

## REVIEW ARTICLE

# Salivary Calcium Levels in Smokers

Raisha Nur Septiani<sup>1</sup>, Sri Tjahajawati<sup>2</sup>, Anggun Rafisa<sup>2</sup><sup>1</sup> Faculty of Dentistry, Universitas Padjadjaran,, 45363 Jawa Barat, Indonesia<sup>2</sup> Department of Oral Biology, Faculty Dentistry, Universitas Padjadjaran,, 45363 Jawa Barat, Indonesia**ABSTRACT**

Cigarettes have a negative impact on the oral cavity and saliva. Saliva is a protective liquid for the oral cavity that is in direct contact with cigarette smoke. Long-term smoking activity can cause taste receptors and the main site for stimulation of salivary secretion to be exposed to tobacco which can affect the salivary reflex. Changes in composition including calcium and salivary flow rate can compromise the integrity of the soft and hard tissues of the oral cavity. Previous studies regarding salivary calcium levels in smokers showed different results between increasing or decreasing salivary calcium levels in smokers, the aim of this study was to review how the salivary calcium levels in smokers are described. The search for articles was conducted using PRISMA- Sc (Preferred Reporting Items for Systematic Reviews and Meta-analyses). The extracted data was then analyzed using the thematic analysis method. After applying the eligibility criteria, 6 articles were selected. Four articles showed an increase in salivary calcium levels, while two articles showed a decrease in salivary calcium levels in smokers. The results of reviewing several articles in this study showed smokers' average salivary calcium levels were 1.139175 mmol/l. Gender, age, duration of smoking, and other comorbidities such as periodontitis are factors that can influence salivary calcium levels.

**Keywords:** Calcium saliva, Saliva, Smoking, Calcium, Smokers, Tobacco**Corresponding Author:**

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**INTRODUCTION**

According to The World Health Organization (WHO), smokers are divided into seven types of categories: current smokers, environmental tobacco smoke, everyday smokers, former smokers, never smokers, quit attempts, and someday smokers (1). The smoker said a current smoker smokes every day for at least one year based on consumption lifetime live 100 sticks of cigarette or more (2) In 2015, early childhood death and disability were major global concerns (3). Since 1990, smoking has claimed over 5 million lives annually and is a major contributor to the rise of certain diseases, particularly in low-income countries. Tobacco consumption has also increased in these developing nations (4). According to the Global Adult Tobacco Survey (GATS), Indonesia ranks third highest in cigarette consumption and fifth highest in tobacco production. Therefore, it requires more attention in terms of management and handling (5).

Smoking cigarettes can be harmful to your oral health as it negatively affects the mouth and saliva (6). Saliva is a protective fluid that comes into direct contact with cigarette smoke when it touches the mouth cavity (7,8). Smoking can have negative effects on oral health,

including bad breath, oral cancer, dental implant failure, receding gingiva, and tooth loss due to periodontal disease (9). Periodontal disease can occur due to a high rate of salivary calcium, which can lead to the formation of plaque and calculus (9). Smoking cigarettes can temporarily increase salivary secretion, but studies have not shown significant effects from long-term smoking (9).

Saliva is a fluid found in the mouth that is secreted by major and minor salivary glands. The major glands include the parotid, submandibular, and sublingual glands. Saliva is primarily composed of water, accounting for 99% of its composition, along with organic and inorganic electrolytes (9,12). Saliva is made up of different components, including salivary calcium, which should be at normal levels of 1-1.5 mmol/L. Smoking can affect the taste buds and salivary glands, leading to thicker and more mucus-like saliva. This change in composition and flow speed can harm the soft and hard tissues in the mouth, such as the gingiva and alveolar bone (13).

Previous studies have shown a decrease in salivary calcium, but there is no evidence that other components have an impact on this reduction (8,11). The decrease in calcium metabolism in female can be linked to hormonal changes, specifically in estrogen and parathyroid levels (8). According to Varghese et al. male smokers may experience an increase in salivary calcium due to smoking (14). According to Abed et al., male smokers have significantly higher levels of salivary

calcium compared to non-smokers subject (15). Factors such as smoking can lower the pH levels inside the oral cavity, which can speed up the loss of calcium from teeth and increasing the amount of calcium released into the saliva. This can impact the rate of salivary calcium enhancement (15).

