ORIGINAL ARTICLE

Incidence of Aphthous Ulcers in All Forms of Tobacco Users, Mixed Habits and Non-Users

Rabia Masood, Hadia Malik, Laiba Gul, Zarmeena Imtiaz, Ume Hani Sajjad

ABSTRACT

Objective: The aim of this study was to test the association between recurrent aphthous ulcers and different forms of tobacco habits.

Study Design: Hospital based cross-sectional study.

Place and Duration of Study: The study population consisted of patients attending the Out Patient Department of Islamic International Dental Hospital Islamabad. A hospital based study is carried out for 2 successive months (July-August) 2018.

Materials and Methods: Study was conducted on 500 patients to assess the presence of aphthous ulcers. Questionnaire based data was collected along with the clinical examination. Questionnaire included both quantitative and qualitative variables. Quantitative variables; Age, Frequency of addictive habits, Duration of addiction, Size of ulcer, No. of lesions, Duration of ulcer and Qualitative variables; All types of Addictive habits (smoking and smokeless tobacco), Medical history, Frequency of recurrence of ulcers, Site of ulceration, Type of aphthous ulcers. Statistical analysis was carried out using SPSS software version 23 and chi-squared test was applied.

Results: Out of 500 subjects, 33 (6.6%) participants presented with aphthous ulcers. 78 subjects had addictive habits of smoking tobacco. Among them, Cigarette Smokers were 75 (15%), Hookah Smokers were 2 (0.4%) and 1 was a Bidi Smoker (0.2%). 23 subjects had addictive habits of using smokeless tobacco. Among which, Paan Chewers were 7 (1.4%), Gutka Chewers were 3 (0.6%) and 13 were Naswar Chewers (2.6%).

Conclusion: Although no significant association has been found between aphthous ulcers and smoking habits but ulcers were found to be lower in patients who are smokers as compared to the non-smokers.

Key Words: *Stomatitis, Aphthous Ulcer, Tobacco Smoking, Smokeless.*

Aphthous ulcer is a common condition, also known as “canker sores” or “aphthous stomatitis”. The term aphthae is derived from Greek word “Aphthi” which means “to set on fire” or “to inflame”.[1,2] It is characterized by the repeated formation of benign and non-contagious ulceration of the oral mucous membrane.[3] The ulcers present as lesions having yellow ulcerated base surrounded by erythematous halos and covered by fibrino-purulent membrane.[4,5] [6]Morbidity of Recurrent Aphthous Ulcer (RAS) is quite high affecting quality of life of patients in a way that they are painful and recurrent mucosal lesions causing discomfort while eating, drinking and speaking.

There are three clinical variations of aphthous stomatitis;

- Minor aphthous ulceration
- Major aphthous ulceration
- Herpetiform aphthous ulceration

Exact etiology of RAS is unknown but the condition is associated with multiple factors including autoimmunity, genetic predispositions, hematologic abnormalities (anemia), HIV, hormonal fluctuations, arthritis, stress/anxiety, nutritional deficiencies, trauma, drugs, food hypersensitivity, smoking cessation and allergies.[1,3,5,7]

RAS is associated with human leukocyte antigen (HLA) and immune-dysregulation. Lymphocytes are the predominant cells in pathogenesis of RAS with a variation in CD4:CD8 ratio during pre-ulceration, ulceration, and healing stage. [4,5] Tobacco reduces immunity and T cell response to various antigens so that the association appears to be biologically plausible. [8]

Department of Oral Pathology
Islamic International Dental College
Riphah International University, Islamabad

Correspondence:
Dr. Rabia Masood
Assistant Professor
Department of Oral Pathology
Islamic International Dental College
Riphah International University, Islamabad
E-mail: drrabiamasood@gmail.com

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The management of patients with RAS comprises application of topical analgesics, corticosteroids, antibiotics and anti-inflammatory agents that only provide symptomatic relief.[13]

There are different types of tobacco being used in Pakistan which includes *smoking tobacco* i.e. cigarettes, cigar, pipe, hookah, shisha and bidi and *smokeless tobacco* include paan, gutka, naswar, oral snuff, snuss (moist snuff), khaini (tobacco and lime) and lozenges.

