Dentistry Section

Association between Lifestyle Factors and Oral Potentially Malignant Disorders among People of Bangalore: A Case-control Study

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ABSTRACT

Introduction: The increase in prevalence of oral premalignant lesions and oral cancer in India is due to cultural, ethnic, geographic factors and varying lifestyle factors like consumption of tobacco, alcohol and standard of living. Some of the risk factors are modifiable and emphasises the need for detailed assessment of these modifiable risk factors and increasing awareness among general public and policy makers.

Aim: The present study was conducted to assess the association between lifestyle factors and Oral Potentially Malignant Disorders (OPMDs).

Materials and Methods: A case-control study was conducted where 154 cases and controls were selected from MS Ramaiah Dental College and Hospital, Bangalore and peripheral outreach centers of MS Ramaiah Dental College and Hospital, Bangalore. Cases diagnosed as oral leukoplakia, erythroplakia and Oral Submucous Fibrosis (OSMF) based on the World Health Organisation (WHO) criteria (1980) were included in the study group. Age and sex (1:1) matched controls without OPMDs were included in control group. The data was collected regarding socio-demographic factors, blood group and lifestyle factors using specially designed proforma. Chi-square test and odds ratio were utilised to association and strength of association between various lifestyle factors and development of OPMDs. Univariate logistic regression test was done followed by multiple logistic regression for identifying the risk factors. The p-value <0.05 was considered as statistically significant. SPSS version 11.0 was used for data analysis.

Results: Out of 154 cases, 84 (54.5%) cases were leukoplakia, 2 (1.3%), cases were erythroplakia, 53 (34.4%) cases were OSMF and 15 (9.7%) cases were with multiple potentially malignant disorders (leukoplakia+OSMF). In univariate analysis, OR for tobacco smoking in individuals who smoked more than 20 times a day was 2.56 (95% CL 1.19-5.5) compared to non-smokers, tobacco chewing who chewed more than 10 times a day was 43.03 (95% CL-17.2-107) in comparison to non-chewers and alcohol consumption who consumed alcohol daily was 3.2 (95% CL 0.6-16.3) in comparison to non-alcoholics. Following multiple logistic regression analysis occupation, smoking, chewing tobacco and vegetable intake was found to be statistically significant as independent risk factors p<0.05.

Conclusion: Occupation, smoking, chewing tobacco and vegetable consumption were identified as independent risk factors for the development of OPMDs. Identifying the risk factors and OPMD at an early stage is important for prevention of oral cancer.

INTRODUCTION

Oral cancer is one of the 10 most common cancers in the world. Each year about 5,75,000 new cases and 3,35,000 deaths occur worldwide. Its high frequency in Central and South East Asian countries (India, Bangladesh, Sri Lanka, Thailand, Indonesia, and Pakistan) has been well-documented [1]. Oral cancers are seen predominantly in both sexes accounting for one-third of all the cancers in South-East Asian countries. India has one of the highest incidences of oral cancer in the world, with estimated incidence of 12.48 cases per 100,000 population in males and 5.52 per 100,000 populations in females [1].

Oral cancer is usually first diagnosed when it becomes symptomatic. Unfortunately, by this stage approximately two-third of the patients would have already developed advanced disease with regional metastasis. The delay in treatment leads to high mortality and morbidity. Treatment of oral cancer can be easy and unaggressive when the diagnosis is early, with a survival rate of around 80% [2,3]. There are also a number of precursor lesions which constitute a detectable preclinical phase. The most important ones are leukoplakia, erythroplakia, OSMF etc. A comprehensive global review points at a prevalence of 2.6%. In India, the prevalence of leukoplakia varies from 0.2 to 5.2%. Erythroplakia represents the most severe oral premalignant lesion. Prevalence rate of as 0.09% is reported in the USA and 0.02% in Indian villagers. OSMF is a precancerous condition with a reported increase in the prevalence 0.16 to 3.2 from the late 1960s to the late 1990s in Bhavnagar, Gujarat. This dramatic increase in OSMF as new epidemic among youth (persons below 35 years) in India has been attributed to gutka and paan masala chewing [3].

