Effect of tobacco, alcohol, and smoking habits in oral precancer with histological proven epithelial dysplasia

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ABSTRACT

Objectives: To assess the effect of risk factors tobacco, alcohol, and smoking habits in oral precancer patients with epithelial dysplasia status.

Material and methods: The study sample included biopsy proven cases of 29 oral submucous fibrosis (OSMF) and 43 cases of clinical leukoplakia. Histopathological diagnosis was made from formalin fixed paraffin embedded tissues as per WHO criteria. The relevant clinical and demographic details were recorded after interviewing the patients. Risk for tobacco, alcohol and smoking was determined by logistic regression analysis by SPSS software.

Results: Presence of epithelial dysplasia was significantly associated with tobacco in OSMF & both tobacco and smoking habits in leukoplakia. In OSMF tobacco was associated with 14.16-fold (95% CI, 1.36–147.07; $p < 0.026$) and in leukoplakia tobacco was associated with 4.66-fold (95% CI, 1.00–21.63; $p < 0.047$) and smoking was associated with 9.20-fold (95% CI, 1.65–51.28; $p < 0.011$) increased risk of epithelial dysplasia.

Conclusion: Tobacco consumption was independent risk factor for epithelial dysplasia in OSMF and both tobacco and cigarette smoking were independent factors for epithelial dysplasia in leukoplakia.

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Keywords: Oral precancer, Epithelial dysplasia, OSMF, Leukoplakia, Tobacco

INTRODUCTION

Oral habits like tobacco chewing in the form of betel quid areca nut, smoking and alcohol consumption are most prevalent in Indian population. India accounts for 86% of the world's oral cancer cases, as per the data from National Institute of Public Health (February 2011). Several factors influence the epithelial dysplasia status; duration of the lesion, age of patient, intra oral site, risk habit and infection with human papillomavirus (HPV) and Candida. It is likely that as the lesion is present for

years and decades there could be changes to dysplasia status, some worsening and other resolving.¹ The presence of epithelial dysplasia is one of the most important predictors of malignant development in pre-malignant lesions.² Oral submucous fibrosis (OSMF) and leukoplakia are clinically distinct precancerous lesions that precede the development of oral cancer.³ Thus, the challenge within the field of oral precancer is to predict which lesions will eventually develop into carcinoma and what are the risk factors that may be involved in development of epithelial dysplasia.

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The aim of this study was to assess the effect of three important risk factors; tobacco, alcohol, and smoking habits in oral precancer patients with histological proven epithelial dysplasia.

MATERIAL AND METHODS

Tissue biopsies were taken from cases of 29 OSMF and 43 clinical leukoplakia from the Departments of Oral and Maxillofacial Surgery and Otolaryngology after obtaining the Institutional Ethical approval and informed written consent from the patients from year 2007 to year 2011. The relevant clinical and demographic details were recorded after interviewing the patients.

Histopathological examination

All oral tissues were fixed in 10% neutral buffered formalin and processed for histopathological examination as per standard procedure. 5 µm thick sections were cut and stained with haematoxylin and eosin (H&E). Sections were reviewed by two independent pathologists and histological diagnosis was made as per WHO criteria.

Statistical analysis

Statistical analysis was performed using version 17.0 SPSS software for windows (SPSS, INC, Chicago, IL). For assessing proportional data, chi-square test was carried out. Logistic regression was applied to evaluate hazard ratios for the dysplasia. Odds ratios (OR) with 95% confidence interval (95% CI) and *p* values were calculated. For all the tests, a *p*-value <0.05 was considered statistically significant.

RESULTS

Clinicopathological characteristics of patients

The study population included 72 cases of oral precancer which included 29 cases of OSMF and 43 cases of oral leukoplakia as shown in Table 1. Epithelial dysplasia was present in 62.07% (18/29) cases of OSMF and 76.74% (33/43) cases of leukoplakia. Buccal mucosa was the most common site for OSMF and leukoplakia. In OSMF tobacco 79.31% (23/29) using habit was most prevalent where as in leukoplakia tobacco and smoking, both habits 58.14% (25/43) were prevalent.

Association of clinical characteristics of patients with dysplasia in OSMF

Epithelial dysplasia status was significantly (*p* < 0.010) associated with presence of tobacco habit in OSMF as

Table 1 Clinical characteristics of patients.

Characteristics	OSMF (n = 29)	Leukoplakia (n = 43)
Age		
<35	13	15
≥35	16	28
Sex		
Male	19	35
Female	10	8
Topological site		
Tongue	1	7
Buccal mucosa	23	28
Lip	1	2
Palate	3	1
Retromolar region	1	1
Buccal vestibule	0	2
Gingivobuccal sulcus	0	2
Dysplasia		
Present	18	33
Absent	11	10
Tobacco		
Present	23	25
Absent	6	18
Alcohol		
Present	8	20
Absent	21	23
Smoking		
Present	11	25
Absent	18	18

shown in Table 2. No association was found with epithelial dysplasia status in OSMF with age, sex, alcohol and smoking habits.

Association of clinical characteristics of patients with dysplasia in leukoplakia

Epithelial dysplasia status was significantly associated with presence of tobacco (*p* < 0.039) and smoking (*p* < 0.005) habits in leukoplakia as shown in Table 3. No association was found with epithelial dysplasia status in leukoplakia with age, sex and alcohol habit.

