World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(REVIEW ARTICLE)

Check for updates

Effect of smoking on salivary flow rate and oral candidiasis incidence

Fayza Devana Wynistilla [1], Reza Agustina [1], Aneu Virgina Tambunan [1,*] and Tantiana [2]

[1] *Undergraduate Student, Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia.*
[2] *Department of Oral Biology, Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia.*

World Journal of Advanced Research and Reviews, 2024, 23(03), 2725–2730

Publication history: Received on 17 August 2024; revised on 24 September 2024; accepted on 27 September 2024

Article DOI: https://doi.org/10.30574/wjarr.2024.23.3.2964

Abstract

Background: The 2014 ASEAN Tobacco Control Atlas (SEACTA), provides evidence that the first country to have the highest number of smoker prevalence in ASEAN is Indonesia, which is 50.68%. Smoking is one of the main risk factors for various diseases. Cigarette smoke and the hot temperature of cigarettes exposed to the oral mucosa will cause tissue damage. This results in damage to taste receptors which affects the decrease in salivary sensitivity and productivity. Damage to oral tissue is one of the factors for the *C. albicans* fungus to colonize in the oral cavity and cause infection so that oral candidiasis appears.

Objectives: To review and investigate the effect of smoking on salivary flow rate and oral candidiasis incidence

Conclusion: There is an effect of smoking on Salivary Flow Rate and Oral Candidiasis Incidence. Smoking will result in decreased salivary secretion and become a factor in the onset of *C. albicans* colonies in the oral cavity.

Keywords: Salivary flow rate; Oral candidiasis; Smoking; Cigarettes

1 Introduction

Based on data from The ASEAN Tobacco Control Atlas (SEACTA) published in 2014, Indonesia ranked first in ASEAN for the highest smoker prevalence, with a rate of 50.68%. According to data from the World Health Organization (WHO), there were 72,723,300 smokers in Indonesia as of 2015; by 2025, that number is predicted to rise to 96,776,800 smokers [1]. One of the biggest risk factors for many diseases is smoking. Cigarette smoke contains tobacco smoke, which affects nearly every organ system in the human body and is primarily responsible for heart disease, cancer, and non-cancerous respiratory disorders [2]. Teenagers aged 10 to 18 had a higher percentage of active smokers in 2018—9.1%—than in 2013 [3].

Cigarette smoke and the heat of cigarettes exposed to the oral membranes cause tissue damage. In addition, it also results in damage to taste receptors that affect sensitivity. This opens ion channels, allowing positively charged sodium ions to enter the cell and depolarize the normal negativity. Thus, a decrease in the sensitivity of taste receptors leads to a decrease in the impulses transmitted by the nerves to the nuclei of the salivary glands, which also leads to a decrease in saliva production [4].

The oral microbiome is defined as the collection of genomes of microorganisms living in the oral cavity [5]. The oral microbiome plays an important role in local and systemic inflammation [6]. The normal temperature of the oral cavity is usually around 37^0 Celsius without varying changes, the pH of saliva is stable around 6.5-7.5, and saliva provides a stable habitat for microbes and keeps bacteria hydrated, as well as facilitates the transport of nutrients in microorganisms. The oral microbiome is said to be associated with the presence of pathological conditions in the oral

* Corresponding author: Aneu Virgina Tambunan

cavity such as periodontitis, caries, and oral cancer. Microbes are most commonly found on tooth surfaces, oral mucosa, periodontal pockets, and the tongue. The transmission of bacteria in the oral cavity is facilitated by saliva [7].

One of the microorganisms often encountered in humans is *C. albicans*. This fungus is an opportunistic fungus that is part of the normal flora in the mucosal areas of humans and animals, such as the oral cavity, digestive tract and vagina. Oral candidiasis appears due to *C. albicans* fungal infection. The relationship between smoking activity and oral candidiasis is that tissue damage caused by smoke and the heat of cigarettes can reduce salivary secretion, making it easier for the *C. albicans* fungus to colonize the oral cavity and cause infections that lead to oral candidiasis [7,8].

The aim of this research is to determine and review the effect of smoking on salivary flow rate and the incidence of oral candidiasis. This research is intended to clarify the relationship based on findings from previous studies, so that this information can serve as a basis for further research in the future.

2 Material and methods

This research uses a Literature Review design with references to literature relevant to the topic and then written systematically. The study was conducted in May 2023.