This increase in the prevalence of OPMDs in India is mainly due to the culture, ethnic, geographic factors, low socio-economic status and varying lifestyle factors like consumption of various forms of tobacco, alcohol, fewer intakes of fruits and vegetable etc. Studies have shown that these are major risk factors for development of premalignant lesions [4-8]. Blood group plays an important role in the immunogenic system. But not much work has been done to find out the genetic relation of these most prevalent potentially malignant disorders of the oral cavity. Therefore, the role of genetics in the aetiology of potentially malignant disorders can be established. A part of this study related to ABO Rh blood group and OPMD is already published [9]. Detection of oral cancer in its premalignant stage becomes very important. Screening and early detection of oral cancer and its pre-invasive intraepithelial stages is still largely based on visual examination of mouth. The site is readily accessible for visual inspection and oral potentially malignant lesions are known to present clinically as white or red patches [10]. And, also there is need for more indepth studies of various modifiable risk factors in India. This would enable us to evolve appropriate interventions and effective preventive

measures to reduce the burden of morbidity and mortality [2]. Thus, the present study was under taken to find the association between the risk factors and OPMD.

MATERIALS AND METHODS

This case-control study was conducted at MS Ramaiah Dental College and Hospital, Bangalore and field practice areas (peripheral outreach centers) located in Kaiwara, Muddenahalli and Mohan Kumar Nagar from January 2009 until July 2010. The study proposal was approved by the Ethical Review Board of MS Ramaiah Dental College and Hospital, Bangalore. The study objectives and procedures were explained in detail to the patients and informed consent was obtained. Sample size of 154 subjects in each group was calculated by using n-Master software based on the study conducted by Campisi G and Margiotta V and sample selection was non-probability sampling (Quota sampling) [11].

Inclusion criteria: Cases with OPMDs like leukoplakia, erythroplakia and OSMF, identified and clinically diagnosed at MS Ramaiah Dental College and Hospital, Bangalore and field practice areas were included in the study. Diagnosis of OPMDs was done based on WHO guidelines for diagnosis of oral premalignant lesions [8]. Age and sex matched hospital patients without potentially malignant disorders and patients' attendees, either their relatives or friends were selected as controls.

Exclusion criteria: Cases and controls not being willing to undergo oral examination and not giving consent or suffering from any systemic disease were excluded from the study.

Group matching was done to ensure comparability between cases and controls. Two-year age group matched cases and controls were selected. Equal numbers of controls were selected (for each case a control was selected who was similar to case in two-year age group).

Study Procedure

A special proforma was prepared by the investigator keeping objectives as guidelines, first part of proforma included- socio-demographic details (name, age, sex, address, education, occupation, family income), second part included lifestyle factors, exposure to risk factors such as tobacco form and frequency, juice swallowing, quid retention, alcohol consumption habit in terms of type used, dose and duration of exposure, socio-economic status, diet history regarding type of food (vegetarian or mixed) and frequency of intake of fruits and vegetables etc., and third part included clinical examination of oral mucosa.

A face-to-face interview was conducted by the trained and calibrated investigator. The investigator was trained and calibrated for data collection and clinical examination of OPMDs in the Department of Public Health Dentistry and Oral Pathology, MSRDC Bangalore, under the guidance of the professor in order to minimise intraexaminer variability. Calibration was carried out on ten subjects and subjected to kappa statistics, Kappa co-efficient value was 0.95 and 0.98. Face to face interview method was selected in order to avoid incomplete submission. Any doubts arising during the filling of the proforma were clarified by the investigator. To avoid bias, data collection and clinical examination were performed by the same expert.

Patients were instructed to rinse their mouth thoroughly with water to dislodge food, tobacco and betel quid debris and thorough clinical examination of oral mucosa was done by visual method under the chair operatory light and mouth mirror was used to retract cheek and tongue. Clinical examination included extraoral inspection of head and neck and palpation of cervical lymph nodes, intraoral inspection and palpation of lip, buccal mucosa, gingiva, tongue, floor of mouth, hard and soft palate and oropharynx.