Previous research on the rate of salivary calcium in smokers has shown varying results, with some indicating an increase while others suggest a decrease. Based on this, researchers are interested in mapping out the factors that differentiate the rate of salivary calcium in smokers. This study will summarize a number of studies in the field and largely present them for easy delivery.

**MATERIALS AND METHODS**

**Reporting Format**

This research uses scoping review technique that can be used to summarize multiple studies in a particular field. This method ensures that the information is presented in a broad and comprehensive manner.

**Inclusion and Exclusion Criteria**

This article discusses research conducted on humans, both in English and Indonesian language, focusing on the effects of smoking on salivary calcium levels. The research includes articles published between 2012 to 2022 and specifically examines male and female smokers. However, articles that include patients with systemic diseases or literature reviews are excluded from the research.

**Research Question**

In this study, the Population, Concept, Context (PCC) framework was utilized to establish research criteria and questions. The JBI recommends using this framework to draft the main research question. It helps to avoid being too specific and includes a wide range of criteria. The population studied in this research consists of individuals who smoke in general. The concept being explored is the influence of cigarette smoking on the rate of salivary calcium. The context includes possible factors that may affect the relationship between smoking and salivary calcium levels, such as age, gender, and the biochemistry method used.

**Study Selection and Screening Methods**

To conduct research, we used a scoping review technique and searched electronic databases such as PubMed, EBSCO, and ScienceDirect. We utilized Boolean operators to search for articles or journals that combined specific keywords using "AND" and "OR." (16). Search technique using keywords combination such as *calcium saliva*, *saliva*, *smoking*, *calcium*, *smokers*, *tobacco*.

The research process followed a protocol called Preferred Reporting Items for Systematic Review and

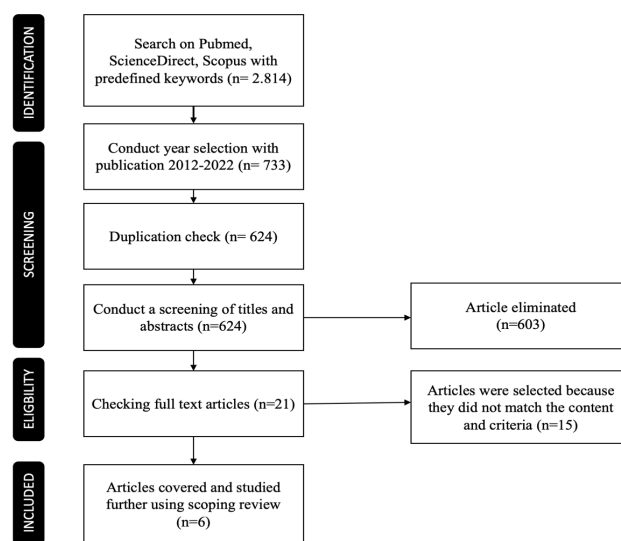
Meta-Analyses for Scoping Review (PRISMA-ScR) (16). Two reviewers were involved in selecting the literature for our study based on inclusion and exclusion criteria. The PRISMA protocol was used to search for literature from PubMed, ScienceDirect, and EBSCO databases. We filtered the literature obtained from these databases by inspecting the year of publication (2012-2022) and removing any duplicates. The remaining articles were screened based on their title and abstract to determine their relevance. The final filtering was done by reading the full text of the articles. The literature that passed through all these stages was reviewed using the scoping review method.

**Data Extraction**

The data collection process involved gathering information such as the author’s name, year of publication, article title, and samples of both male and female individuals of various ages. The collected data was analyzed and presented in a table showing the rate of salivary calcium. The data presented in the table will be analyzed descriptively using the approach of thematic analysis to examine quantitative data by identifying a pattern or finding a theme from the collected data.

**RESULTS**

Searches on three databases resulted in 2,814 articles. A total of 2,081 articles were excluded because the year of publication did not match, and the remaining 733 articles were obtained. A total of 109 duplicate articles were issued at the next screening. Subsequent screening of 603 articles was excluded because the title or abstract was unrelated to the research question, and the remaining 21 articles were screened in full text. Fifteen articles were excluded due to non-compliance with predetermined research inclusion criteria. The final results of the screening obtained six articles. The flow of the literature search using PRISMA-ScR is shown in Figure 1.



