

# Association of Recurrent Aphthous Ulcer among Tobacco Users - A Retrospective Study

**Running title:** Recurrent aphthous ulcer among tobacco users

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## **Abstract:**

Recurrent Aphthous Ulcer (RAU) is one of the most common painful, recurrent oral mucosal disease that can be single or multiple seen among patients. These present as round, or ovoid ulcers, with circumscribed margins, having yellow or gray floors and are surrounded by erythematous haloes. The etiology of Recurrent Aphthous Ulcer always remains unclear. Symptomatic treatment is usually done which usually includes topical corticosteroids. The aim of the study is to find out the association of recurrent aphthous ulcer among the people who use smoking and smokeless form of tobacco. The study was carried out for a 1 year period (June 2019 to April 2020). 229 patients data (213 males and 16 females) who visited Saveetha dental college and hospitals, Chennai were included. Statistical analysis was done by chi square test. In the study, it is observed that only 3.5% of the males who had tobacco usage habits were diagnosed with Recurrent Aphthous Ulcer. The patients aged between 31-40 years had higher prevalence of Recurrent Aphthous Ulcer (61.15%) compared to other age groups. Among the tobacco users only 1.75% of RAU was prevalent among smoking and smokeless groups respectively. There is no significant association between tobacco users and recurrent aphthous ulcer p value 0.625, p (>0.05). Minor aphthous ulcer (87.5%) were more commonly present compared to major aphthous ulcer among tobacco users. Within the limitations of the study, among the tobacco usage patients, males are more prevalent for Recurrent Aphthous Ulcer than females and occurrence of RAU among tobacco users were less. Though there is no association, anti tobacco counselling to be conducted frequently to educate them from harmful effects of tobacco.

**Keywords:** Recurrent aphthous ulcer (Recurrent Aphthous Ulcer), TNF-alpha, Interleukin-1.

## INTRODUCTION

Recurrent aphthous ulcer is canker sore affecting the oral mucosa, characterised by ulcerations affecting patients quality of life. (Kalpana, 2016). They are usually seen on the buccal, labial mucosa, floor of the mouth, tongue and palate (Sawair, 2010). It is characterised by the presence of a yellowish, gray base surrounded by an erythematous halo. These lesions are extremely painful and aggravates on eating, speaking and swallowing (Abdullah, 2013), (Subramanyam, 2011; Kumar and Ananthakrishnan, 2014).

Recurrent aphthous ulcer is classified based on size as minor, major, herpetiform (Sciubba, 2007). The minor aphthous ulcers are small (<1 cm in diameter), well defined, shallow, and heals within 2 weeks. The majority of aphthous ulcers are shallow ulcers that are bigger, deeper and take many weeks to heal and leave a scar behind. Herpetiform ulcers are multiple, small, (3-6 cm), shallow ulcers that take weeks to heal (Rajmaneet *et al.*, 2017).

There are several possible risk factors for initiation of Recurrent Aphthous Ulcer, they are hereditary, auto immunity, haematological stress, viral infections (Tuzunet *et al.*, 2000). 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 (Scully and Felix, 2005). In Spite of various factors the usage of smoking and smokeless forms of tobacco is still a debatable issue.

According to the Global Adult Tobacco Survey (GATS), India 2010, the prevalence of tobacco use among Indian adults is 35%. Smoking tobacco in the form of cigarettes or bidis is a common practice in India and a major chewing form is pan with tobacco. Thousands of chemical compounds are detected in both smoked as well as smokeless forms of tobacco which act not only as irritants and toxins, but also are deadly carcinogens. Nicotine, an alkaloid, is mainly

accountable for addiction, which along with tobacco-specific nitrosamines, polycyclic aromatic hydrocarbons, and many others act as potent carcinogens (Naveen-Kumar *et al.*, 2016)

Reasonably the consumption of tobacco should lead to Recurrent Aphthous Ulcer due to chronic irritation of oral mucosa. Shamaz *et al* in his study had stated that significantly higher percentage of smokers were diagnosed with Recurrent Aphthous Ulcer (Mohamed and Janakiram, 2014). On an opposing note, there are several studies that show a negative relationship between Recurrent Aphthous Ulcer and tobacco usage (Axéll and Henricsson, 1985; Atkin, Xu and Thornhill, 2002). Aim of this study is to find out the association of Recurrent Aphthous Ulcer among the patients with smoking and smokeless form of tobacco usage.