STATISTICAL ANALYSIS

Data obtained was entered on an excel sheet and was analysed using Statistical Package For The Social Sciences (SPSS) software version 11.0. Descriptive statistics to summarise the data, Chi-square test and Odds ratio was calculated to asses association and strength of association between various lifestyle factors and development of OPMDs. Univariate logistic regression test was done followed by multiple logistic regression tests for identifying the risk factors. The p-value <0.05 was considered statistically significant.

RESULTS

Cases were selected from kaiwara (84), Muddenahali (20), MK nagar (10) and MSRDCH (40) Bangalore and controls were selected simultaneously (1:1). Mean age was 49.06 years with standard deviation 10.7 years. There were 88 males and 66 females. Out of 154 cases, 84 (54.5%) cases were of leukoplakia, 2 (1.3%) erythroplakia, 53 (34.4%) OSMF and 15 (9.7%) cases were with multiple oral potentially disorders (leukoplakia+OSMF).

[Table/Fig-1] shows socio-demographic characteristics of cases and controls. A total of 88 cases were illiterate, and three had completed their college and above. None of the cases were semiprofessional and professional, whereas 83 controls were unskilled workers and one semiprofessional and two professional workers. Socio-economic status of the family was assessed based on modified BG Prasad's classification by considering per capita monthly income of family [12]. Majority of cases belonged to class III and class IV whereas majority of the controls belonged to class III and class II.

Variables	Cases n=154 (%)	Controls n=154 (%)	Total n (%)	Chi-square value	df	p-value
1. Marital status						
Married	111 (72.08)	113 (73.38)	224 (72.73)	4.4	3	0.21
Unmarried	19 (12.34)	26 (16.88)	45 (14.61)			
Widow	15 (9.74)	12 (7.79)	27 (8.77)			
Widower	9 (5.84)	3 (1.95)	12 (3.30)			
2. Education status						
Illiterate	88 (57.14)	60 (38.96)	148 (48.05)	18.5	4	<0.001**
Primary school	21 (13.64)	31 (20.13)	52 (16.88)			
Middle school	27 (17.53)	38 (24.68)	65 (21.105)			
High school	15 (9.74)	19 (12.34)	34 (11.04)			
College and above	3 (1.95)	6 (3.9)	9 (2.92)			
3. Occupation						
Unemployed	34 (22.08)	24 (15.58)	58 (18.83)	7.2	6	0.21
Unskilled	81 (52.60)	83 (53.90)	164 (53.25)			
Semiskilled	23 (14.94)	31 (20.13)	54 (17.53)			
Skilled	11 (7.14%)	11 (7.14)	22 (7.14)			
Clerk, shop/farm owner	5 (3.25)	2 (1.30)	7 (2.27)			
Semi profession	-	1 (0.65)	1 (0.32)			
Profession	-	2 (1.30)	2 (0.655)			
4. Socio-economic status						
Class I	2 (1%)	21 (13%)	23 (7.47)	31.5	4	<0.001**
Class II	24 (15%)	42 (27%)	66 (21.43)			
Class III	50 (32%)	47 (30%)	97 (31.49)			
Class IV	52 (33%)	34 (22%)	86 (27.92)			
Class V	26 (16%)	10 (6%)	36 (11.69)			

[Table/Fig-1]: Socio-demographic characteristics of cases and controls.
*Chi-square test was used for the calculation of p-value

[Table/Fig-2] shows odds ratio for potentially malignant disorders according to smoking, chewing tobacco and alcohol intake. The odds of developing OPMDs were higher in smokers who smoked more than 20 times a day (OR 2.56 compared to non-smokers)

and OR 43.03 among tobacco chewers who chewed more than 10 times a day when compared to non-chewers. It was observed that odds ratio was 3.2 times higher among people who consumed alcohol daily compared to non-alcoholics.

