Correlation between Salivary pH in Menopausal Women and Oral Lactobacillus: A Rapid Review

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Abstract

Numerous studies have reported clinical manifestations in the oral cavity caused by hormonal changes during menopause. Hyposalivation, often complained by menopausal women, impacts decreasing salivary pH, driving normal flora in the oral cavity becomes pathogenic, including Lactobacillus sp., which is often associated with caries. This study aims to determine the association between salivary pH in menopausal women and Lactobacillus.

A rapid review method following PRISMA guidelines was performed in this literature review. The research question was structured according to the PICO framework. Relevant articles searches were conducted in online databases, including MEDLINE/PubMed, Google Scholar, Science Direct, and SAGE Journal.

After selection based on inclusion and exclusion criteria, four papers were identified through PRISMA and four others through hand searching. Two articles reported that the number of Lactobacillus in the oral cavity of menopausal women was higher than non-menopausal and premenopausal women. Another study revealed that of 141 older women in the study (63.8%), 48.2% of them had high amounts of Lactobacillus in their saliva (>10⁵). Five other articles reported lower salivary pH in menopausal women than non-menopausal women. This review showed that the number of lactobacilli increased in the oral cavity of menopausal women, in line with the decrease of salivary pH to become acidic compared to non-menopausal women.

The salivary pH of menopausal women, which tends to be acidic, correlates with increased Lactobacillus in the oral cavity in menopausal women.

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Introduction

Menopause is a permanent cessation of menstruation that commonly occurs in 45-55 years of women. This period occurs after a woman has experienced amenorrhea for 12 consecutive months (no longer has her usual menstruation) because the ovaries no longer produce ovarian follicles^{1,2}. The World Health Organization (WHO) estimates that the number of menopausal women in Asia in 2025 will increase from 107 million to 373 million. In Indonesia, in 2020, as many as 19.67% of women entered menopause from a total of 133

***Corresponding author:** Qonita Faizulhyrza Tabayyana Faculty of Dentistry, Padjadjaran University, West Java, Indonesia. E-mail: <u>tabayyana@gmail.com</u> million Indonesian women with a reasonable age range for menopause³. The increase in the number of menopausal women is due to the rise in life expectancy every year³. The female reproductive system is influenced by two hormones, namely follicle-stimulating hormone (FSH) and luteinizing hormone (LH), which play a role in stimulating the secretion of estrogen and progesterone and play a role in oocyte maturation in a woman's ovaries⁴. When the productive period of the ovary runs out or can no longer produce follicle growth until the follicle matures, the ovary will become less responsive to stimulation of the FSH and LH. Consequently, estrogen production in the ovaries will decrease, which will affect other processes in the woman's body system^{4,5}. The decrease in total estrogen production during menopause affects salivary gland function, reducing salivary flow (hyposalivation). Hyposalivation in menopausal

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women has been reported to be significantly associated with complaints of oral discomfort^{6,7}.

Decreased salivary flow by 40-50% or even experiencing xerostomia will also affect the quality of life, mainly the essential functions of speaking, chewing, swallowing, and changes in the oral cavity that have a domino effect⁶. The other impact of hyposalivation on the oral cavity is decreased salivary pH. Additionally, the oral environment becomes acidic, which will cause the self-cleansing function and saliva buffering ability to fall⁸. The acidic conditions of the oral cavity and the inability of buffer capacity will stimulate the growth of opportunistic bacteria, especially acidophilic and acidogenic bacteria, in the mouth so that they have the potential to become pathogens⁹. Streptococcus mutans and Lactobacillus sp. are normal flora of the oral cavity, which is acidophilic and acidogenic and has been reported in an acidic oral environment to exacerbate the demineralization process into caries¹⁰. Apart from Streptococcus mutans, Lactobacillus sp. is often associated with cariescausing bacteria¹¹. In menopausal women with hyposalivation or even xerostomia, an increase in acidogenic bacteria such as Lactobacillus in the oral cavity should be wary of because it can have adverse effects.