**Figure 1: Flow chart study according to PRISMA-ScR**

Table I displays descriptive data extracted from a total of 6 studies conducted between 2012 and 2021. The majority of studies were conducted in India (n=3), followed by Croatia (n=1), Iraq (n=1), and Indonesia

(n=1). The 616 participants included both males and females aged between 18-64, with an unclear distribution between genders. Only one study focused on teenage smokers.

**Table I: Data extraction results**

No	Author name & Year publication	Title Article	Study Design	Sample	Results
1.	Ivana Sutej , <i>et al.</i> (2012) (17)	<i>Salivary Calcium Concentration and Periodontal Health of Young Adults in Relation to Tobacco Smoking</i>	<i>Cross-sectional Study</i>	Sample smokers and non- smokers age 22-26 years (12 female and 5 male )	The rate of salivary calcium in smokers is $38.64 \pm 16.9 \mu\text{g/ml}$ , while non-smokers have a rate of $18.72 \pm 8.2 \mu\text{g/ml}$ .
2.	Abhay P. Kolte, <i>et al.</i> (2012) (8)	<i>Effect of smoking on salivary composition and periodontal status</i>	<i>Cross-sectional Study</i>	Sample smokers and non- smokers healthy and experienced periodontitis aged 30-60 years (Female and male)	According to the results, there is a steady decrease in calcium levels among smokers. Healthy smokers had an average of $9.99 \pm 9.64 \text{ mg/dL}$ , while smokers with periodontitis had an average of $3.47 \pm 1.49 \text{ mg/dL}$ . In comparison, non-smokers had an average of $13.89 \pm 10.34 \text{ mg/dL}$ , and those with periodontitis who do not smoke had an average of $6.16 \pm 2.84 \text{ mg/dL}$ .
3.	Hayder Hamed Abed, <i>et al.</i> (2012) (15)	<i>Evaluation of calcium concentration in saliva of Iraqi male smokers</i>	<i>Cross-sectional Study</i>	Sample smokers 15 people and non-smokers 15 males ages 49-52 years .	The results indicate that the level of value is higher in the sample of smokers at $0.538 \pm 0.410 \text{ mmol/l}$ compared to the non-smokers sample at $0.323 \pm 0.2857 \text{ mmol/l}$ .
4.	Megha Varghese, <i>et al.</i> (2015) (14)	<i>Quantitative Assessment of Calcium Profile in Whole Saliva From Smokers and Non-Smokers with Chronic Generalized Periodontitis</i>	<i>Cross-sectional Study</i>	Sample smokers 25 people and non - smokers 25 males aged 20-50 years	According to the results, smokers had a higher enhancement rate of salivary calcium with a value of $2.27 \pm 24838 \text{ mmol/l}$ , compared to non-smokers with a value of $1.726 \pm 0.103 \text{ mmol/l}$ .
5.	Preeti Kambalyal , <i>et al.</i> (2015) (18)	<i>Comparison of salivary calcium level in smokers and non-smokers with chronic periodontitis, aggressive periodontitis, and healthy controls</i>	<i>Cross-sectional Study</i>	Study done using 56 subjects with divided between the ages of 25-55 years into 5 groups (Females and males)	The salivary calcium levels were measured in different groups of people. The group of healthy individuals had an average of $2.01 \pm 0.02 \text{ mmol/l}$ . Non-smokers with chronic periodontitis had a higher average of $2.24 \pm 0.08 \text{ mmol/l}$ , while smokers with chronic periodontitis had an even higher average of $2.66 \pm 0.02 \text{ mmol/l}$ . Smokers with aggressive periodontitis had an average of $2.62 \pm 0.01 \text{ mmol/l}$ , whereas non-smokers with aggressive periodontitis had a lower average of $2.11 \pm 0.01 \text{ mmol/l}$ .
6.	Sri Tjahajawati , <i>et al.</i> (2021) (9)	<i>The effect of smoking on salivary calcium levels, calcium intake, and bleeding on probing in females</i>	<i>Cross-sectional Study</i>	subject study is female with range ages 18-64 years with a total of 26 females smokers and 37 non- smokers females.	The results indicate a decreasing trend in salivary calcium levels. Individuals who smoke have a lower average salivary calcium level of $1.16 \pm 0.93 \text{ mmol/l}$ compared to non-smokers who have an average level of $1.80 \pm 0.96 \text{ mmol/l}$ .