Although studies have failed to find the exact etiology of Recurrent Aphthous Stomatitis but tobacco use is the one most debatable and confused anticipated factor as tobacco usage is associated with various oral pathologies such as Oral squamous cell carcinoma, periodontitis, gingivitis, tobacco pouch keratosis, oral sub mucous fibrosis and nicotine stomatitis etc., so tobacco usage should logically lead to occurrence of Recurrent Aphthous Stomatitis. However, in contrast to this a number of studies have shown negative correlation between RAS and tobacco usage and positive therapeutic effects of smoking. [3] Tobacco usage causes thickening (keratinization) of oral mucosa which renders the mucosa less susceptible to ulceration. [4 5] Smokers quitting with nicotine chewing gums have less chances to develop ulcers than those without nicotine replacement therapy. [9]

Previous studies have suggested negative association between tobacco usage and RAU but most of those studies assessed relationship between RAS and tobacco by using methods that were based on interviews, questionnaire, or on self-reporting of smoking status.[3,10,11]

However, the studies that were previously carried out did not evaluate occurrence of aphthous ulcers in different forms of tobacco users, mixed habits and non-users. In our study we wanted to evaluate the strength of association between occurrence of aphthous ulcer and tobacco usage and incidence of aphthous ulcer among different types of tobacco users in our population and comparing them with non-users because no such study has been done in our community.

The objective of this study was to assess the association between recurrent aphthous ulcers and different forms of tobacco habits.

Materials and Methods

Hospital based cross-sectional study design was used to assess the incidence of aphthous ulcers in tobacco users, non-users and those with mixed habits.

The study population consisted of patients attending the Out Patient Department of Islamic International Dental Hospital Islamabad. A hospital based study was carried out for 2 successive months (July-August) 2018. Study was conducted on 500 patients who visited OPD of dental hospital for seeking dental treatment. All subjects were interviewed and a structured questionnaire was developed to record their details. The questionnaire contained four main sections (addictive habits/tobacco usage history, aphthous ulcer related medical history, ulcer characteristics and demographics). The *Addictive habits section* had two domains; Smoking tobacco domain comprised of six tobacco usage habits (smoking cigarettes, cigar, hookah, pipe, shisha, bidi) and Smokeless tobacco domain also had six habits (paan, ghutka, naswar, snuff, lozenges, other habits). *Medical history* associated with the occurrence of aphthous ulcers included Anemia, HIV, Hormonal fluctuations, GI disorders, Arthritis, Stress/anxiety, Allergies and genetic predisposition. *Ulcer characteristics* comprised size of ulcer, number of lesions, site of ulceration, frequency of recurrence and duration of ulcers.

Informed Consent was taken from all the participants before conducting the study. The participants were asked whether they had oral ulcers (aphthous ulcers) present in their mouth after describing aphthosis to them as recurrent painful ulcers. Additional information about ulcers like duration, location, size, recurrence, and no. of ulcers was noted. Moreover, risk factors that might be related to condition were inquired (stress, hormonal factors, GD disorders, allergies).

Participants were classified into 3 groups and the selection criteria for the groups are given below:

Control Group:

Inclusion criteria included male and female of 15 years and above, subjecting without any ulcers and without any addictive habits.

Exclusion criteria included patients under 15 years, subjecting with ulcers and with addictive habits

Smokers group:

Inclusion criteria included male and female patients of 15 years and above, subjecting with smoking habits (Cigarette, cigar, pipe, hookah, shisha, bidi) and with/without ulcers.

Exclusion criteria included patients under 15 year

subjecting without any smoking habits.

Non-smokers group:

Inclusion criteria included male and female patients of 15 years and above, Subjecting without any smoking habits, with smokeless tobacco habits (paan, gutka, naswar, snuff, lozenges) and with/without ulcers.

Exclusion criteria included patients less than 15 years, subjecting with smoking habits and without any smokeless tobacco habits.

To assess the presence of aphthous ulcers, oral mucosal examination and questionnaire were completed for 500 patients reporting to the OPD over a 2-month interval by four examiners. History of addictive habits was taken and tobacco usage was measured on the basis of type of tobacco used, frequency of consumption per day and the duration for which the individual maintained this frequency. To avoid confounding, patients with known history of systemic diseases and other conditions that might influence occurrence of aphthous ulcer were also recorded. And finally on the basis of ulcer characteristics, aphthous ulcerations were categorized into minor, major and herpetiform ulcers.

Both quantitative and qualitative variables were part of this study.

Quantitative variables; age, frequency of addictive habits, duration of addiction, size of ulcer, no. of lesions, and duration of ulcer.

Qualitative variables; All types of Addictive habits (smoking and smokeless tobacco), Medical history, Frequency of recurrence of ulcers, Site of ulceration and types of aphthous ulcers.