Based on the increase in the number of menopausal women every year, information about the association between menopausal conditions and the tendency to cause oral diseases also needs to be promoted. Manifestations in the oral cavity of menopausal women. such as decreased salivary pH compared to non-menopausal women, have been extensively studied. However, research reporting on the number of microbiotas in menopausal women, especially Lactobacillus sp, is rarely investigated. In particular, the research was conducted to provide and disseminate information of menopausal women regarding the prevention of oral diseases.

Materials and methods

The study used the rapid review method. The research questions were designed based on the concept of the PICO framework, Population (P): menopausal women; Intervention (I): salivary pH; Comparison (C): Lactobacillus; Outcome (O): association. Research tools and materials used are laptops, internet access, Microsoft Office software, Mendeley, and electronic article databases, namely, National Library of Medicine (MEDLINE/PubMed), Google Scholars, ScienceDirect, and SAGE Journal. The research was carried out for approximately three months, from December 2021 to February 2022.

The search and selection of articles in the electronic database refer to the Preferred Reporting Items for Systematic Review without (PRISMA)¹². Meta-Analvses The PRISMA flowchart of the article selection process is shown in Figure 1. Article identification was first performed using keywords combined with boolean operators. namely: ((salivary pH) AND ((hyposalivation) (menopause) AND OR (xerostomia)) AND (oral lactobacillus)). The search focus for relevant articles on MEDLINE/PubMed used Medical Subject Headings (MeSH), and free text was used to search other electronic databases. The selected articles in the identification stage were then screened based on duplication, title, and abstract.

Additional article searches were carried out by hand searching using Google search engine for articles listed in the article reference list selected through PRISMA. Still, the report did not appear when identified using keywords. The last extraction stage, article eligibility, was carried out based on the suitability between the contents of the article and the inclusion criteria as well as exclusion criteria (Table 1). The complete contents of the last extracted articles were then analyzed thematically based on the title of the article, the name of the author, the year of publication, the number of research samples, the results of the study, and the conclusions of the study. Complete data on the results of the thematic analysis of selected articles are summarized in a simple quantitative measure to describe the research results of each piece (Table 2).

Results

Three hundred five articles were identified in the first stage of the search, with 22 articles from the PubMed electronic database, 118 articles from Google Scholar, 124 pieces from Science Direct, and 41 articles from the SAGE Journal. Selection of articles based on duplication obtained 277 articles, and 28 were excluded. In the title and abstract screening stage of 277 pieces, only 32 articles were relevant to the title of this study, and 245 articles were excluded. The total number of reports for the next extraction stage was 32 articles. Article selection was based on inclusion and exclusion criteria, 28 articles were excluded, and only four entered the analysis stage (Figure 1). Additionally, hand searching on Google Scholar based on the literature of the included articles resulted in four others. Therefore, eight papers were analyzed from searching through the PRISMA guidelines and hand searching.

The research articles analyzed were divided into two types, namely five articles of which described the differences in salivary pH of menopausal and non-menopausal women. In contrast, the other three articles explained Lactobacillus in menopausal women.

The difference in salivary pH between menopausal and non-menopausal women described in 5 articles studied used samples of menopausal and non-menopausal women, both fertile and pregnant women, with a different number of participants. The results of the five research articles recognized that the salivary pH of menopausal women is lower than that of nonmenopausal women^{7,13-16}. The salivary flow rate of menopausal women, considered lower than that of non-menopausal women, tends to cause a low salivary pH^{7,14–16}. Examination of high OHI-S and DMF-T indexes in menopausal women indicates а poor oral environment for menopausal women compared to nonmenopausal women^{7,14}, except in the study by Foglio-Bonda et al. which reported higher DMF-T index results in non-menopausal women than their counterparts, albeit not significantly. The caries experience in menopausal women was substantially higher than that of non-menopausal women¹³.

The following three articles describe Lactobacillus in the oral cavity of menopausal women. Semiguantitative enumeration of Lactobacillus on de Man, Rogosa, and Sharpe (MRS) medium agar showed that Lactobacillus from oral and rectal smears in menopausal women were twice as high as in pregnant women¹⁷. Based on multiplex PCR results, 99 Lactobacillus colonies were identified from 30 pregnant women, and 37 colonies were identified from 30 menopausal women. It shows that the spread of Lactobacillus strains in oral, vaginal, and rectal menopausal women is lower than in pregnant women. Members of the L. delbrueckii

group (*L. crispatus*, *L. gasseri*, *L. johnsonii*, L. jenseni, *L. acidophilus*) predominated in pregnant women, while the *L. casei* members (*L. paracasei* and *L. rhamnosus*) dominated in postmenopausal women¹⁷.