2.1 Research Strategy

Literature search was conducted using the article search strategy used in this study using the Boolean Operator strategy, namely AND/OR/NOT. The search was conducted online and accessed the database using the keywords: (Smoking AND Salivary flow rate AND Oral Candidiasis). The article search was focused on journal articles in English with a publication year range from 2013 to 2023.

2.2 Inclusion and Exclusion Criteria

The literature search for this research used inclusion and exclusion criteria. The inclusion criteria used is literature available in full text and open access in English, published, and using original research design in the last 10 years, while the exclusion criteria used is literature using languages other than English, literature reviews or systematic reviews, literature not available in full text or open access and more than 10 years.

2.3 Synthetic Data

The literature that has been collected is continued with the data synthesis process for further analysis. The data extraction stage is carried out by looking at the entire published article including the research title, author, year of publication, objectives, methods and appropriate research conclusions, then writing down the important findings of the article. Then, continue with the analysis to draw conclusions and recommendations that can answer the research questions and objectives. Literature was selected via keyword search and filtered based on title and abstract. The full text of each piece of literature was screened to determine its relevance to the inclusion and exclusion criteria established in this study.

3 Results and discussion

Oral disorders like caries, candidiasis, periodontal disease, and oral cancer are all made more likely by smoking. The ingredients contained in cigarettes are more than 4,000 of which are chemicals including tar, nicotine, carbon monoxide, cyanide, aromatic hydrocarbons, ammonia, pyridine, acetone. Of all these ingredients 50 of them are cariogenic for humans. Nicotine contained in cigarettes will initially increase the rate of salivary secretion. However, continuous exposure to nicotine in the salivary glands will cause fatigue of acinar cells resulting in decreased secretion of salivary products by the acinar cells of the salivary glands [9,4].

When there is an imbalance in the salivary pH and secretion of saliva, leading to an alteration in the oral cavity's microbiota. The most prevalent fungal pathogen in humans is *Candida albicans*, which can cause systemic infections as well as infections of the mucosal membranes [10]. Several fitness traits and virulence variables support the ability of *C. albicans* species to infect multiple host niches. The capacity to morphologically switch between yeast and hyphal forms, adhesin and invasive agent expression on the cell surface, biofilm formation, phenotypic alterations, and hydrolytic enzyme production are examples of virulence factors [11].

