Original Article

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# Recurrent Aphthous Ulcers Among Tobacco Users- Hospital Based Study

Dentistry Section

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## ABSTRACT

**Context:** Current evidence shows ambiguous relationship between tobacco use and the occurrence of aphthous.

**Objectives**: We studied the relationship between the occurrence of recurrent aphthous ulcers and various forms of tobacco usage.

**Materials and Methods**: A hospital based case control study was carried out in a dental teaching hospital in Cochin, India. One hundred and two outpatient subjects (Males 56.9%) were identified having aphthous ulceration using Natha's diagnostic criteria and were classified as cases. One hundred and eight subjects (Males, 70.4%) with no aphthous ulceration were selected randomly as controls. Exposure ascertainment of tobacco usage was done by structured interview.

**Results**: The adjusted odd ratio was found to be 0.41 (95% CI 0.19-0.87) for tobacco usage and occurrence of aphthous ulceration compared to non tobacco users. The odds ratio of 0.41 for tobacco usage infers that subjects using tobacco were 59% less likely to have aphthous ulcerations compared to nontobacco users.

**Conclusion**: The tobacco consumers have less frequency of aphthous ulceration compared non users.

**Keywords:** Aphthous ulcer, Smoking tobacco, Smokeless tobacco

## INTRODUCTION

Recurrent aphthous ulcers (RAU), also known as "canker sores" or "aphthous 'stomatitis," are characterized by ulcerations of the oral mucous membranes. RAU is poorly understood mucosal disorder and is found in men and women of all ages, races, and geographic regions [1]. Morbidity is quite high in recurrent aphthous ulceration; quality of life of patients with aphthous ulceration is affected in that the recurrent and painful intraoral mucosal lesions give discomfort while eating, drinking, and speaking [2]. Several possible risk factors like auto immunity, food allergy, hematological disorders, heredity, psychological stress, viral infections, immunodeficiency and local trauma have been proposed as initiating factors of aphthous lesions [3]. The exact aetiology of recurrent aphthous ulceration is still unknown; most patients with recurrent aphthous ulceration are usually given some medications to relieve their symptomatic pain only, instead of an etiologic screening [3].

Recurrent aphthous ulceration may be associated with several systemic diseases and despite extensive investigations; studies have failed to find the exact aetiology and pathophysiology of recurrent aphthous ulceration [4]. Among the various proposed factors tobacco use is the one which is most debatable and confused one. Logically tobacco usage should lead to occurrence of aphthous ulcers as it causes injury or chronic irritation to the oral tissues. A study has shown that smoke known to increase the occurrence of the RAU [5]. However in contrary number of studies [5-7] have shown negative relationship between occurrence of the RAU and smoking. The positive therapeutic effects of smoking and the symptomatic alleviation of aphthous ulcerations have been studied [8]. The negative correlation between the RAU and tobacco undermines harmful effect of tobacco to health. It nevertheless provokes thought in the direction of the potential use and inhibitory effects of smoking on the occurrence of aphthous ulceration. Does smoking play a significant role in inhibiting the formation of aphthous lesions? The previous studies have used the descriptive designs to understand the association. In present study we tested association between the occurrence of recurrent aphthous ulcers and various forms of tobacco usage using analytical methods.

## MATERIALS AND METHODS

**Study Design:** We used hospital based case control design to assess the association between aphthous ulcer and usage of tobacco.

**Study settings:** The study population consists of out-patients attending the Department of Public Health Dentistry and Oral Medicine of a dental college in India, from the period of June to July 2012.

The study was cleared by the institutions ethics committee of a medical institution in India. Written informed consent was obtained and documented from the selected eligible subjects for the participation in the study.

### Subject selection

**Case definition and selection:** Those patients having aphthous ulcer in the oral cavity using diagnostic criteria of Nathas [9] were classified as cases. The patient aged 18 y and above visiting the Department of Oral Medicine of dental school seeking treatment for Aphthous ulcer or other reasons were selected for the study. The patients with known history of systemic disease like gastrointestinal disorders, on medication were excluded.