Aerobic bacteria identified from subgingival plaque in premenopausal and postmenopausal women were dominated by Staphylococcus Streptococcus sp., mutans. Enterococcus. Lactobacillus, and Neisseria catarhaalis. The predominant anaerobic bacteria were Peptostreptococcus and Veillonella, but other bacteria showing high numbers were Stomatococcus, Peptostreptococcus, Prevotella, Porphyromonas gingivalis, and Fusobacterium¹⁸. The rate of chronic periodontitis was more elevated in postmenopausal women (80%) than in premenopausal women (41.8%). In contrast, the percentage of mild periodontitis/gingivitis was more increased in premenopausal women (58%) than in postmenopausal women (20%)¹⁸.

A total of 67.8% of 142 older people had Streptococcus mutans in high numbers or more than 10^5 , while the number of *Lactobacillus sp.* more than 10^5 were identified only in 48.2% of 141 elderly. As many as 83.7% of the elderly reported to have an average salivary flow rate, and the rest experienced hyposalivation (<1mL/min). The buffering capacity of saliva with alkaline saliva was more dominant than the capacity of neutral and acidic saliva¹⁹. The article did not report exactly how the study results were based on gender, but of the 141 elderly studied, 63.8% of them were women.

Discussion

The number of ovarian follicles present since a woman was born is related to the reproductive period. Ovarian follicles will respond to hormonal stimulation so that they secrete estrogen. This condition will have a negative feedback effect on the pituitary and cause an increase in the secretion of Gonadotropin-Releasing Hormone (GnRH). It triggers an increase in FSH and LH secretion even in excess in menopausal women^{4,5,20}. Hormonal imbalances that occur in menopausal women have an important effect on the overall body, such as decreased development of reproductive organs, skin aging, increased bone resorption that leads to osteoporosis, and cavity^{6,13,21}. decreased pН in the oral

Estrogen receptor β is an estrogen receptor subtype predominantly expressed in human oral epithelium, salivary gland acinar cells, and salivary gland ductal cells. Estrogen receptor β in these places indicates that the hormone estrogen affects the functional activity of the human oral cavity, especially in regulating the growth of epithelial cells of the oral mucosa, gingiva, and salivary glands²². The decrease in estrogen in menopausal women causes hypofunction of the salivary glands, which in turn causes a reduction in the quality and quantity of saliva (hyposalivation). This situation leads to xerostomia which is often complained of by women²³. Hyposalivation menopausal experienced by menopausal women can reduce the salivary pH in the oral cavity⁹, and is indirectly related to a decrease in estrogen. The study results explain that the salivary pH of menopausal women tends to be lower than that of non-menopausal women. The acidic environment in the oral cavity of menopausal women can be a good niche for forming colonies of acid-fast (acidophilic) bacteria such as Streptococcus mutans, sobrinus, Lactobacilli sp., Actinomyces, Bifidobacteria, and yeasts⁹.

Lactobacillus generally live in an anaerobic environment with a low pH or acidic atmosphere and the availability of carbohydrates for fermentation. Like Streptococcus mutans, Lactobacillus can tolerate low pH and produce acid from carbohydrate fermentation¹¹. The human bodies that meet these niche specifications are caries lesions in the oral cavity, stomach, and vagina¹¹. Lactobacillus are often found in the oral cavity, especially in biofilms or deep caries lesions initiated by Streptococcus mutans. Therefore, Lactobacillus is believed to associate with the formation of dental caries. Its characteristic that approves acidic an environment (acidophilic) allows this bacterium to be found in the oral cavity of menopausal women (the pH of the oral cavity tends to be acidic), especially those who do not maintain health in their oral cavity¹⁴. Petricevic et al. reported that the number of Lactobacillus from oral specimens of menopausal women was twice as high as that of pregnant women¹⁷, and salivary pH in menopausal women was lower compared to non-menopausal women¹⁵. The saliva of menopausal women was also more inadequate and tended to be more acidic than that of non-menopausal women^{7,13–16}. The

results of this study clarify that the number of Lactobacillus tends to increase at the pH of an acidic oral environment.