## MATERIALS AND METHODS

### Study setting

The study is university based single setting study. This is a retrospective study conducted on 229 patients (223 males and 6 females) who reported to Private Dental College, Chennai with recurrent aphthous ulcer on tobacco users. The population chose were patients whose habit history is tobacco in either smoking or smokeless form and had Recurrent Aphthous Ulcer in oral mucosa. Advantage of study is data collection flexibility and disadvantage is data not location specific. Cons of the study were location specific. Patients who use smoking and smokeless forms of tobacco were included in this study. Insufficient available data without proper history of tobacco usage and insufficient intra oral photographs were excluded from the study.

### Ethical Approval

Ethical clearance for the retrospective study was obtained from the Institutional committee (IEC), Saveetha Dental College. Ethical approval number: SDC/SIHEC/2020/DIASDATA/0619-0320.

**Data collection/ Tabulation**

The data was collected by reviewing the patients records from June 2019 to March 2020. The details of the patients age, gender, oral habits, site of recurrent aphthous ulcer were obtained. The age of the patients were grouped as follows: 31-40years, 41- 50 years, 51- 60 years, >60 years. Cross verification was done by referring case sheets and photographs. To minimise sampling bias all available data were included. All data were reviewed by 2 reviewers. All the available data obtained were entered in microsoft excel documents.

**Statistical analysis**

After excel tabulation, the data was transferred to SPSS. The analysis was done by SPSS statistical software version 23. Descriptive statistics were used to assess the frequency and association of age, gender, smoking and smokeless status. The dependent variable is recurrent aphthous ulcer. Independent variables were smoking and smokeless status, age, gender. The statistical analysis was done by pearson chi square test. The level of significance was set at  $p < 0.05$  to find the association.

**RESULTS & DISCUSSION**

Out of 229 tobacco usage patients, the majority of tobacco usage population lies between 31-40 years and was reported as 61.14% ( figure 1).

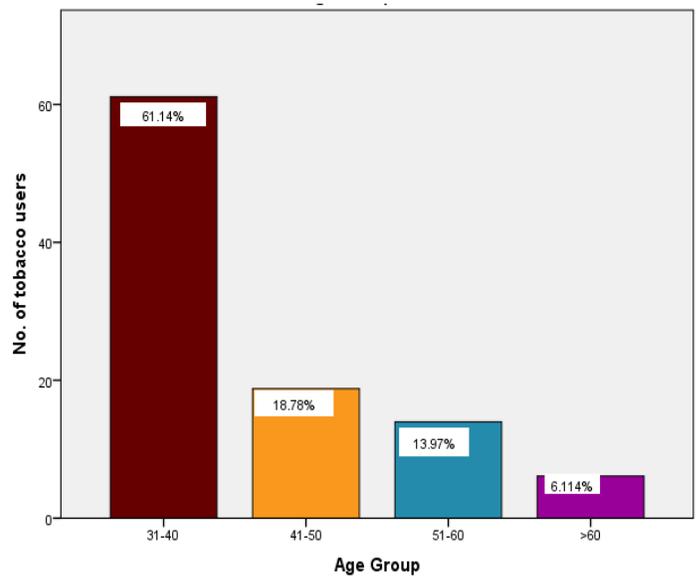


Figure 1: Bar graph depicts the percentage of age distribution in tobacco users . X axis represents age group and Y axis represents the number of tobacco users. The prevalent age group was 31-40(brown) years which was 61.1% followed by 41-50 years(orange) which was 18.78%.