\*  $\mu\text{g}$  = Micrograms ;  $\text{mg}$  = Milligrams ;  $\text{mmol}$  = Millimole ;  $\text{ml}$  = Milliliter ;  $\text{l}$  = liters

**Table II: Characteristics Reviewed Research**

Characteristics	Frequency	Percentage
<b>Year Publication</b>		
2012	3	50%
2015	2	33%
2021	1	17%
<b>Research Design</b>		
<i>Cross-sectional</i>	6	100%
<b>Country</b>		
India	3	50%
Croatian	1	17%
Indonesia	1	16%
Iraq	1	17%
<b>Age</b>		
0-18 years	1	7%
19-35 years	4	28%
36-50 years	5	36%
51-70 years	4	29%
<b>Gender</b>		
Females and males	3	50%
Females	1	17%
Male	2	33%
<b>Method Measurement of Saliva Calcium Levels</b>		
<i>Atomic Absorption Spectrophotometer</i>	3	50%
<i>Cresolphtaleine Complexone</i>	2	33%
<i>Electron Analyzer</i>	1	17%
<b>Amount Sample (person)</b>		
<25	1	17%
26-50	2	33%
>50	3	50%

**Table III: Content results salivary calcium**

	Sutej et al. (2012)	Kolte et al. (2012)	Abed et al. (2012)	Var-ghese et al. (2015)	Kam-balyal et al. (2015)	Tjaha-jawati et al. (2021)
Healthy and non-smoker subjects	0.466 ± 0.205 mmo/l	0.3469 ± 0.2581 mmo/l	0.323 ± 0.2857 mmo/l	1.726 ± 0.103 mmo/l	2.01 ± 0.02 mmo/l	1.80 ± 0.96 mmo/l
Healthy and smokers subjects	0.963 ± 0.422 mmo/l	0.2492 ± 0.2402 mmo/l	0.538 ± 0.410 mmo/l	2.27 ± 24838 mmo/l	2.24 ± 0.08 mmo/l	1.16 ± 0.93 mmo/l
Chronic periodontitis and non-smokers subjects		0.1536 ± 0.0708 mmo/l	-	-	2.11 ± 0.01 mmo/l	-
Chronic periodontitis and smokers subjects		0.0865 ± 0.0372 mmo/l	-	-	2.66 ± 0.02 mmo/l	-

CONTINUE

**Table III: Content results salivary calcium (CONT.)**

	Sutej et al. (2012)	Kolte et al. (2012)	Abed et al. (2012)	Var-ghese et al. (2015)	Kam-balyal et al. (2015)	Tjaha-jawati et al. (2021)
Aggressive periodontitis and non-smokers subjects		-	-	-	2.62 ± 0.01 mmo/l	-
Aggressive periodontitis and smokers subjects		-	-	-	2.01 ± 0.02 mmo/l	-
Average	0.7145 mmo/l	0.20905 mmo/l	0.4305 mmo/l	1.726 mmo/l	2.275 mmo/l	1.48 mmo/l
				1.139175 mmo/l		

mmol = Millimole ; l = liters

Two studies were conducted using samples of smokers and non-smokers with periodontitis, while another study used samples of smokers and non-smokers without periodontitis (n=4). One study focused on using samples of females, while two studies focused on using samples of males. However, three studies did not specify the gender of the samples. The studies used different methods to analyze biochemistry. The most common method used was the Atomic Absorption Spectrophotometer (AAS) (n=3), while other studies used the Electrolyte Analyzer method (n=1) and Cresolphtaleine complexone method (n=2) for analysis. The study found that there was a higher rate of enhancement in salivary calcium in smokers (n=4) compared to the study that found a decline in salivary calcium rate in smokers (n=2).

