 500 patients and the Without OPML group constituted 900 patients.

Individuals of both groups were subjected to a questionnaire that included details regarding their socio-demographic characteristics, various risk factors for oral premalignant lesions, and conditions like the duration and frequency of tobacco usage, information regarding wearing of dentures, other irritational factors, food habits, and alcohol consumption. Individuals in the With OPML group underwent vital staining using toluidine blue dye followed by incisional biopsy and histopathology to reach a final diagnosis.

Statistical analysis

Statistical analysis was done using Statistical Package for the Social Sciences (SPSS Version 23; Chicago Inc., IL, USA). Shapiro Wilk test was performed to determine the normality of the data. Variables were compared using numbers and percentages. The Chi-square test was applied to find significant differences between the groups for tobacco habits, denture wear, and other risk factors. For all analyses, a *p*-value <0.05 was considered to be statistically significant.

RESULTS

The prevalence of OPML and conditions in our study was found to be 31%.

The demographic characteristics of the study patients are shown in Table 1. The study showed that the age group 41-50 years had a higher number of participants in both the With OPML group (28.45%) and the Without OPML group (25.5%).

Table 1: Sociodemographic characteristics of the patients

Sociodemographic characteristics	with OPML		without OPML		P value	Sociodemographic characteristics	with OPML		without OPML		P value
	no	%	no	%			no	%	no	%	
A) Age in years						E) Occupation					
18-20years	7	1.4%	25	2.7%		Business	31	6.2%	259	28.7%	.038*
21-30 years	90	18%	176	19.55%		Govt service	144	28.8%	72	8%	
31-40 years	91	18.2%	169	18.7%		Agriculture	32	6.4%	64	7.1%	
41-50 years	142	28.45%	230	25.5%		Housewife	56	11.2%	96	10.6%	
51-60 years	123	24.6%	204	22.66%		Student	71	14.2%	108	12%	
61-70 years	47	9.4%	84	9.33%		Laborer	54	10.2%	77	8.5%	
71-80 years	0	0	12	1.33%		Unemployed	25	5%	50	5.5%	
						Self-employed	87	17.4%	174	19.3%	
B) Sex						F) SES					
Male	366	73.2%	506	56.2%	.000*	Lower	15	3%	22	2.4%	.000*
Female	134	26.8%	394	43.8%		Lower middle	185	37%	117	13.0%	
C) Religion						Upper	8	1.6%	30	3.3%	
Hindu	422	84.4%	810	90.0%	.007*	Upper lower	268	53.6%	643	71.4%	
Christian	53	10.6%	57	6.3%		Upper middle	24	4.8%	88	9.8%	
Muslim	25	5%	33	3.7%							
D) Marital status											
Married	400	80.0%	634	70.4%	.000*						
Unmarried	99	19.8%	261	29.0%							
Widow	1	0.1%	5	0.4%							

The tobacco chewing habits among the study participants- the commonest form of smokeless tobacco use among the study participants was Pan masala [betel quid mixture may or may not contain tobacco](Talab/saajan), khaini (roasted tobacco flakes with slaked lime), saajan (scented khaini) and betel quid (betel leaf, areca nut, with/without slakes lime, tobacco, catechu, condiments. [Table 2]

Table 2: Tobacco habits of patients

Habits		with OPML		without OPML		P value
Tobacco chewers		no	%	no	%	
a) Talab Duration	<1 year	9	28.1%	23	57.5%	0.023*
	1-5years	10	31.2%	8	20.0%	
	6-10years	5	15.6%	7	17.5%	
	>11years	8	25.1%	2	5.0%	
b) Saajan Duration	<1 year	5	12.8%	15	46.8%	.002*
	1-5years	4	10.2%	7	22.0%	
	6-10years	17	43.5%	6	18.7%	
	>11years	13	33.5%	4	12.5%	
c) Betal quid Duration	<1 year	12	21.0%	13	9.5%	0.007*
	1-5years	14	24.5%	24	54.7%	
	6-10years	27	47.5%	5	11.3%	
	>11years	4	7.0%	2	4.5%	
d) Khaini Duration	<1 year	3	14.2%	29	19%	0.036*
	1-5years	2	9.5%	56	36.8%	
	6-10years	7	33.3%	33	21.7%	
	>11years	9	42.8%	34	22.5%	
Mixed habit		36	11.6%	27	10.2%	0.590

*=Significant

The risk factors other than tobacco associated with OPMDs were found to be alcohol consumption, ill-fitted dentures or sharp edges of broken teeth repeatedly contacting the mucosa, stress, and diet. [Table 3]

Table 3: Dissection of other risk factors other than tobacco associated with premalignant lesions and conditions.

Risk factors		with OPML		without OPML		P value
		no	%	no	%	
Alcohol		162	32.4%	204	22.7%	0.000*
Denture wearers		38	7.6%	55	6.2%	0.283
Sharp edges/ill-fitted dentures causing trauma		7	19%	6	11%	0.304
Stress	Feeling neglected	137	27.4%	56	6.2%	<0.001*
	Feeling tried	286	57.2%	105	11.6%	<0.0001*
	Feeling nervous	249	49.8%	84	9.3%	<0.001*
	Sleepless night	175	35.0%	53	5.9%	<0.0001*

*=Significant

The type of oral premalignant lesions and conditions, tobacco pouch keratosis showed the highest prevalence of 70.4%. [Table 4]

Table 4: Dissection of cases based on the type of oral mucosal lesions

Type	Number	Percentages	Type	Number	Percentages
Tobacco pouch keratosis	352	70.4	Leukoplakia	85	17
Oral submucous fibrosis	34	6.8	Lichen planus	29	5.8

Table 5 shows the histopathological data where 62.8% of individuals were associated with epithelial dysplasia in the epithelium indicating abnormal cells confined to the oral epithelium.