Gender predilection shows that tobacco usage was higher in males (97.38%) compared to females (2.62%) ( figure 2). The prevalence of recurrent aphthous ulcer among tobacco usage population was reported to be 3.49% ( figure 3).

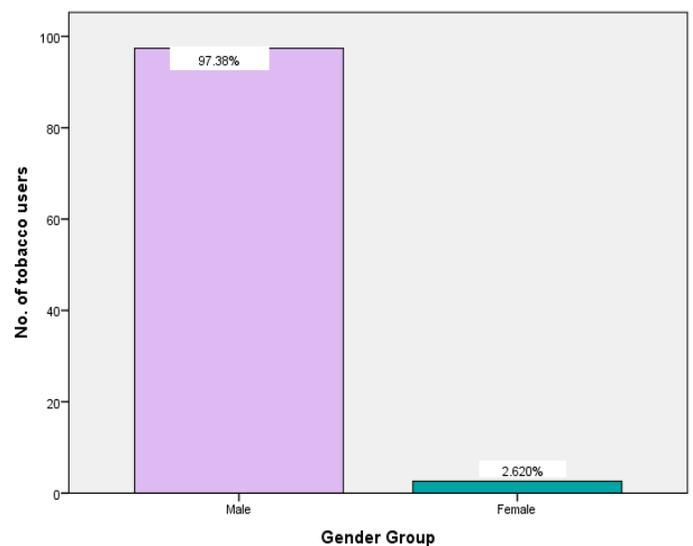


Figure 2: The bar graph depicts the percentage of gender variation among tobacco users. X axis

represents the gender group and the Y axis represents the number of tobacco users. The males(purple) were 97.4% and females( bluish green) were 2.6%.

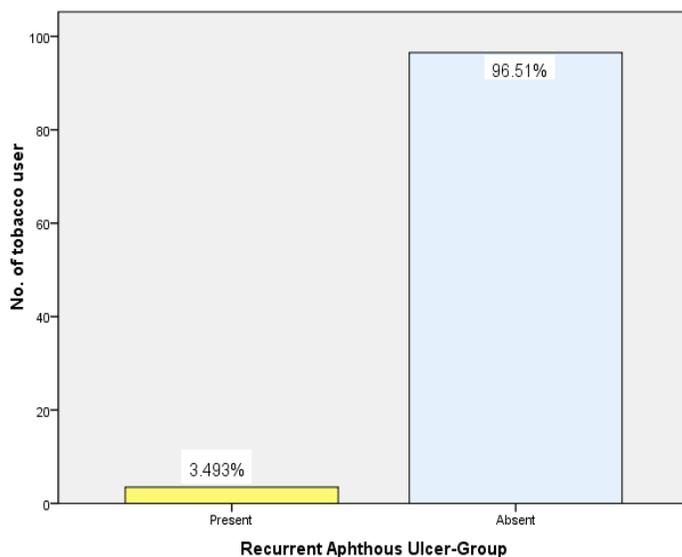


Figure 3: Bar graph depicts the percentage of Recurrent Aphthous Ulcer among tobacco users. X axis represents the Recurrent Aphthous Ulcer group and Y axis represents percentage of tobacco users. It is evident that the Recurrent Aphthous Ulcer was present ( Yellow) in 3.5% and absent (sky blue) in 96.5% of the given population.

On analysing the association between age and Recurrent Aphthous Ulcer. It is evident from the bar chart, the occurrence of Recurrent Aphthous Ulcer is prevalent in 31-40 years and was recorded 2.18%, followed by 0.87% reported between 51-60 years and 0.44% in the >60 years age group ( figure 4). Less than 30 years and between 41-50 years no Recurrent Aphthous Ulcer cases were recorded among tobacco users . The p value was 0.42 and Pearson chi square value is 2.833. There is no significant difference between age and Recurrent Aphthous Ulcer among tobacco users. Not statistically significant ( p value >0.05).