**DISCUSSION**

First substance to be exposed to cigarette smoke is saliva, which is a fluid biological material. The hot smoke from a cigarette directly stimulates and irritates the mucous membrane in the mouth, causing changes in blood flow and a decrease in salivary secretion (18). One of the contents found in cigarettes is nicotine, which can stimulate the sympathetic nerve to produce neurotransmitters. This can lead to vasoconstriction, which can decrease the functioning of salivary glands and cause a decline in salivary secretion. As a result, the composition of saliva changes and the rate of salivary flow decreases. Cigarette smoke contains carbon monoxide (CO), which causes blood vessels to constrict and reduces the amount of oxygen in the body. This leads to a decrease in bicarbonate ions and a drop in salivary pH (18,19).

Research Abed et al. also explained that the rate of salivary calcium increase in smokers was observed using 15 samples from smokers (15). Increased salivary

calcium levels are associated with a decrease in salivary pH value. Smoking leads to the formation of hydroxyapatite in the mouth, which affects calcium levels in saliva regardless of tooth enamel (20). In line with study by Kambalyal et al., smoking can increase the rate of salivary calcium with lower density bone structure. Continuous exposure to tobacco can affect the salivary reflex and levels of salivary calcium, as well as the receptors responsible for taste (18). Research conducted by Kolte et al. and Tjahajawati et al. indicates a decrease in salivary calcium levels among smokers. However, there may be variations in the results due to differences in samples and methods used.

Previous research on salivary calcium levels in smokers has shown varying outcomes, with some reporting an increase and others a decrease in levels compared to the average value of 1.139175 mmol/l for smokers. These differences in results could be attributed to factors such as age, gender, and variations in the biochemistry methods used in the study.

#### **Salivary calcium levels based on age and smoking duration**

The research study involved subjects of various ages, with an average age range of 22-64 years old. The results showed an increase in the rate of salivary calcium among teenagers aged 22-26, men aged 20-50 years and 49-52 years, and subjects aged 25-55 years (11,17,18,14). However, research conducted on subjects aged 30-60 years and 18-64 years showed a decrease in the rate of salivary calcium among smokers (8,9). Difference in results could be attributed to the amounts of cigarettes consumed and the duration of smoking, as well as the age of the subjects.

Smoking can increase salivary gland activity and lead to the development of tolerance to the salivating effects, resulting in existing smokers who have been smoking for a longer period of time producing more saliva compared to novice smokers (14). Singh et al. conducted research that shows an initial increase in activity in the salivary glands when smoking starts, but over time, tolerance to the resulting saliva develops with prolonged smoking (21). According to a study by Sutej et al., teenagers who have a history of smoking experience a decrease in their salivary flow rate (17). Duration and amounts of cigarettes consumed can affect the rate at which nicotine is absorbed into the body through changes in salivary flow. The more cigarettes smoked, the higher the level of nicotine in the body, and this can cause a decrease in salivary flow. This decrease in flow can lead to a decrease in the secretion of bicarbonate ions and a decrease in salivary pH, which can cause damage to tooth enamel and affect the levels of calcium present in the saliva<sup>20</sup> The study of how age affects the body varies based on the individual. In the aging process, some change can occur in the salivary system, including decrease saliva production and changes

salivary composition (22,23). The composition of saliva is affected by the salivary flow rate, volume, and pH. Salivary glands control these three salivary parameters. As salivary flow rate increases, calcium concentrations in saliva are also expected to increase. Conversely, as salivary flow rate decreases, salivary calcium levels decrease. The physiological condition of saliva secretion under the regulation of the parasympathetic nervous system with the parotid gland being the highest producer of calcium saliva secretion. The parotid glands is the largest gland, and as the secretion flow increases, the calcium concentration also increases (24).

This statement discusses the link between smoking habits, age, and salivary calcium levels. As smokers age, their salivary function and composition change, leading to different rates of salivary calcium compared to younger smokers. However, research has not found significant differences in salivary calcium levels based on age.