Variables	Cases n (%)	Controls n (%)	OR (95%CI)	p-value (chi-square)
Type of smoking				
Bidi	52 (33.77)	25 (16.23)	2.55 (1.4-4.4)	
Cigarette	10 (6.49)	16 (10.39)	0.7 (0.3-1.7)	<0.002**
Non-smokers	92 (59.74)	113 (73.38)	1	
Frequency of smoking (no. per day)				
Up to 10	16 (10.39)	10 (6.49)	1.96 (0.8-4.53)	
10-20	23 (14.94)	20 (12.99)	1.41 (0.73-2.7)	<0.046*
More than 20	23 (14.94)	11 (7.14)	2.56 (1.19-5.5)	
Non-smokers	92 (59.74)	113 (73.38)	1	
Duration of smoking (Years)				
Up to 10	18 (11.66)	10 (6.49)	2.21 (0.9-5.02)	
11 to 20	18 (11.66)	15 (9.74)	1.47 (0.7-3.08)	
21 to 30	19 (12.34)	15 (9.74)	1.5 (0.74-3.23)	<0.335
31 to 40	7 (4.55)	1 (0.65)	8.3 (1.0-71.15)	
Type of chewing habit				
Paan with tobacco	106 (68.83)	31 (20.13)	36.0 (16.3-79.6)	
Gutaka	30 (19.48)	18 (11.69)	17.59 (7.153-0.067)	
Paan without tobacco	9 (5.84)	10 (6.49)	9.5 (3.0-29.4)	<0.001**
Non-chewers	9 (5.84)	95 (61.69)	1	
Frequency of chewing (times per day)				
<=5	9 (5.84)	17 (11.04)	5.58 (1.9 -9.390)	
6-10	83 (53.90)	29 (18.83)	30.2 (13.5-67.4)	<0.001**
>10	53 (34.42)	13 (8)	43.03 (17.2-107)	
Non-chewers	9 (5.84)	95 (61.69)	1	
Duration of quid retention				
Up to 15 min	61 (39.61)	29 (18.83)	22.2 (9.8-50.1)	
Half to 1 hour	64 (41.56)	25 (16.23)	27.0 (11.8-61.6)	<0.001**
More than hour	20 (2.99)	5 (3.25)	42.22 (12.7-139)	
No quid retention	9 (5.84)	95 (61.69)	1	
Juice swallowing				
Yes	65 (42.21)	23 (14.94)	1.2717 (0.686-2.357)	
No	80 (51.95)	36 (23.38)	1	<0.44
Type of alcohol consumption				
Locally made	13 (8.34)	5 (3.25)	2.8 (0.9-8)	
IMFL	9 (5.84)	5 (3.25)	1.9 (0.63-5.9)	
Beer	6 (3.90)	8 (5.19)	0.8 (0.273-2.3)	<0.1
Non-alcoholics	126 (81.82)	136 (88.31)	1	
Quantity of alcohol consumption				
Up to 60 mL	8 (5.19)	5 (3.25)	1.7 (0.5-5.4)	
60-120 mL	11 (7.14)	9 (5.84)	1.3 (0.52-3.2)	<0.3
>180 mL	9 (5.84)	4 (2.60)	2.4 (0.7-0.8)	
Frequency of alcohol consumption				
Daily	6 (3.9)	2 (1.3)	3.2 (0.6-16.3)	
Three times weekly	13 (8.44)	7 (4.55)	2 (0.7-5.1)	
Weekly	7 (4.55)	4 (02.60)	1.8 (0.5-6.6)	<0.1
Monthly	2 (1.30)	5 (3.25)	0.43 (0.08-2.26)	

[Table/Fig-2]: Odds ratio and 95% confidence intervals for Oral Potentially Malignant Disorder (OPMDs) according to tobacco smoking, chewing, alcohol consumption.
IMFL: Indian-made foreign liquor; OR: Odd ratio; CI: Confidence interval; p-value <0.05 considered statistically significant; p<0.05 significant*; p<0.001 highly significant**

A total of 121 cases were consuming mixed diet compared to 143 controls and the odds ratio was 3 (95%CL 1.5-5.7) for vegetarians compared to individuals who consumed mixed diet [Table/Fig-3]. It was observed that the odds of developing OPMDs were 3.7 times higher among those who consumed vegetables 3-4 times per week compared to everyday consumers. Similarly, odds of developing OPMDs were 3.6 times higher among those who consumed fruits 3-4 times per week compared to daily consumer.