**Control definition and selection:** Controls were those presenting without any type of ulcers as assessed by using criteria of Natha's criteria's [9] and those who did not experience ulceration for past six months. The patients or patient attendant aged 18 y and above visiting the same department for treatment for other than aphthous ulcer were included as controls.

**Assessment of Aphthous ulceration:** The aphthous ulceration were assessed according to size, site of location, duration and number of ulcers etc., both visual and tactile examination were carried out. Natha's criteria's were used by the investigators which included four major and ten minor criteria's. The diagnosis of aphthous ulceration is established if all four major and one minor criteria is established. The screening for cases and controls was carried out by the two dentists trained for this purpose.

**Ascertainment of exposure:** All the selected cases and controls were interviewed for tobacco usage. A pretested interview schedule developed specifically for this study was used in the face-to-face interview by a trained recorder. The pretested, questionnaire consisting of both open and closed ended questions was used to record the demographic details, tobacco usage history etc. as a part of interview. To avoid the interviewer bias the clinical proforma was coded and was not known to interviewer during the ascertainment

| Variable Place of residence | Cases | | Controls | |
|---|---|---|---|---|
| | N | % | n | % |
| Rural | 93 | 91.2 | 97 | 89.9 |
| Urban | 09 | 8.8 | 11 | 10.1 |
| **Age (years)** | | | | |
| 18 – 25 | 12 | 11.8 | 10 | 9.3 |
| 26 – 35 | 27 | 26.5 | 24 | 22.2 |
| 36- 45 | 19 | 18.6 | 29 | 26.8 |
| 46- 55 | 21 | 20.6 | 11 | 20.2 |
| 56 and above | 23 | 22.5 | 34 | 31.5 |
| **Gender** | | | | |
| Male | 58 | 56.9 | 76 | 70.4 |
| Female | 44 | 43.1 | 32 | 29.6 |
| **Education** | | | | |
| Primary school | 12 | 11.8 | 13 | 12.2 |
| Middle school | 08 | 7.8 | 19 | 17.4 |
| High school | 60 | 5.8 | 54 | 50 |
| Graduate | 22 | 21.6 | 19 | 17.4 |
| No tobacco usage | 81 | 79.4 | 69 | 63.8 |
| Tobacco usage | 21 | 20.6 | 39 | 36.1 |
| Smoking tobacco | 16 | 15.7 | 28 | 25.9 |
| Chewing tobacco | 01 | 9.8 | 05 | 4.6 |
| Usage of both forms of tobacco | 04 | 3.9 | 06 | 5.5 |

**[Table/Fig-1]:** Descriptive characteristics of the study population

| Variable | Reference | p-value | Odds ratio | C I Lower | 95% Upper |
|---|---|---|---|---|---|
| Tobacco user | Non tobacco user | 0.02 | 0.41 | 0.19 | 0.87 |
| Male | Female | 0.31 | 0.70 | 0.35 | 1.39 |
| Urban | Rural | 0.50 | 1.43 | 0.51 | 3.87 |
| 18 to 25 years | > 56 years | 0.97 | 1.01 | 0.34 | 3.04 |
| 26 to 35 years | > 56 years | 0.18 | 2.13 | 0.69 | 6.59 |
| 36 to 45 years | > 56 years | 0.23 | 0.47 | 0.13 | 1.62 |

**[Table/Fig-2]:** Regression of occurrence of aphthous ulceration, Dependent variable is occurrence of Aphthous ulcer

of the exposure. Hence, interviewer did not know the disease status during the exposure ascertainment. A set of clinical photographs of aphthous ulcerations were used to show to the subjects, which would help them in easy recognition and understanding of the aphthous ulcers for which they need to answer the questions in relation to history of aphthous ulceration. This was done to eliminate the recall or memory bias. The standardization and calibration of interviewer and clinical examiner with regard to clinical examination of ulcer and interview technique were carried out before and during the study.

**Sample Size:** The sample size estimation was done using N Master 2006 version 1.0 software developed Christian Medical College, Vellore, India (Permission obtained and there is no conflict of interest with the authors or Christian Medical College, Vellore). The sample size estimation was done using alpha at 5% and power of 80%. The prevalence of aphthous ulceration in patients using tobacco was estimated at 0.18% [10]. Risk difference was estimated to be 0.13. The calculated sample size was 93 in each arm (case and control). To ensure adequate numbers for other covariates, 10% excess was added to the total sample size. We identified 102 cases and 108 controls.