Statistical analysis was carried out using SPSS software version 23. Frequency and percentages of different variables were calculated using SPSS and formulated in tables 1, 2, and 3.

Results

All 500 subjects were asked about their medical histories. Out of 500, only 5 subjects (1%) were anemic. 10 subjects (2%) had hormonal disorders related with puberty, menstrual cycle and pregnancy, 83 subjects (16.6%) had GI disorders related to acidity, 7 subjects (1.4%) had arthritis, 74 subjects (14.8) experienced stress related ulcerations during exams or social issues. 61 subjects (12.2%) were allergic to dust, pollen and medications, and 5 subjects (1%) presented with family history of recurrent ulcers.

Table I: Self-Reported Medical History of Patients

	Anemia	Hormonal	HIV	GI disorders	Arthritis	Stress	Allergies	Genetics
Frequency	5	10	0	83	7	74	61	5
Total	500	500	500	500	500	500	500	500
Percentage	1	2	0	16.6	1.4	14.8	12.2	1

Out of 500 subjects, 78 subjects had addictive habits of smoking tobacco. Among those 78, *Cigarette Smokers* were 75 (15%), *Hookah Smokers* were 2 (0.4%) and 1 was a *Bidi Smoker* (0.2%). (Graph 1). From 500 subjects, 23 subjects had addictive habits of using smokeless tobacco. And of those 23, *Paan Chewers* were 7 (1.4%), *Gutka Chewers* were 3 (0.6%) and 13 were *Naswar Chewers* (2.6%). (Graph 2). From a group of 101 subjects that presented with addictive habits of either smoking or smokeless tobacco 46 were addicted for more than a period of 7 years. Table-II illustrates distribution of duration of addiction among addicts:

Table II: Duration of Tobacco Addiction

Duration of Addiction	Frequency (percentages)
Less than 2 years	8 (1.6%)
2-5 years	22(4.4%)
5-7 years	25 (5%)
7-10 years	12 (2.4%)
More than 10 years	34 (6.8%)
Total	101 (20.2%)

33 (6.6%) participants presented with aphthous ulcers. Pertaining to the ulcer characteristics given in **Table III**, 2 patients presented with Major Aphthous Ulceration and 31 patients presented with Minor Aphthous Ulcerations. None of the patients presented with Herpetiform Aphthous Ulcerations during the period of sample collection. And out of these 33 subjects who presented with aphthous ulcers, 5 were cigarette smokers while remaining 28 had no history of any addictive habits (smoking or smokeless tobacco).

Presence of aphthous ulcers was correlated with self-reported medical conditions; 5 out of 33 subjects (15.1%) were allergic, 9 (27.2%) had GI disorders, 3 (9%) had hormonal disorders, 12 (36.4%) had stress-related ulcers, 4 (12.1%) had genetic association and 6 (18.2%) subjects presented without any significant medical history. Occurrence of RAU is affected by a number of other variables, with no statistically significant influence of tobacco usage.

Table III: Ulcer Characteristics

Ulcer Characteristics	Variables	Frequency (percentages)
Duration	7-14 days	28 (5.6%)
	2-6 weeks	2 (0.4%)
	5-7 days	3 (0.6%)
	Total	**33 (6.6%)**
No. of Lesions	1-5	30 (6%)
	1-10	2 (0.4%)
	10-100	1 (0.2%)
	Total	**33 (6.6%)**
Frequency of Recurrence	Non recurrent	4 (0.8%)
	Recur frequently	25 (5%)
	Recur rarely	4 (0.8%)
	Total	**33 (6.6%)**
Site of Ulceration	Non keratinized	25 (5%)
	Keratinized	8 (1.6%)
	Total	**33 (6.6%)**
Size of Individual Lesion	1-3mm	21 (4.2%)
	3-10mm	10 (2%)
	3cm	2 (0.4%)
	Total	**33 (6.6%)**
TOTAL		500

Incidence of RAU in tobacco users and non-users was statistically analyzed by using Chi-squared test. Cigarette smoking was considered to represent tobacco usage as significant number of tobacco users were cigarette smokers as compared with negligible amount of other tobacco variables. Cigarette smoking was compared with presence of RAU and type of ulcers if present. Statistical analysis of our study showed no significant association between the presence of aphthous ulcers and cigarette smoking (p value = 0.98) and between cigarette smoking and type of aphthous ulcers (p value = 0.72) as shown in the **Table IV and Table V.**

Table IV: Relationship of Cigarette Smoking with Aphthous Ulcer

Type of Ulcer	Cigarette smoking	
	Yes	**No**
Minor aphthous ulcers	5	26
Major aphthous ulcers	0	2