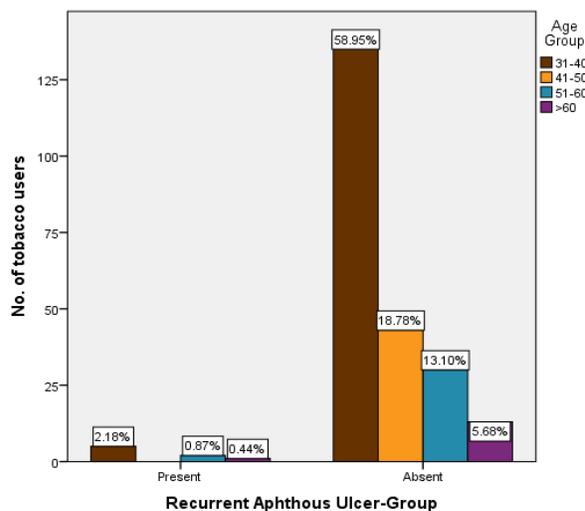


Figure 4: Bar graph depicts the association between age and Recurrent Aphthous Ulcer among tobacco users. X axis represents recurrent aphthous ulcer and Y axis represents number of tobacco users. Recurrent Aphthous Ulcer was more commonly seen in 31- 40 years(brown) compared to other age groups among tobacco users . Pearson chi square value is 2.833, p value- 0.42(<0.05), statistically not significant,hence no association between age and RAU.

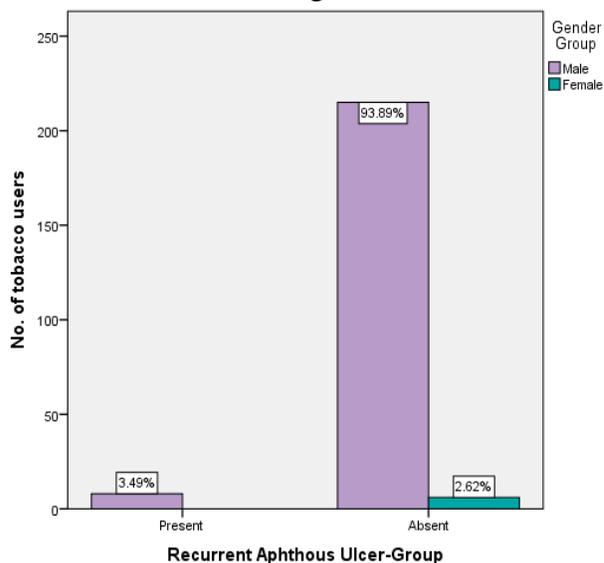


Figure 5: Bar chart depicts the association between gender and Recurrent Aphthous Ulcer among tobacco users. X axis represents the Recurrent Aphthous Ulcer and Y axis represents the number of tobacco users . Recurrent Aphthous Ulcer was present only in males(purple) among tobacco users.Chi square value is

0.223 , p value- 0.637 (>0.05),statistically not significant. There is no association between gender and Recurrent Aphthous Ulcer among tobacco users.

The relation between gender and Recurrent Aphthous Ulcer is reported that 97.4% of males and 2.6% of females in the given population consume tobacco( figure 5). Out of which 3.5% males were reported with Recurrent Aphthous Ulcer and there is no case of Recurrent Aphthous Ulcer diagnosed among female tobacco users. The p value was 0.637 and Pearson chi square value is 0.223. There is no significant difference between gender and Recurrent Aphthous Ulcer among tobacco users. Not statistically significant ( p value >0.05) .

On analysing the association of distribution between Recurrent Aphthous Ulcer and tobacco users. It is evident that smokeless tobacco users were more prevalent than smoking groups and were reported 84.3% of total population. Out of which less frequency of 1.75% of smokeless tobacco users were observed with Recurrent Aphthous Ulcer. Among smoking groups 1.75% of RAU were prevalent among 13.97% of total population. Pearson chi square value is 0.001 and p value was 0.625( p value >0.05)( figure 6). There is no significant association between occurrence of Recurrent Aphthous Ulcer among smoking and smokeless tobacco users.