#### **Salivary calcium levels based on gender**

This research study screens both males and females to determine salivary calcium levels based on sex. Sutej et al. conducted the study, which included a sample of 12 teenage females and 5 teenage males (15). The results indicate that smokers have a higher rate of salivary calcium compared to non-smokers. This finding aligns with research conducted by Kambalyal et al. that found similar results in both male and female subjects, although the exact amounts were uncertain for each gender (18). Research conducted by Varghese et al., they found that the enhancement rate of salivary calcium in a male subject increased to a value of  $2.27 \pm 24838$  mmol/l. This value was compared to non-smokers who had a value of  $1.726 \pm 0.103$  mmol/l (14). Abed et al. found that smokers (consisting of 25 samples) have an increased salivary calcium rate of  $0.538 \pm 0.410$  mmol/l as compared to non-smokers (consisting of 25 samples) with a rate of  $0.323 \pm 0.2857$  mmol/l. The study also accounted for differences in gender and manifold smoking habits (11). The research results were compared to a study conducted by Tjahajawati et al. which focused on female subjects. The study showed a decrease in the rate of salivary calcium in smokers, with a marked salivary calcium level of  $1.16 \pm 0.93$  mmol/l, compared to non-smokers who had a level of  $1.80 \pm 0.96$  mmol/l (9).

Difference in results can be attributed to the gender factor, which determines the rate of salivary calcium. This supports the finding of Tjahajawati et al. that nicotine can decrease the levels of estrogen and parathyroid hormones (PTH) (9). Hormones have an influence on the rate of salivary calcium. Estrogen plays a known role in changing the composition of saliva. When estrogen levels decrease, salivary calcium levels can also change. In female who smoke and have decreased estrogen levels, the absorption of calcium in the small intestine

can be lowered by 20-25%, resulting in a lower rate of calcium in the blood. Female who smokes also experience a decrease in PTH hormone which has a role in balancing the rate of calcium in the blood by releasing calcium from the bone into the blood. When calcium levels in the blood decrease, PTH increases. However, female who smoke may have PTH not working to its maximum capacity, leading to reduced calcium levels in the blood and a lower rate of calcium in the saliva (9). The research conducted by Varghese et al., Abed et al., and Tjahajawati et al. strengthens the statement that gender can be a causative factor in the difference in results from the rate of salivary calcium in smokers.

#### Salivary calcium levels based on measurement method

Various methods have been used to study the rate of salivary calcium in different ways. These include Atomic Absorption Spectrophotometer (AAS), cresolphthaleine complex, and Electrolyte Analyzer. Research by Sutej et al. using AAS found that smokers had slightly higher salivary calcium levels than non-smokers, with values of  $0.963 \pm 0.422$  mmol/l compared to  $0.466 \pm 0.205$  mmol/l for non-smokers, although this difference was not statistically significant (15). These findings are consistent with similar research by Varghese et al., who also used AAS and found that salivary calcium levels were higher in smokers with values of  $2.27 \pm 24838$  mmol/l compared to  $1.726 \pm 0.103$  mmol/l for non-smokers (14).

A study by Kolte et al. found that smokers have a lower rate of salivary calcium compared to non-smokers. The research showed that the rate of salivary calcium was  $0.3469 \pm 0.2581$  mmol/l in healthy non-smokers and  $0.2492 \pm 0.2402$  mmol/l in healthy smokers, while the rate in non-smokers with chronic periodontitis was  $0.1536 \pm 0.0708$  mmol/l and in smokers with chronic periodontitis was  $0.0865 \pm 0.0372$  mmol/l (8). Research done used the cresolphthaleine complexona method in the Selectra E automatic machine, which showed some issues with reagent stability, linearity, and recovery due to magnesium interference (8). The most reliable method is the Atomic Absorption Spectrophotometer (AAS), but it requires a special and expensive instrument and is not suitable for routine testing in a clinical laboratory (25). It is important to note that different methods may yield different salivary calcium results, which can be influenced by the limitations of the method used. Limitations Study

This research has limitations during the drafting process in the form of limits set in finding sources or literacy that fits the inclusion criteria. Articles or journals published in 2012-2022 with the appropriate criteria are very limited and many articles were published ten years ago. The research samples covering age, gender, and biochemical methods included in this study varied.

#### CONCLUSION

The results of reviewing several articles in this study showed that the average value of salivary calcium levels in smokers was 1.139175 mmol/l. Gender, age, duration of smoking, and other comorbidities such as periodontitis are factors that can influence salivary calcium levels.

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