Lactobacillus often found in the human oral cavity are L. casei, L. fermentum, L. rhamnosus, L. acidophilus, L. salivarius, and L. oris^{11,24}. Lactobacillus, which dominates menopausal women, is L. casei, L. paracasei, and L. rhamnosus¹⁷. Research reported that teichoic acids had been found from species L. fermentum, L. plantarum, and L. casei adhering to the tooth surface. It explains that teichoic acid, as a wall component of Gram-positive bacteria, in this case, Lactobacillus, plays a role in biofilms²⁵. formation of supporting the Streptococcus mutans and Lactobacillus sp. grow faster at pH 5.0 than Streptococcus nonmutans and Actinomyces. Prolonged acidic conditions in the oral cavity, such as conditions in teeth that have caries, can also cause an increase in the pathogenicity of Streptococcus *mutans* and *Lactobacillus sp.* in the oral cavity¹⁰.

The paradigm of caries states that in the formation of dental caries, acidogenic bacteria are involved, which produce lactic acid from the anaerobic fermentation of carbohydrates and bacteria with aciduric properties that can live in an acidic environment. Streptococcus mutans and Lactobacillus, both of which have acidogenic and aciduric properties, are most likely involved in caries formation. Streptococcus mutans and other acidogenic oral bacteria create pre-caries lesions that can provide retention for Lactobacillus so that Lactobacillus can bind mechanically through the pre-caries lesion. Lactobacillus then works to aggravate the caries condition.¹¹ In the end, the acidic environment from the low salivary pH in the oral cavity environment of menopausal women can change Lactobacillus, which was initially a normal flora, into opportunistic pathogenic bacteria that can increase the risk of caries in menopausal women.

In addition to caries, Lactobacillus is also found in periodontal tissues, such as subgingival or supragingival. The number of subgingival Lactobacillus in postmenopausal women has also been intensely investigated¹⁸, compared to subgingival non-menopausal women²⁶. An increase in the number of Lactobacillus or other pathogenic bacteria in periodontal tissues also allows an increase in oral cavity disease in menopausal women. It is proven that the DMF-T index, CPI (Community Periodontal Index) and

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LoA (Loss of Attachment) in menopausal women are higher than in non-menopausal women⁷. The increase in acidogenic and other acidophilic bacteria due to an acidic oral cavity can also harm the host. In addition to the increased risk of caries previously described, the increased risk of biofilm formation and gingival inflammation (gingivitis) by the *Streptococcus sanguis* and *Actinomyces israelii* bacteria is also a cause for concern²⁷. An increase in Streptococcus species will also increase the risk of odontogenic infections²⁸.

Research reporting information related to menopausal conditions with a tendency to develop oral diseases caused by pathogenic bacteria is expected to assist health workers in preventing possible complaints and the onset of diseases in the oral cavity of menopausal women. Dental and oral health checks should be carried out regularly, extra care for dental and oral health needs to be done independently, and reduce carbohydrate consumption²⁹. Menopausal women also need to visit an endocrinologist to get hormone therapy to minimize the incidence of hyposalivation, which can create an acidic atmosphere for the mouth. Dentists also need to emphasize the importance of maintaining oral hygiene through educational programs for menopausal women.

Conclusions

This study concludes a correlation between the salivary pH of menopausal women and Lactobacillus. The decrease in salivary pH in menopausal women due to hormonal changes triggers an increase in Lactobacillus. Consequently, it can increase the incidence of caries in the oral cavity of menopausal women.

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Declaration of Interest

The authors report no conflict of interest.

Inclusion Criteria	Exclusion Criteria
1) Articles are available in full text	1) Experimental research on non-
2) Articles were published in the last	humans or animals
ten years (2011-2021)	2) Articles with research designs of
Articles are in English or Indonesian	systematic review, meta-analyses, and
4) Articles with the following types of	other research designs that have a level of
research: cross-sectional, case-control,	validity below RCTs based on an evidence-
cohort, and Randomized Control Trials	based pyramid
(RCTs)	
5) Articles with experimental and	
observational research types that discuss	
Lactobacilli in the oral cavity and salivary pH	
in menopausal women	

Table 1. Inclusion and exclusion criteria for article extraction.