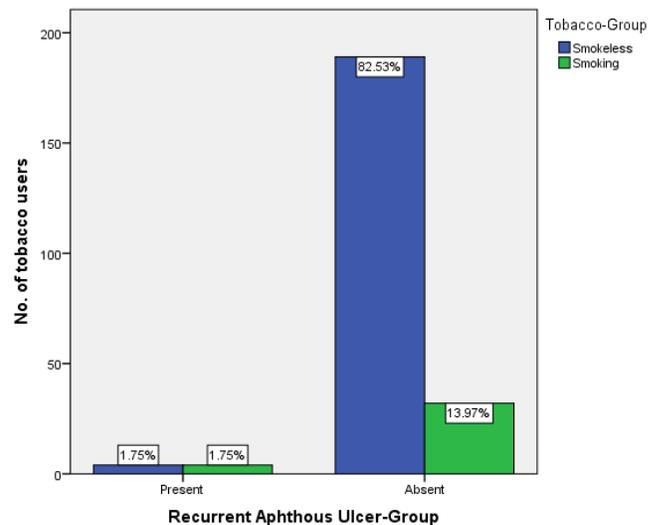


Figure 6: Bar chart depicts the association between Recurrent Aphthous Ulcer and tobacco users. X axis represents recurrent aphthous ulcer and Y axis represents number of tobacco users. Recurrent Aphthous Ulcer was equally present between smoking (green) and smokeless tobacco (blue) users. Chi square value is 0.001, p value was 0.625 (p < 0.05), statistically not significant. There is no significant association between tobacco users and Recurrent Aphthous Ulcer.

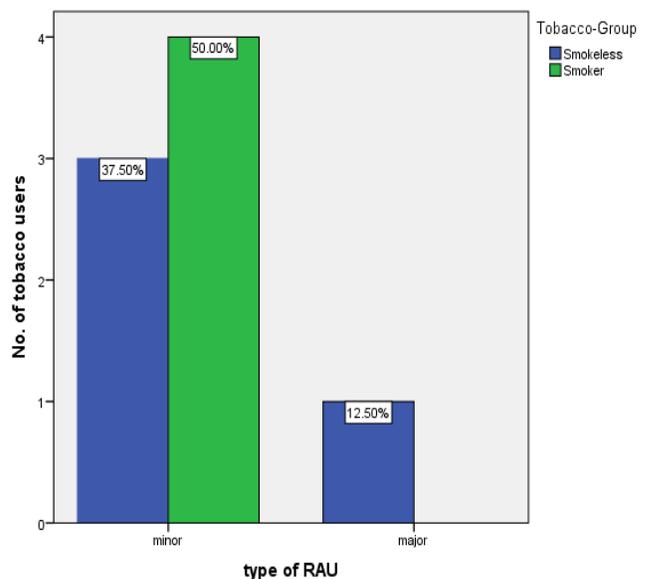


Figure 7: Bar chart depicts the association between types of Recurrent Aphthous Ulcer and tobacco users. X axis represent types of Recurrent Aphthous Ulcer and Y axis represents number of tobacco users.

Y axis represents number of tobacco users. Minor aphthous ulcer were more prevalent than major aphthous ulcer among tobacco users. Chi square value is 1.143, p value is 0.285( $p < 0.05$ ), statistically not significant. There is no significant association between types of recurrent aphthous ulcer and tobacco users.

The results from this study shows that there is a negative epidemiological association between occurrence of recurrent aphthous ulcer and tobacco usage. In this study the mean age for Recurrent Aphthous Ulcer was 38.56 years who accounted 61.1% of total population. This is in consent with the study done by Yojari et al, where she reported the mean age in her study was 31.36 years (Rajmanee *et al.*, 2017). There are several studies that depict the high prevalence of Recurrent Aphthous Ulcer in the 2<sup>nd</sup> and 3<sup>rd</sup> decade of life.