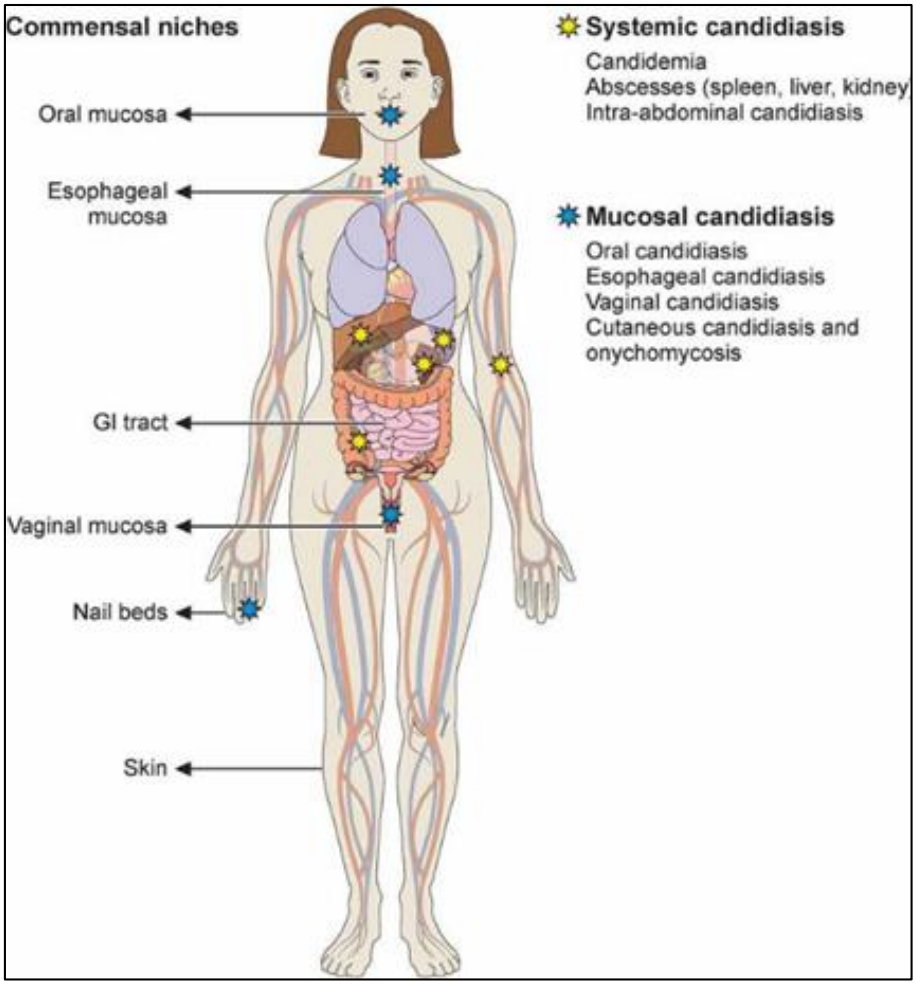

Figure 1 The human body has commensal sites of *Candida albicans*, and the pathogen can cause invasive diseases (yellow star) and mucosal diseases (blue star) in certain tissues. It can also infect the mucosal surfaces of the mouth, genitalia, and the gastrointestinal tract [10]

A balanced combination of bacteria species living in biofilms in particular oral cavity crevices is essential for oral health. Dental caries, periodontal disease, endodontic infections, and tooth loss are caused by homeostasis being disrupted by variables such altered food, altered salivary flow, poor oral hygiene, and altered host immune response [12]. Oral candidiasis has been linked to eating disorders, malnutrition, and malabsorption. According to Vila et al, salivary pH is a factor that can be a factor in the incidence of oral candidiasis. Candidiasis is an infection caused by the fungus *C. albicans* which most often causes lesions in the soft tissues of the oral cavity. The appearance of yellow or white patches on the tongue, gums, inner cheeks, base of the throat, and lips is one of the hallmarks of oral candidiasis [13,14].

In the opinion of Osman & Papon, tobacco smoke (TS) exposes people to a variety of minor to severe oral health issues, such as oral leucoplakia (OLK) and oropharyngeal candidiasis (OPC), due to its complex blend of oxidants and many reactive oxygen species (ROS). OPC, also called "thrush," is characterized by superficial tissue invasion and Candida fungal overgrowth at many oral mucosal locations. On the other hand, OLK contains plaques or potentially cancerous white patches that form in the oral cavity. The oral epithelial barrier, the initial line of defence against fungal infections, can be weakened and its structure altered by smoking-induced oxidative stress and cellular redox state abnormalities [15].

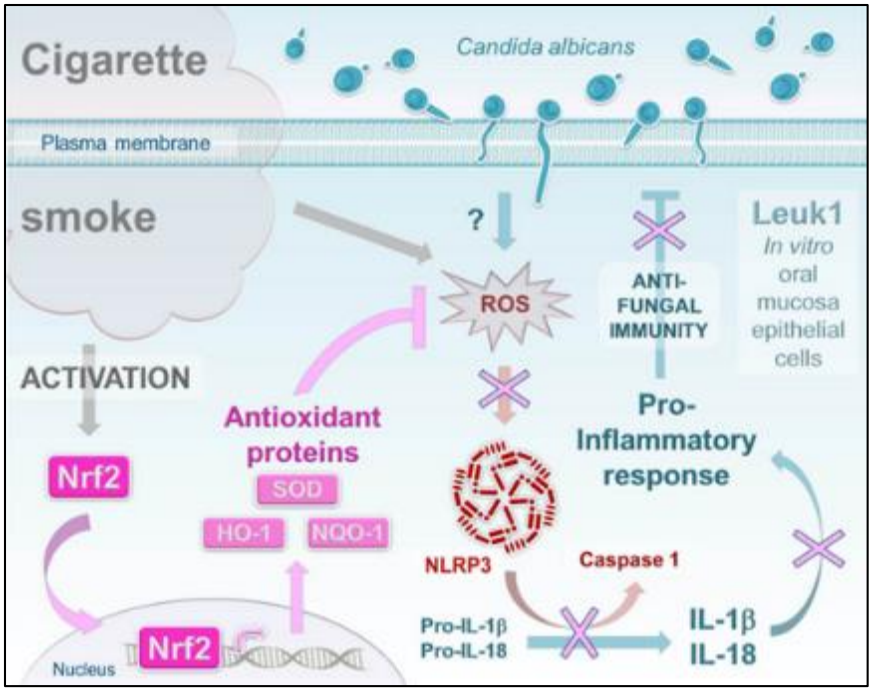

Figure 2 According to a hypothesized model in oral epithelial cells, smoking enhances the vulnerability of oral mucosa to *C. albicans* infection by activating the Nrf2 pathway, which in turn negatively regulates NLRP3 inflammation. Smoking-induced oxidative stress causes Nrf2 to become phosphorylated and translocate into the nucleus, where it activates the expression and functions of target antioxidant proteins such as superoxide dismutase (SOD), haem-oxygenase-1 (HO-1), and NAD(P)H dehydrogenase quinone-1 (NQO-1). Crucially, while a number of investigations have clarified how ROS and NQO-1 regulate the connection between Nrf2 and NLRP3, the precise molecular mechanism behind this antagonistic relationship is still unknown [15].