Table 5: shows descriptive data of Histopathological findings

Dysplastic changes	no	%
Dysplasia	314	62.8%
Without dysplasia	186	37.2%

DISCUSSION

This study identifies the prevalence of Oral premalignant lesions and conditions in Manipur and tries to identify the possible risk factors associated with OPMDs. It was identified from our study that the prevalence of OPMLs and conditions in this region was exceptionally high (31%). Additionally, it was also identified that the main etiological factor was the consumption of smokeless forms of tobacco. The NFHS 2005-06^[5] and GATS 2009-10^[6] state that the consumption of smokeless tobacco is exceptionally high as it is accepted socially and plays an integral role in the culture of these states.^[7] The peak age group of OPMDs in our study was seen to be 41-60 years which is predominantly the working age group with the highest external exposure and the fact that the premalignant lesions develop much before the development of cancers in accordance to the study by Swati et al.^[8,9,10] As the age increases, the frequency and duration of intake of tobacco also increases. Socioeconomic status^[11] was strongly associated with adverse habits. Maximum participants belonged to the upper lower economic class even though the majority were literate, they were engaged in low-paying, high physical activity and stress in combination with peer desire which resulted in the consumption of harmful habits like tobacco.^[12] Smokeless forms of tobacco are more likely to cause OPMDs due to their longer contact time which increases the carcinogenic potential of nicotine.^[8] Higher concentrations of nitrosamines constitute smokeless tobacco and are readily extracted by saliva ultimately increasing the toxic levels in tobacco users.^[13,14] Our study showed that the use of smokeless tobacco was for longer durations and frequency in With OPML group in accordance with other studies.^[8]

Some studies have explained that alcohol acts as a promoter rather than an initiator of OPMDs, doubling the risk of malignant transformation.^[15] Individuals in our study who wore ill-fitted dentures or had sharp edges of broken teeth repeatedly contacting the mucosa and had the presence of OPMLs due to irritation to the mucosa. This can be attributed to chronic mechanical irritation of the oral mucosa may hypothetically contribute to the formation or severity of oral cancer and by almost four times increases the cancer risk.^[16] In Stress has been linked with various effects on the oral mucosa. Oxidative stress might be involved in the etiology of oral premalignant lesions.^[17] Chronic inflammation associated with OPMLs is linked with increased production of reactive oxygen species that cause impairment to macromolecules including DNA. A higher mutation rate in chronically inflamed tissues increases the risk for carcinogenesis.^[18] The data on diet justifies that the vegetarian diet had the potential to reduce the risk of the development of OPMLs or conditions even though the control patients were also tobacco users. A variety of nutrients, micronutrients, and food components can act as protective elements these can be obtained from fruits, vegetables, and certain vitamins, low consumption of fruit and vegetables has been associated with an increased risk of oral cancer.^[19] Reactive oxygen species are reduced by the action of antioxidants contained in the green leafy vegetables. Additionally, many of the traditional Manipuri foods contain phytonutrients having antioxidants and other health-promoting properties, which may be one of the reasons for not developing OPMLs in the Without OPML group despite the high consumption of smokeless tobacco and the presence of other risk factors.^[20] Some complexes found in vegetables are thought to have anti-tumoral properties, such as glycate and indol-3 carbonol (inducing phase II enzymes) responsible for eliminating reactive oxygen species and DNA repair.^[21]

Axell *et al.*^[22] identified that tobacco pouch keratosis may occur due to chronically stretched tissues in the area of tobacco placement and the lesion is confined to areas in direct contact with spit tobacco. After 5 to 10 years of tobacco habit, the admittance of smokeless tobacco keratosis becomes apparent and retreats with cessation of the habit. The development of tobacco pouch keratosis is reliant on the category of habit popular among general people. The definite brand of tobacco consumed, extended duration of the habit, the frequency used, excessive daily contact hours of tobacco on oral mucous membranes, and a lack of beta-carotene or vitamin A also contribute to a high risk of keratosis.^[23] Oral premalignant lesions and conditions such as tobacco pouch keratosis and oral leukoplakia are often seen in the initial stages and are diagnosed on normal clinical examination of individuals with habits. Other premalignant lesions and conditions initially at the subclinical level don't show any signs and symptoms and could go undiagnosed. Hence the higher prevalence of tobacco pouch keratosis and oral leukoplakia could be due to this reason in our study.

LIMITATIONS

Our study is a community-based study and thus only provides the baseline data regarding the OPMLs and conditions and their risk factors in this region. We suggest that many more studies should be conducted to derive a definitive conclusion. Another limitation was that the participants didn't provide complete/ true information about tobacco chewing habits or alcohol consumption as it is considered a social taboo resulting in misinformation. Additionally, many individuals who had signs of OPMDs but were asymptomatic refused to undergo biopsy presuming it to be a painful process.

CONCLUSION

This study was conducted to assess the prevalence of oral premalignant lesions and conditions in Manipur, India. This study helps us to analyze the associated risk factors and the situation of tobacco-associated oral lesions which in turn helps in planning a program to prevent tobacco-related oral habits and its associated oral lesions such as potentially malignant disorders and oral cancers through early detection and primary prevention, hence emphasis should be given for cessation of habit through counseling, proper referral and treatment procedures for better control over the prevention of such oral premalignant lesions and conditions.

DISCLOSURE

Ethical clearance no: Research Ethics Board A/206/REB/Prop(faculty)111/38/2019 dated 4th November 2019

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