In this study, the males (97.4%) were predominant tobacco users than females (2.6%), out of which only 3.5% of males were reported with Recurrent Aphthous Ulcer. Faleh et al, in his study, have reported that prevalence of Recurrent Aphthous Ulcer among tobacco users was high in males ( $p < 0.001$ ) (Sawair, 2010). However a high prevalence of Recurrent Aphthous Ulcer was found in US female student nurses (60%) (Ship, 1972).

Shapiro, McRobbie in their studies have suggested that there is increased keratinization of the oral mucosa among the smokers that leads to protective effect against Recurrent Aphthous Ulcer and bacterial penetration (Shapiro, Olson and Chellemi, 1970; McRobbie, Hajek and Gillison, 2004). This is also evident in our study that among the smoking population (50.7%) only 3.4% of the population was prevalent for Recurrent Aphthous Ulcer.

D Grady in his study determined to find the association between smokeless tobacco usage and Recurrent

Aphthous Ulcer. In which he found that smokeless tobacco had significantly reduced the incidence of Recurrent Aphthous Ulcer which is in agreement with our study that smokeless group 84.3% had a lower rate 1.75 % than smoking group incidence for Recurrent Aphthous Ulcer. (Grady *et al.*, 1992). Mohammad et al, had also reported prevalence of Recurrent Aphthous Ulcer in smokeless groups was only 9.8% while those in the smoking group was 15.7% (Tuzunet *et al.*, 2000).

Some authors state that nicotine is known to affect the immune response to inflammatory reaction by producing adrenal steroid through hypothalamus pituitary axis thereby decreasing the production of TNF-  $\alpha$  and interleukin 1 and 6 by attaching on macrophages. They decrease the secretion of anti inflammatory cytokines (Sawair, 2010; Kumar and Ananthkrishnan, 2014).

Marakoglu et al, have reported those who quit smoking are less likely to develop Recurrent Aphthous Ulcer if they use nicotine replacement therapy (Marakoğlu *et al.*, 2007). Some authors suggest the protective effect of nicotine as subjects who quit smoking often complain of Recurrent Aphthous Ulcer and resumption of smoking leads to faster resolution (Ussher, 2003).

Previously our team had conducted numerous systematic reviews and reviews (Venugopal and Uma Maheswari, 2016; Chaitanya *et al.*, 2018; Maheswari *et al.*, 2018; Muthukrishnan and Warnakulasuriya, 2018), surveys (Subashri and Maheshwari, 2016), case reports (Choudhury *et al.*, 2015; Misra, Shankar and Recurrent Aphthous Ulcer, 2015; Dharman and Muthukrishnan, 2016; Muthukrishnan, Bijai Kumar and Ramalingam, 2016; Muthukrishnan and Bijai Kumar, 2017), randomised controlled studies (Steele *et al.*, 2015; Chaitanya *et al.*, 2017; Rohini and Kumar, 2017; Patil *et al.*, 2018; Subha and Arvind, 2019).

## CONCLUSION

Within the limitation of the study, the occurrence of Recurrent aphthous ulcer among the tobacco users were present only in males in 31-40 years Among the tobacco users only 1.75% of RAU was prevalent among smoking and smokeless groups respectively. There is no significant association between tobacco users and RAU. It is also evident that occurrence of recurrent aphthous ulcer was comparatively less among tobacco users. However it is not encourageable to use tobacco in order to prevent aphthous ulceration. Hence anti tobacco programs should be conducted in order to provide awareness among the general public regarding harmful effects of tobacco consumption.

## AUTHORS CONTRIBUTION

Aishwarya performed the data collected by reviewing the patient details, filtering required data, analysing and interpreting statistics and contributed to manuscript writing

SreedeviDharman contributed to conception of the study title, the study design, analysed the collected data, statistics and interpretation and also critically revised the manuscript.

Suresh.V participated in the study and revised the manuscript. All the three authors have discussed the results and contributed to the final manuscript.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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