Table 1 Summary of study results

No.	Author Name, Year	Objective	Research Result
1	Haghighi *et al*, 2022	To illustrate how nicotine affects the proliferation of *C. albicans*, the creation of biofilms, and its combined antifungal activity	When *C. albicans* is treated with antifungals at sub-MIC concentrations, the effect of nicotine on virulence-related gene expression is diminished. Nicotine influences the pathogenic properties of *C. albicans*, such as hyphal development, biofilm formation and morphology, and virulence-related gene expression.
2	Semlali *et al*, 2014	To demonstrate the impact of condensed tobacco smoke on *C. albicans* adhesion, proliferation, and biofilm formation in addition to activating EAP1, HWP1, and secreted aspartic protease 2.	The adherence, proliferation, and biofilm formation of *C. albicans* were all enhanced by cigarette smoke condensate (CSC). Certain significant genes may be activated in support of these characteristics. We showed by quantitative RT-PCR that *C. albicans* exposed to CSCs expressed significant quantities of EAP1, HWP1, and SAP2 mRNA, and that the expression of these genes rose as the concentration of CSCs increased.
3	Khalili et al., 2023	To clarify the relationship between the prevalence of oral candidiasis and the use of cigarettes, tobacco, alcohol, and opium in Rafsanjani, an area in southeast Iran.	7.94% of 8682 individuals, whose mean age was 49.94 years, had oral candidiasis. In fully adjusted models, there was a direct correlation between the chances of oral candidiasis in current and past smokers (OR: 3.26, 95% CI: 2.46–4.33 and OR: 1.63, 95% CI: 1.18–2.25, respectively). The odds of oral candidiasis showed a dose-response association with the number of cigarettes smoked in the 4th quartile

			compared to the reference group (OR: 3.01, 95% CI: 2.02–4.50), time (OR: 2.48, 95% CI: 2.04–3.95), and dose (OR: 3.31, 95% CI: 2.38–4.60).
4	Yendri *et al*. 2018	To understand how smokers' salivary flow rate is represented, as well as how long they smoke for and how many cigarettes they consume,	When the Kruskal-Walls test was used to examine the effects of salivary flow rate, the results showed that the mean (SD±) salivary flow rate among smokers was 0.36 (±0,207) ml/min (p=0,012). The results of the study demonstrated a substantial relationship between salivary flow rate and the length of time spent smoking and the quantity of cigarettes smoked.
5	Gani *et al*, 2017	To determine how cigarette smoke condensate (CSC) affects *C. albicans* biofilm formation.	*C. albicans* was sensitized using CSC kretek and non-kretek, which demonstrated a rise in biofilm production ($p<0.05$) as compared to the control, particularly over the course of a day. It is associated with the mass of biofilm formation observed under a 400x microscope, as well as the fact that CSC non-kretek outperforms CSC kretek in biofilm formation of *Candida Albicans*, primarily in 24 and 48 hours. In addition, although the disingenuity is lower than 24 hours, 12 hours were the most dominant biofilm figuration of *C. albicans* sensitized by CSC kretek.

Cigarette smoke can be a mediator that causes *C. albicans* fungal infection to increase, in this case the antibodies contained in saliva can decrease, then can weaken the ability of saliva to maintain the oral cavity, so that smoking activity causes an imbalance in oral flora. Changes in the oral mucosa in the form of thinning of the oral mucosal epithelium and decreased salivation make *C. albicans* easy to colonize and then invade the oral mucosal epithelium, causing oral candidiasis [4,8,9]. Chemical compounds in cigarette smoke such as acetaldehyde, benzene, 1,3-butadiene, and isoprene, can increase gene mutations in *C. albicans*. These compounds can reduce the pathogenicity of *Candida spp.* by affecting the External Associated Protein 1 (EAP1) and Secreted Aspartyl Protease 2 (SAP2) genes, which play a role in regulating attachment, growth, and biofilm formation. The EAP1 gene in *Candida* encodes an epithelial cell wall protein that promotes adhesion to the oral mucosa. The SAP2 gene plays a role in the virulence of *Candida spp.* [8,13,16]

The results of previous studies show that the longer a person smokes, the less saliva, and the more cigarettes smoked, the less saliva. This is related to the nicotine content in cigarettes. Initially, nicotine increases saliva, but subsequent doses decrease it. This is because nicotine in cigarettes causes morphological and functional abnormalities in the salivary glands. The length of time you smoke and the number of cigarettes you smoke can affect saliva. The more nicotine accumulates in the salivary glands, the faster pathology appears in the salivary gland cells, leading to morphological and functional abnormalities in the salivary glands [4].