Logistic regression analysis of risk factors in precancer with dysplasia status

Risk with age, sex, tobacco, alcohol and smoking habits for epithelial dysplasia was evaluated by univariate logistic regression and found that tobacco and smoking habits were associated with 4.43-fold (95% CI, (1.47–12.75); *p* < 0.008) and 4.96-fold (95% CI, 1.56–15.67;

Table 2 Association of clinical characteristics of patients with epithelial dysplasia in OSMF.

Characteristics	OSMF with epithelial dysplasia (n = 18)	OSMF without epithelial dysplasia (n = 11)	p-Value
Age			
<35	8	5	0.958
≥35	10	6	
Sex			
Male	13	6	0.331
Female	5	5	
Tobacco			
Present	17	6	0.010
Absent	1	5	
Alcohol			
Present	13	8	0.976
Absent	5	3	
Smoking			
Present	10	8	0.335
Absent	8	3	

$p < 0.006$) increased risk of epithelial dysplasia in pre-cancer, respectively as shown in Table 4. In OSMF tobacco was associated with 14.16-fold (95% CI, 1.36–147.07; $p < 0.026$) and in leukoplakia tobacco was associated with 4.66-fold (95% CI, 1.00–21.63; $p < 0.047$) and smoking was associated with 9.20-fold (95% CI,

Table 3 Association of clinical characteristics of patients with dysplasia in leukoplakia.

Characteristics	Leukoplakia with epithelial dysplasia (n = 33)	Leukoplakia without epithelial dysplasia (n = 10)	p-Value
Age			
<35	12	3	0.711
≥35	21	7	
Sex			
Male	27	8	0.897
Female	6	2	
Tobacco			
Present	11	7	0.039
Absent	22	3	
Alcohol			
Present	15	5	0.801
Absent	18	5	
Smoking			
Present	23	2	0.005
Absent	10	8	

Table 4 Logistic regression analysis of risk factors with dysplasia status in OSMF, leukoplakia and precancer.

Variables	OR (95% CI)	p-Value
OSMF (n = 29)		
Age	1.04 (0.23–4.70)	0.958
Sex	0.46 (0.09–2.22)	0.335
Tobacco	14.16 (1.36–147.07)	0.026
Alcohol	1.02 (0.19–5.50)	0.976
Smoke	2.13 (0.42–10.78)	0.359
Leukoplakia (n = 43)		
Age	0.75 (0.16–3.45)	0.712
Sex	0.88 (0.14–5.29)	0.897
Tobacco	4.66 (1.00–21.63)	0.047
Alcohol	0.83 (0.20–3.43)	0.801
Smoke	9.20 (1.65–51.28)	0.011
Precancer (n = 72)		
Age	0.95 (0.33–2.71)	0.929
Sex	0.55 (0.17–1.69)	0.298
Tobacco	4.43 (1.47–12.75)	0.008
Alcohol	1.04 (0.36–2.98)	0.929
Smoke	4.96 (1.56–15.67)	0.006

1.65–51.28; $p < 0.011$) increased risk of epithelial dysplasia.

DISCUSSION

The present study evaluated the risk factors that were responsible for presence of epithelial dysplasia in pre-cancer. The study samples included only biopsy proven cases of OSMF and leukoplakia with and without epithelial dysplasia. In this study we observed that tobacco consumption was found to be an independent risk factor for OSMF patients with epithelial dysplasia. The relative risk (OR) for having epithelial dysplasia in OSMF for tobacco was 14.16. Ahmad et al⁴ found that 152 out of 157 patients used gutka and other areca nut products. Tobacco contains up to 50 potential carcinogens, such as nitrosamines and polycyclic aromatic hydrocarbons. Some of them may cause mutations of the p⁵³ tumour-suppressor gene or other genes that disrupt cell-cycle regulation and modulation of the immune systems.⁵ We found that tobacco was strongly associated with both OSMF and leukoplakia. This study showed that the risk of OSMF at each exposure level of tobacco was stronger than that of leukoplakia. C H Lee et al³ also suggested that tobacco in the form of betel quid chewing was strongly associated with both these oral diseases, the attributable fraction of leukoplakia being 73.2% and of OSMF 85.4%. They suggested that although betel quid chewing was a major cause for both leukoplakia and OSMF, its effect might be different between the two diseases.

Cigarette smoking has an important role in the development of epithelial dysplasia in oral leukoplakia. It was found that tobacco and smoking habits were the risk factors associated with epithelial dysplasia in leukoplakia patients. Kulasegaram et al⁶ found the relative risk of having a dysplastic lesion for smokers compared with non-smokers, or ex-smokers for more than 10 years, was 7.00. We found the relative risk for having epithelial dysplasia in precancer for smoking was 9.20 and for tobacco it was 4.66.

We did not find significant risk for alcohol consumption for epithelial dysplasia in OSMF and leukoplakia. Other studies also did not find overall increased risk with alcohol.^{3,6} Although ethanol has been recognized as a solvent that may damage the oral cells and increase the mucosal penetration of certain oral carcinogens,⁷ the role of alcohol drinking in the development of precancer is still unclear.

In summary tobacco was independent risk factor for epithelial dysplasia in OSMF and both tobacco and cigarette smoking were independent factors for epithelial dysplasia in leukoplakia.

CONFLICTS OF INTEREST

All authors have none to declare.

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