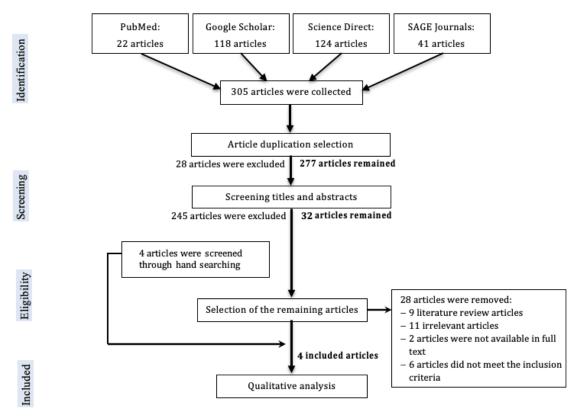


Figure 1. Research flowchart following PRISMA.

Author (Year)	Research Title	Sample	Result	Conclusion
Bhat, Suraksha et al. ¹⁴ (2010)*	A Study on Evaluation of the Effect of Menopause on Saliva and Dental Health	Study group: 20 menopausal women (average age of 52 years) Control group: 20 fertile women (average age of 26 years)	OHI and DMF-T Index Study group = 1.89 ± 0.82 and 8.20 ± 4.58 Control group = 0.99 ± 0.57 and 2.30 ± 2.07 Salivary pH Study group = 5.67 ± 0.49 Control group = 7.02 ± 0.41 Salivary flow rate Study group = 4.50 ± 1.93 Control group = 8.95 ± 1.84	OHI and DMF-T indexes for menopausal women are higher than for non- menopausal women. The salivary pH and salivary flow rate for menopausal women are lower than fertile (non-menopausal) women.
Rukmini, JN et al. ⁷ (2018)*	Effect of Menopause on Saliva and Dental Health	Study group: 40 postmenopausal women (41-60 years) Control group: 40 non-menopausal women (21-31 years)	Salivary flow rate Study group = 55% normal and 45% hyposalivation Control group = 100% normal Salivary pH Study group = 50% normal and 50% acidic pH Control group = 100% normal OHI-S Index Study group = 17.5% good and 82.5% poor Control group = 82.5% good and 17.5% poor DMF-T Index (Significant with P<0.001) Study group = 5.15 \pm 2.94 Control group = 1.38 \pm 1.56	Postmenopausal women tend to have lower salivary flow rates and hyposalivation than non- menopausal women. The salivary pH of postmenopausal women tends to be acidic compared to the salivary pH of non-menopausal women. OHI-S and DMF-T indexes in postmenopausal women are higher than in non- menopausal women.