Variables	Cases n (%)	Controls n (%)	OR (95%CI)	p-value (chi square)
Diet				
Mixed	121 (78.6%)	143 (92.9%)	0.8 (0.7-0.9)	<0.001**
Vegetarian	33 (21.4%)	11 (7.1%)	3 (1.5-5.7)	
Frequency of consumption of fruits				
3-4 times per week	27 (17.53%)	39 (25.32%)	3.6 (0.6-19.9)	
1-2 times per week	69 (44.81%)	83 (53.90%)	3 (0.5-15.9)	<0.01*
1-2 times per month	53 (34.42%)	30 (19.48%)	1.4 (0.2-7.7)	
Every day	5 (3.25%)	2 (1.30%)	1	
Frequency of consumption of vegetables				
3-4 times per week	79 (51.30%)	37 (24.03%)	3.7 (0.6-19.9)	
1-2 times per week	15 (9.74%)	11 (7.14%)	2.4 (0.7-8)	<0.001**
Every day	60 (38.96%)	106 (68.83%)	1	

[Table/Fig-3]: Odds ratio and 95% confidence intervals for Oral Potentially Malignant Disorder (OPMDs) according to diet, fruits and vegetable intake.
OR: Odd ratio; CI: Confidence interval; p-value <0.05 considered statistically significant

Multiple regression analysis showed occupation (p=0.014), smoking (p<0.001), chewing habit (p<0.001) and vegetable intake (p=0.018) as the risk factors significantly associated with development of OPMDs [Table/Fig-4].

Variables	Estimate	SE. of estimate	Wald statistics	Sig. (p value)	Exp(B) or OR	95.0% CL for Exp(B) or OR Lower	Upper
Constant	-5.9880	1.9880	9.0680	0.0030	0.003		
Age	-0.0050	0.0100	0.2630	0.6080	0.995	0.975	1.015
Sex	0.3890	0.3500	1.2310	0.2670	1.475	0.742	2.931
Education	-0.0380	0.1720	0.0500	0.8240	0.962	0.686	1.349
Occupation	0.4070	0.1660	5.9900	0.0140	1.502	1.084	2.080
SES	0.0280	0.1540	0.0330	0.8570	1.028	0.761	1.390
Smoking	2.0430	0.5260	15.0750	<0.001	7.711	2.750	21.623
Chewing	4.2660	0.5590	58.3420	<0.001	71.268	23.847	212.984
Alcohol	-0.1270	0.5210	0.0600	0.8070	0.881	0.317	2.443
Diet	0.8600	0.5250	2.6890	0.1010	2.364	0.845	6.608
Fruits	-0.2470	0.2310	1.1460	0.2840	0.781	0.497	1.228
Vegetable	0.5970	0.2540	5.5530	0.0180	1.817	1.106	2.987

[Table/Fig-4]: Unadjusted multiple logistic regressions.
Chi-square=168.197, p<0.0001; -2log likelihood=258.7812; p<0.0001;
SES: Socio-economic status; SE: Standard error; OR: Odd ratio; CI: Confidence level

DISCUSSION

The term 'OPMDs' was recommended by WHO in the year 2005 [2]. It includes both oral premalignant lesions and conditions. The present study was conducted to study the association between various lifestyle factors and OPMDs. In the present study, oral leukoplakia, erythroplakia and OSMF were included as cases. In cases, where more than one lesion or atleast two different premalignant lesions under study were present in the oral cavity than it is considered as multiple OPMDs [2,3]. Lifestyle denotes the way people live, reflecting a whole range of social values, attitudes and activities. It is composed of cultural and behavioural patterns and lifelong personal habits that have developed through the process of socialisation [3,5,13]. Visual examination method was used for clinical examination, since it is more conventional method for oral cancer screening [10,14]. This method is a non-invasive technique for examination of oral cavity. It can be carried out in a simple and

easy manner without use of any additional diagnostic equipment by all healthcare professionals across a multitude of disciplines. A study conducted by Mathew B et al., showed that visual examination test performance is satisfactory in terms of sensitivity, specificity and predictive value [15]. It was observed that majority of the cases were illiterate, unskilled and belonged to lower socio-economic group. OPMDs were more in lower socio-economic groups (class IV group 33% and class V group 16%). The difference in the proportion between cases and controls according to socio-economic status was statistically significant p<0.001. These findings are also consistent with another study done by Hashibe M et al., in which they found that higher the Socioeconomic Status (SES) index, education and income were associated with decreased risk of oral premalignant lesions [6]. It was noted that higher the frequency and duration of smoking, higher the risk for OPMDs. Similar findings were noted in the study done by Nagao T et al., where 50% of the leukoplakia cases were found in males who were heavy smokers (20 or more per day) [7].