TABLE V: Incidence of Aphthous Ulcer among Smokers and Non-Smokers

		Cigarette smoking	
Ulcer	**Yes**	5	28
	No	70	397

Discussion

Aphthous ulcers are recurrent and painful condition of oral mucosa, etiology of which is still unknown.[3] There are certain risk factors that are associated with occurrence of RAU including immune reaction, genetic factors, hormonal factors, stress, infections, GI disorders etc. No randomized control trial have shown any treatment, that could help in preventing or curing RAU.[4]

RELATIONSHIP BETWEEN TOBACCO HABITS AND RAU: An inverse relationship is observed between RAU frequency and smoking habits according to previous studies held.[3,5,9] The observations previously made by Tony Axell and Vingent Henricsson also presents that there is a negative association between tobacco habits and RAU. According to them, surface structures like leukoedema and keratin prevent the penetration of antigenic substances into the oral epithelium.[9] Shapiro et al. found that there is a negative relation between RAU and smoking. They pointed that genetic, familial, psychological and environmental factors are important considerations in the formation of recurrent aphthous ulceration. They suggest that meaningful data can be obtained by multidisciplinary longitudinal studies. According to Banoczy and Sallay there is a negative association between keratinization of oral mucosa and aphthae.[12] The findings of the case control study given by PA Atkin, X Xu, and MH Thornhill indicate that patients with RAU have low levels of smoking than in matched controls, and they support that there is a negative correlation between minor RAU and smoking.[4] The negative correlation of smokeless tobacco with recurrent aphthous stomatitis is also given in a study by Grady et al.[3] The case control study given by Shamaz Mohamed and Chandrashekar Janakiram found the statistical association between the RAU and usage of tobacco smoking. The association that exists between smoking and aphthous mouth ulcers is negative. The non- tobacco users tend to have 55% more chance of occurrence of RAU than tobacco users.[1]

However, study carried out by Slebioda Z and Dorocka, showed there is no significant association found between smoking tobacco habits and occurrence of Recurrent Aphthous ulcers.[13]

Protective Effect of Smoking

Epidemiological studies suggest a protective effect of smoking. These studies show that mouth ulcers are more common in nonsmokers than in smokers.[4,14,15] The reason that might be associated with this protective effect of tobacco use could be increased keratinization of oral mucous membrane [3] or some substances present in cigarette smoke absorbed

causing decrease in frequency of RAU. Case studies suggest that the nicotine chewing gums are helpful for the nonsmokers who have mouth ulcers.[16] Most of the population, on cessation of smoking appear to develop RAU for the first time or any previous RAU that existed, has exacerbated.[4,17] This might possibly be due to increased keratinization of oral mucosa, antibacterial effect of tobacco smoke[17,18] or smoking cessation have effects on immune system like stress generated due to withdrawal.[17]

Comparison with Literature: Most of these previous studies assessed relationship between RAU and tobacco by using methods that were based on interviews, questionnaires, or on self-reporting of smoking status.[3,10,11]

Our study also used the same method as special questionnaire was designed according to which significantly smaller population of RAU patients were smokers (15%) as compared to control group who were nonsmokers (84.4%) in a sample of 500 patients. Most of the incidences of RAU were found among sample population who were non tobacco users. Some daily tobacco habits were found in patients among which smoking was most common habit especially cigarette smoking while some in rest of the sample were addicted to other forms of tobacco (smoking and smokeless) and no ulcers were found among them. In contrast to other studies [1 3 5 15] our study showed no significant association between presence of ulcers and cigarette smoking and no association between cigarette smoking and type of ulcers.

Limitations and Future Recommendations

The factors that might have affected our results could be that these lesion are not fixed long standing lesions, that can be evaluated at any time by the physician , but are short lived that may not be present at the time of examination[15] statistical evaluation of RAU might have been affected by this fact. In addition, the methods of assessing smoking status could be inaccurate as smokers may hide their smoking status or underestimate their level of smoking. Our study was unable to show incidence of aphthous ulcers between different genders and the medical conditions that might affect the occurrence of aphthous ulcers in our community, so in future we would suggest that further studies be carried out on these aspects.

Conclusion

Incidence of RAU in tobacco users and non-users has been assessed and statistically analyzed showing that occurrence of ulcers is lower in patients who are smokers as compared to non-smokers. However, no significant association has been found between ulcer occurrence and smoking habits. These findings substantiate with the previous similar studies and can serve as a base for further research in future.

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