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	Replacement Therapy a Remedy?		2. The rate of chronic periodontitis was higher in postmenopausal women (80%) than in premenopausal women		
Thomas, Kanakam Elizabeth. ¹⁸ (2014)**	Prevalence of Chronic Periodontitis Among Post- Menopausal Women-Hormone	110 premenopausal women and 110 postmenopausal women	1. The dominating aerobic bacteria isolated from the two subjects were <i>Streptococcus mutans</i> and <i>Lactobacillus</i> <i>sp.</i> Aerobic bacteria that showed high significance were <i>Staphylococcus sp.</i> , <i>Streptococcus mutans</i> , <i>Enterococcus</i> , <i>Lactobacillus</i> , and <i>Neisseria catrhaalis</i>	the h subg samp (43%	bbacillus sp. showed igh significance of ingival plaque bles in premenopausa and nenopausal women b)
			slightly higher than in postmenopausal women 2. Members of the <i>L. delbrueckii</i> (<i>L. crispatus, L. gasseri, L. johnsonii, L. jenseni, L. acidophilus</i>) dominated in pregnant women, while members of the <i>L. casei</i> (<i>L. paracasei</i> dan <i>L. rhamnosus</i>) predominated in postmenopausal women		
Petricevic, Ljubomir et al. ¹⁷ (2011)**	Characterization of the oral vaginal and rectal Lactobacillus flora in healthy pregnant and postmenopausal women	postmenopausal	1. Examination of Lactobacilli concentrations using semiquantitative enumeration on MRS agar showed that oral and rectal Lactobacillus concentrations in postmenopausal women were two times higher than those seen in pregnant women. In contrast, the concentration of Lactobacilli from vaginal specimens in pregnant women was	in po are h pregi distri diver postr	bbacilli concentrations stmenopausal womer igher than in hant women, but the bution of strains and sity of Lactobacilli in nenopausal women is r than in pregnant en
Aisyah, Rosita et al. ¹³ (2021)*	The Difference of Salivary Volume, pH and Oral Conditions Between Menopausal and Non-Menopausal Women	27 menopausal women & 27 non- menopausal women	Salivary volume (Significant with $p = 0.0016$; P<0.05) Menopause = $1.4 \pm 1.1 $ Non- menopause = 2.4 ± 1.4 Salivary pH (Significant with $p = 0.019$; P<0.05) Menopause = $6.2 \pm 0.5 $ Non- menopause = 6.6 ± 0.6 Caries (Significant with $p = 0.014$; P<0.05) Menopause = $70\% $ Non-menopause = 41%	saliva wom of no wom expe meno highe	salivary volume and ary pH of menopausal en are lower than that n-menopausal en, and caries rienced by opausal women are er than that of non- opausal women.
et al. ¹⁹ (2021)*	Correlation Between Microbial Host Factors and Caries Among Older Adults	A total of 141 participants aged 60-99 years (63.8% women and 36.2% men)	1. The mean DMF-T of coronal caries was 11.08. 9.9% of participants had at least one decayed tooth (DT), 52.5% had at least one missing tooth (MT), and 86.5% had at least one filled tooth (FT). A total of 34% of the study sample had DMF-T > 12 2. In SM bacterial examination, 67.4% of participants had MS > 10 ⁵ (high), while 32.6% of participants had MS < 10 ⁵ (high), while 32.6% of participants had MS < 10 ⁵ (high), while 51.8% of participants had LB > 10 ⁵ (<i>high</i>), while 51.8% of participants had LB < 10 ⁵ (<i>high</i>), while 51.8% of participants had normal salivary flow or hypersalivation (>=1mL/min), while 16.3% had hyposalivation (<1mL/min) 5. In the saliva buffer capacity examination, 61% of participants had alkaline salivar, and only 10.6% had acidic saliva.	corre and l expe The r low e relati show vary envir phys cond the n	e is a positive elation between SM _B with caries rience in older adults. mean DMF-T can be even though SM is vely high. The result vs that other factors according to the host onment or iological & biological itions that can affect umber of SM and LB e oral cavity.

			mild periodontitis/gingivitis was more elevated in premenopausal women (58%) than in postmenopausal women (20%)	
Saluja, Pulin et al. ¹⁵ (2014)**	Comparative Evaluation of the Effect of Menstruation, Pregnancy, and Menopause on Salivary Flow Rate, pH and Gustatory Function	Study group: 30 menstruating women, 30 pregnant women, 30 postmenopausal women Control group: 30 women with a regular menstrual cycle	Salivary flow rate Study group: 1.09 ± 0.4 (menstruating group); 1.29 ± 0.5 (pregnant group); 0.93 ± 0.2	The salivary flow rate and salivary pH of postmenopausal women are the lowest compared to other groups
Foglio- Bonda, P.L. et al. ¹⁶ (2019)*	Salivary pH and Flow Rate in Menopausal Women	60 menopausal women & 60 nonmenopausal (fertile) women	Salivary pH (0.11; p<0.05) Menopause = 6.75 ± 0.34 Non- menopause = 6.86 ± 0.24 Salivary flow rate (0.19; p<0.0001) Menopause = 0.29 ± 0.17 mL/min Non- menopause = 0.48 ± 0.19 mL/min	Salivary pH and salivary flow rate of postmenopausal women are lower but not significant compared to non-menopausal women

Table 2. Results of thematic analysis of the articles reviewed.

*= Articles obtained following the PRISMA guidelines; ** = Articles obtained through hand searching method.

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