4 Conclusion

Several ingredients in cigarettes, especially nicotine, cause damage to salivary gland cells. As a result of this damage there is a decrease in the production of salivary secretions. A decrease in the rate of salivary secretion in the oral cavity will create abnormal conditions so that *C. albicans* colonies can infect the oral cavity resulting in oral candidiasis disease.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Analysis of the Implementation of Earmarking Tax Policy from Tobacco Excise Revenue Sharing Funds on Public Health [internet]. National Symposium on State Finance; © 2020 [cited 2023 May 2023] Available from https://jurnal.bppk.kemenkeu.go.id/snkn/article/view/561/298

[2] Chaffee BW, Couch ET, Vora MV, Holliday RS. Oral and periodontal implications of tobacco and nicotine products. Periodontology 2000. 2021; 87(1):241-253

[3] Kemenkes RI. Riset Kesehatan Dasar (Riskesdas), Kemenkes RI, Jakarta ; 2018

[4] Yendri L, Nelis S, Alioes Y. The Effect of Smoking To Salivary Flow Rate. Jurnal Kesehatan Gigi. 2018; 5(2):38

[5] Lim Yenkai, Fukuma N, Totsika M, Kenny L, Morrison M, Punyadeera C. The Performance of an Oral microbiome Biomarker Panel in Predicting Oral Cavity and Oropharyngeal Cancers, Frontiers in Cellular and Infection Microbiology. 2018; 8(287) :1-2

[6] Jiyeon Si, Cheonghoon Lee, Gwangpyo Ko. Oral Microbiota: Microbial Biomarkers of Metabolic Syndrome Independent of Host Genetic Factors, Frontiers in Cellular and Infection Microbiology. 2017; 7(516):1-12

[7] Adrianto AWD, Hartomo BT, Putri DA. Oral microbiome variation as a biomarker in the field of dentistry: Literature Review. Indonesian Journal of Dentistry. 2022; 2(1):1-6.

[8] Semlali A, Killer K, Alanazi H, Chmielewski W, Rouabhia M. Cigarette smoke condensate increases C. albicans adhesion, growth, biofilm formation, and EAP1, HWP1 and SAP2 gene expression. BMC Microbiology, 2018; 14(1):1–9.

[9] Haghighi F, Andriasian L, Tran NC, Lux R. Effect of Cigarette and E-Cigarette Smoke Condensates on C. albicans Biofilm Formation and Gene Expression. International Journal of Environmental Research and Public Health. 2022; 19(8):4262

[10] Ponde NO, Lortal L, Ramage G, Naglik JR, Richardson JP. C. albicans biofilms and polymicrobial interactions. Critical reviews in microbiology. 2021; 47(1):91–111.

[11] Pereira R, Dos Santos Fontenelle RO, de Brito EHS, de Morais SM. Biofilm of C. albicans: formation, regulation and resistance. Journal of applied microbiology. 2021; 131(1):11–22.

[12] Bhambri, Taranum. Role of Oral Microbial Flora in Health and Illness. Journal of Advanced Medical and Dental Sciences Research. 2020; 8(3): 53-60.

[13] Khalili P, Atekeh M , Farimah S , Fatemeh MP, Zahra J. Oral candidiasis and cigarette, tobacco, alcohol, and opium consumption in Rafsanjan, a region in the southeast of Iran. BMC Oral Health. 2023; 23(262):1-8

[14] Vila, T. et al. Oral candidiasis: A disease of opportunity. Journal of Fungi. 2020; 6(1):1–28

[15] Osman M, Papon N. Smoking-aggravated oral candidiasis: Nrf2 pathway dampens NLRP3 inflammasome. Journal of cellular and molecular medicine. 2021; 25(19): 9473–9475.

[16] Gani BA, Al Ghassani AQ, Mubarak Z, Bachtiar EW, Bachtiar BM. Potential of cigarette smoke condensate to increase biofilm formation of C. albicans isolate ATCC 10261. J Syiah Kuala Dent Soc. 2017; 2(3):33-4