## STATISTICAL ANALYSIS

The statistical analysis was carried out using SPSS software version 17. Chi-square test, Odds ratio and Logistic analysis tests were employed to check the statistical variations for significance and to ensure that the other variables are controlled and the effect of tobacco is accurately determined.

## RESULTS

Descriptive characteristics of cases and controls are given in [Table/Fig-1]. Because it was an unmatched case–control study, there were variations in the distribution of cases and controls in terms of characteristics. Among the tobacco users, smoking tobacco users had the odds of 0.48 (95% CI 0.97-0.24), when compared to smokeless tobacco users who had odds ratio of 0.17 (95% CI 1.49-0.01) for getting aphthous ulceration.

The multivariate analysis was carried out to find out influence of covariates on occurrence of the aphthous ulcer. The adjusted odd ratio was found to be 0.41 (95% CI 0.19-0.87) for tobacco usage and occurrence of aphthous ulceration compared to non tobacco users. The odds ratio of 0.41 for tobacco usage infers that subjects using tobacco 59% less likely to have aphthous ulcerations compared to nontobacco users. Males had odds of 0.70 (95% CI 0.35-1.39) for having aphthous ulceration compared to females. Subjects within the age group of 36 to 45 y had the odd ratio of 0.47 (95% CI 0.13–1.62) compared to 56 y and more aged subjects for experiencing aphthous ulceration [Table/Fig-2].

## DISCUSSION

The results of this study showed occurrence of aphthous ulceration in both tobacco and nontobacco users among cases and control groups. The prevalence between tobacco users and nontobacco users was significantly different among cases and controls. Our findings are in line with previous studies that found a negative epidemiological association between tobacco use and aphthous ulceration [5-7]. However these studies were observational studies on fewer patients or recruited a small number of patients with aphthous ulceration [11] compared to our study which was a case control study. The results of this study revealed that the tobacco use was widespread and was found to be 36.1% [12].

The confounding factors for the occurrence of the RAU were controlled at design stage by restriction of those subjects. Later at the analysis stage using the regression models, the natural confounders like demographic confounders were adjusted for the association between tobacco users and occurrence of the RAU. The adjusted strength shows the 51% (OR.41 (95% CI 0.19-0.87) protective effect by the use of the tobacco on the occurrence of RAU. This effect is considerable but the biological plausibility is very important to understand the association. The literature on the "protective effect" of tobacco use particularly smoking on aphthous ulceration has been debated particularly with respect to a possible underlying mechanism. It has been suggested smokers have increased keratinization of the oral mucosa [6,13,14]. The keratinization protects the oral tissues against the trauma or bacterial penetration. Multiple substances are systemically absorbed from cigarette smoke, however, and it is possible that one of these absorbed constituents promotes keratinization may be hyperkeratosis and also it is typically localized to the mucosal area where the smokeless tobacco is held. Although hyperkeratosis may be a premalignant condition, it is possible that it prevents aphthous ulcers through a local protective effect on the oral mucosa [14]. Also there are confusions whether nicotine present in tobacco induces the protective effect or one of the constituents of the tobacco products [11]. Since, nicotine is systemically absorbed in smokers compared to smokeless tobacco, hence former should have less protective effect than latter.

The theory that nicotine is the protective factor is supported by a recent report that aphthous ulcers were prevented among those nonsmokers with recurrent aphthous ulcers while they used nicotine gum [13,14].

Even though it was hospital based study the exposure (tobacco usage) prevalence among controls was consistent with prevalence

of tobacco use in general population in Kerala state. The distribution of case and controls was skewed in demographic variables as it was unmatched design. It is worthy to note that this is not absolute proof that tobacco use is responsible for decrease in aphthous ulceration as found in our study, since other factors could be involved which were not considered in our study such as increased stress and depression, which usually affect these subjects and also the sample size was not to large enough to generalize the findings.