According to chewing habit, paan chewing with tobacco had 36 times higher odds for the development of OPMDs. Also, the duration of chewing habit also led to a higher risk for the development of OPMDs. Similarly, in a study done by Kadashetti V et al., showed that odds for developing PMDS in tobacco chewers was 33 times than non-chewers [16]. Another study done by Amarasinghe HK et al., showed odds of 14.9(4.5-49.3) in daily betel quid chewers with tobacco compared to nonchewers [17]. Retention of betel quid in the buccal vestibules for more than one hour had higher odds of developing OPMDS, as buccal mucosa loses its smoothness and the rough area retains the quid for more time, this increases the permeability of mucosa for carcinogens [17]. Cases who swallowed the juice had odds ratio of 1.27 compared to non-juice swallowers. Swallowed juice contains carcinogens or pro-carcinogens causing onset of cancer in the upper alimentary tract. Another study done by Chung CH et al., found similar findings (OR-11.4, CI-4.0-32.0 p<0.001) [18].

Subjects who consumed alcohol daily and for longer durations were at a higher risk for development of OPMDs. Further it was noticed that majority of the cases 92.9% consumed mixed diet (OR=0.8). Several components of the diet are seen as tumour promoters or anti promoters. They may enhance or impede the delivery of carcinogens or alter the susceptibility of the target tissue to carcinogens. Mixed diet supplies all the required nutrients to the individuals when compared to vegetarians. Similar results were noted in a study done by Carley KW et al., which showed that South Indian females tobacco/betel chewers consumed a diet deficient in foods of animal origin and they appeared to have a more significant risk for oral premalignancies (OR 3.38. CL 2.07-5.54, p<0.001) [19]. The antioxidant property of vegetables and fruits plays a vital role in preventing the occurrence of OPMDs [20]. Odds ratio for those who consumed fruits 3-4 times per week was 3.6(0.6-19.9). In a study done by Amarasinghe HK et al., found that more than half of the cases and controls consumed less the two portion of fruits and vegetables per day and intake of B-carotene containing fruits and vegetables significantly reduced the risk of having an OPMD and leukoplakia (OR 0.5; 95%CL -0.3-0.9) [20]. Gupta PC et al., in a study found that intake of fruits, vegetables and beta-carotene evidenced inverse trends in risk of oral precancerous lesion after controlling tobacco use (p<0.05) [21].

Multiple logistic regression analysis showed risk factors like occupation, smoking, chewing tobacco and vegetable intake were significantly associated with development of OPMDs p<0.05. In a study done by Kadashetti V et al., multivariate analysis showed risk factors like occupation, education, income smoking habits, duration and frequency of chewing habits were significantly (p<0.001)

associated with development of OPMDs and oral cancer [16]. In the present study many inherent bias of case-control design were eliminated by matching (age and sex matching) and adjusting the confounding factors in multiple logistic regression analysis. The question of Berkesonian bias was eliminated by selecting cases and controls from field areas. The risk factors which are found to statistically significant are highly amendable for primary and secondary level of prevention.

Limitation(s)

Though, the study could control many of the inherent biases, memory/recall bias couldn't be completely eliminated. But this was minimised by asking the subject to remember certain important local events of life. In Univariate and multiple logistic regression analysis, even though odds ratio was high for alcohol and fruits intake, it was not found to be statistically significant. So further studies with larger sample size are recommended.

CONCLUSION(S)

The risk factors such as occupation, smoking, chewing tobacco, and vegetables intake were significantly associated with the risk of development of OPMDs. The oral premalignant lesion is an intermediate clinical state with increased risk of cancer, which can be recognised and treated with a much better prognosis compared to the fullblown malignancy. Thus, there is a great need to augment tobacco control measures, health education to the public about harmful effects of tobacco consumption.

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