The negative association of occurrence of RAU and usage of tobacco needs to have substantial biological plausibility. However, it does not amount to conclude that the usage of the tobacco is beneficial to prevent aphthous ulceration. It is not compatible with general health principles advocated by the health professions for the harmful use of tobacco effects, a factor related to smoking or smoking habits may nevertheless be influential in providing some directional indicators for the symptomatic alleviation of these ulcerations in extreme cases. It is not the object of this report to prove that smoking is therapeutic or beneficial; rather, we want to emphasize the need for researching even the remote variables associated with aphthous ulcerations of the mouth. The highly statistical negative associations presented at this time between smoking and decreased experience with aphthous ulcerations indicates that certain predisposing unknown factors of immunity may be present in tobacco products or unknown confounders. To understand the natural history of the RAU and its association with tobacco needs to be evaluated by the cellular to histopathologically to clinical research or should have continuation of science bandwagon. Using the animal models of testing the association would be ideal to know the biological plausibility.

However, it should be further emphasized that, although there is an association between the two variables, it is difficult to conclude a causative relationship between them. One can merely suggest that there is some sort of association. The problem of causation cannot be answered solely by the statistical analysis of data.

## CONCLUSION

The study found the statistical association between the occurrence of recurrent aphthous ulceration and usage of tobacco. The association that exists between smoking and aphthous ulcerations of the mouth is in a negative direction. The tobacco users tend to have 45 % less chance of occurrence of recurrent aphthous ulcer than non-tobacco users.

## REFERENCES


[1] Embil JA, Stephens RG, Manuel FR. Prevalence of recurrent herpes labialis and aphthous ulcers among young adults on six continents. *Canadian Medical Association Journal.* 1975;113:627.

[2] Jurge S, Kuffer R, Scully C, Porter SR. Number VI recurrent aphthous stomatitis. *Oral diseases.* 2006;12:1–21.

[3] Preeti L, Magesh KT, Rajkumar K, Karthik R. Recurrent aphthous stomatitis. Journal of oral and maxillofacial pathology: *JOMFP.* 2011;15:252.

[4] Scully C, Felix DH. Oral medicine--update for the dental practitioner. Aphthous and other common ulcers. *Br Dent J.* 2005;199:259–64.

[5] Tüzün B, Wolf R, Tüzün Y, Serdaro\uglu S. Recurrent aphthous stomatitis and smoking. *International journal of dermatology.* 2000;39:358–60.

[6] Axéll T, Henricsson V. Association between recurrent aphthous ulcers and tobacco habits. *Scand J Dent Res.* 1985;93:239–42.

[7] Atkin PA, Xu X, Thornhill MH. Minor recurrent aphthous stomatitis and smoking: an epidemiological study measuring plasma cotinine. *Oral Dis.* 2002;8:173–76.

[8] Chellemi SJ, Olson DL, Shapiro S. The association between smoking and aphthous ulcers. A preliminary report. *Oral Surg Oral Med Oral Pathol.* 1970;29:832–36.

[9] Natah SS, Konttinen YT, Enattah NS, Ashammakhi N, Sharkey KA, Häyrinen-Immonen R. Recurrent aphthous ulcers today: a review of the growing knowledge. *Int J Oral Maxillofac Surg.* 2004;33:221–34.

[10] National Oral Health Survey & Fluoride Mapping 2002. *Dental Council of India.* 2002- 2003; 33pp.

[11] Rivera-Hidalgo F, Shulman JD, Beach MM. The association of tobacco and other factors with recurrent aphthous stomatitis in an US adult population. *Oral Dis.* 2004;10:335–45.

[12] Thankappan KR, Thresia CU. Tobacco use & social status in Kerala. *Indian J Med Res.* 2007;126:300–08.

[13] Shapiro S, Olson DL, Chellemi SJ. The association between smoking and aphthous ulcers. *Oral Surg Oral Med Oral Pathol.* 1970;30:624–30.

[14] McRobbie H, Hajek P, Gillison F. The relationship between smoking cessation and mouth ulcers. *Nicotine Tob Res*. 2004;6:655–59.



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