

The efficacy of scaling root planing to inflammation biomarker of periodontitis patients with atherosclerosis

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Received; March 2 2021, Revised, May 10, 2021, Accepted, June 2, 2021

ABSTRACT Periodontitis is a disease of surrounding dental tissue with a prevalence of 74.1% in Indonesia. Many studies show periodontitis plays a role in the progression of atherosclerosis. The relationship between these two conditions shows that scaling root planing intervention can reduce the risk of atherosclerosis. This study aimed to know the efficacy of scaling root planing on changes in inflammatory biomarkers in periodontitis patients with atherosclerosis. This systematic literature review was conducted using the Rapid Review method, referring to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines. Electronic searches were carried out from 4 electronic databases, including the National Library of Medicine (Medline / PubMed), The Cochrane Library, EbscoHOST, and SAGE Journal. Inclusion and exclusion criteria selected 6 RCT articles to be analyzed qualitatively. Within 2 to 6 months, research in 6 RCT articles showed the results in significantly reducing CRP levels as the main biomarkers of atherosclerosis after scaling root planing intervention. Other biomarkers that were also assessed are cytokines levels, lipid profile components, WBC, and fibrinogen. Overall results showed a positive effect of scaling root planing intervention in reducing the inflammatory biomarker levels of atherosclerosis in periodontitis patients with atherosclerosis. The treatment of scaling root planing is considered effective in reducing the inflammatory biomarker levels of atherosclerosis in periodontitis patients with atherosclerosis to reduce the level of risk.

KEYWORDS: scaling root planing, inflammatory biomarker, atherosclerosis

INTRODUCTION

Periodontal disease is a disease of surrounding dental tissue that is often found in the community, especially in Indonesia.¹ The most common periodontal disease is Periodontitis. According to Riskesdas 2018, the prevalence of Periodontitis in Indonesia is relatively high, reaching 74.1%.² Periodontitis occurs due to complex interactions between bacteria and inflammatory cells that develop in the periodontal tissue.^{1,3}

Some studies explain the relationship between Periodontitis and systemic diseases. One of them is cardiovascular disease.^{4,5} Cardiovascular disease is a disorder of the heart and blood vessels,

including stroke, coronary heart disease, myocardial infarction, and other conditions.⁶ According to the World Health Organization (WHO) in 2018 regarding the profile of Non-Communicable Diseases (NCD) in Indonesia, cardiovascular disease is a disease with the highest mortality among other NCDs.⁷ One of the conditions found in cardiovascular disease is atherosclerosis, which is the dominant cause of cardiovascular disease.⁶ Atherosclerosis is the accumulation of plaque due to the collection of fat in the walls of the arteries.⁸ Common risk factors for atherosclerosis include tobacco smoking, abnormal lipid levels in the circulation, and diabetes mellitus.⁹

How to cite this article: Safitri S, Susanto A, Hendiani I. the efficacy of scaling root planing to inflammation biomarker of periodontitis patients with atherosclerosis . JDS. 2021; 6 (1): 41-50

Over the past ten years, several studies have identified an association between periodontal disease and cardiovascular disease based on the inflammatory process in both conditions.^{10,11} There is strong evidence that periodontal pathogens can translocate from the oral cavity to systemic blood vessels. *Porphyromonas gingivalis* bacteria and its products in lipopolysaccharides (LPS) can cause endothelial cell damage in blood vessel walls and increase inflammatory activities that induce atherogenesis thromboembolic events.¹ Increased inflammatory cells and their activities are identified as the leading cause of atherosclerotic plaque formation and thromboembolic event that manifests in symptoms of cardiovascular disease.⁸

Several studies have also shown that Periodontitis is associated with several

inflammatory biomarkers such as CRP, TNF- α , and IL-6, known as biomarkers of the risk level for atherosclerosis.^{5,12-13} Several studies have also stated that periodontal treatment in the form of scaling root planing has been shown to reduce the level of serological risk factors for atherosclerosis in patients diagnosed with Periodontitis with atherosclerotic conditions.^{1,14-15} Based on the possible relationship between Periodontitis and cardiovascular disease, scaling root planing treatment in periodontitis patients with atherosclerosis has the potential to influence the level of atherosclerosis risk that can be seen through the story of inflammatory biomarkers. The purpose was to review the literature about the efficacy of scaling root planing interventions on changes in inflammatory biomarkers in periodontitis patients with atherosclerosis.

MATERIALS AND METHODS

This research was conducted using the rapid review method. The specific research question was designed based on the PICO framework concept, as follows: Population: articles that discuss the effect of periodontal treatment on chronic periodontitis patients with atherosclerosis; Intervention: scaling root planing treatment; Comparison: individual without scaling root planing treatment; Outcome: changes in inflammatory biomarkers as a risk factor for atherosclerosis after scaling root planing treatment. Search and selection of articles to be analyzed qualitatively were carried out according to the guidelines of Preferred Reporting of Systematic Reviews and Meta-Analyses (PRISMA).¹⁶ An electronic search for appropriate studies was carried out from four electronic literature databases. These included the National Library of Medicine (MEDLINE/PubMed), The Cochrane Library, EBSCOhost, and SAGE Journal. The search was performed using keywords combined with boolean operators as follows: ((*atherosclerosis*) OR (*coronary heart disease*)) AND ((*periodontal therapy*) OR (*nonsurgical periodontal therapy*) OR (*scaling root planing*)). To focus the search and find more relevant references, the authors used Medical Subject Headings (MeSH) to search the MEDLINE/PubMed and The Cochrane Library databases and used free text for searches on other electronic databases. Inclusion criteria for the articles are studies published within the last ten years, written in

English, available in full-text, and conducted in randomized controlled trial study design with the following conditions: aimed at assessing the risk of cardiovascular disease, including human subjects with Periodontitis or atherosclerosis or cardiovascular disease due to atherosclerosis, the test group was the group that received the scaling root planning intervention, and the outcome variable is the biomarkers of atherosclerosis-related to the risk level. Exclusion criteria for the articles collected are experimental studies on non-humans or animals and themes with a systematic review study design, meta-analysis, and other study designs that have a validity level below RCT based on an evidence-based pyramid. In the initial search, 109 articles were collected from 4 electronic databases, and two articles were collected from the hand manual searching process by reviewing the reference list from relevant studies. Thirty-three articles then were excluded due to duplication. Collectively, the search process resulted in 78 themes. Then 31 articles that not available in full-text were excluded. Forty-seven full-text articles that remained were further assessed by inclusion and exclusion criteria summarized in **Table 1**. At the end of the search process, six pieces were collected to be analyzed qualitatively. The PRISMA flow chart as an article selection process can be seen in **Figure 1**.

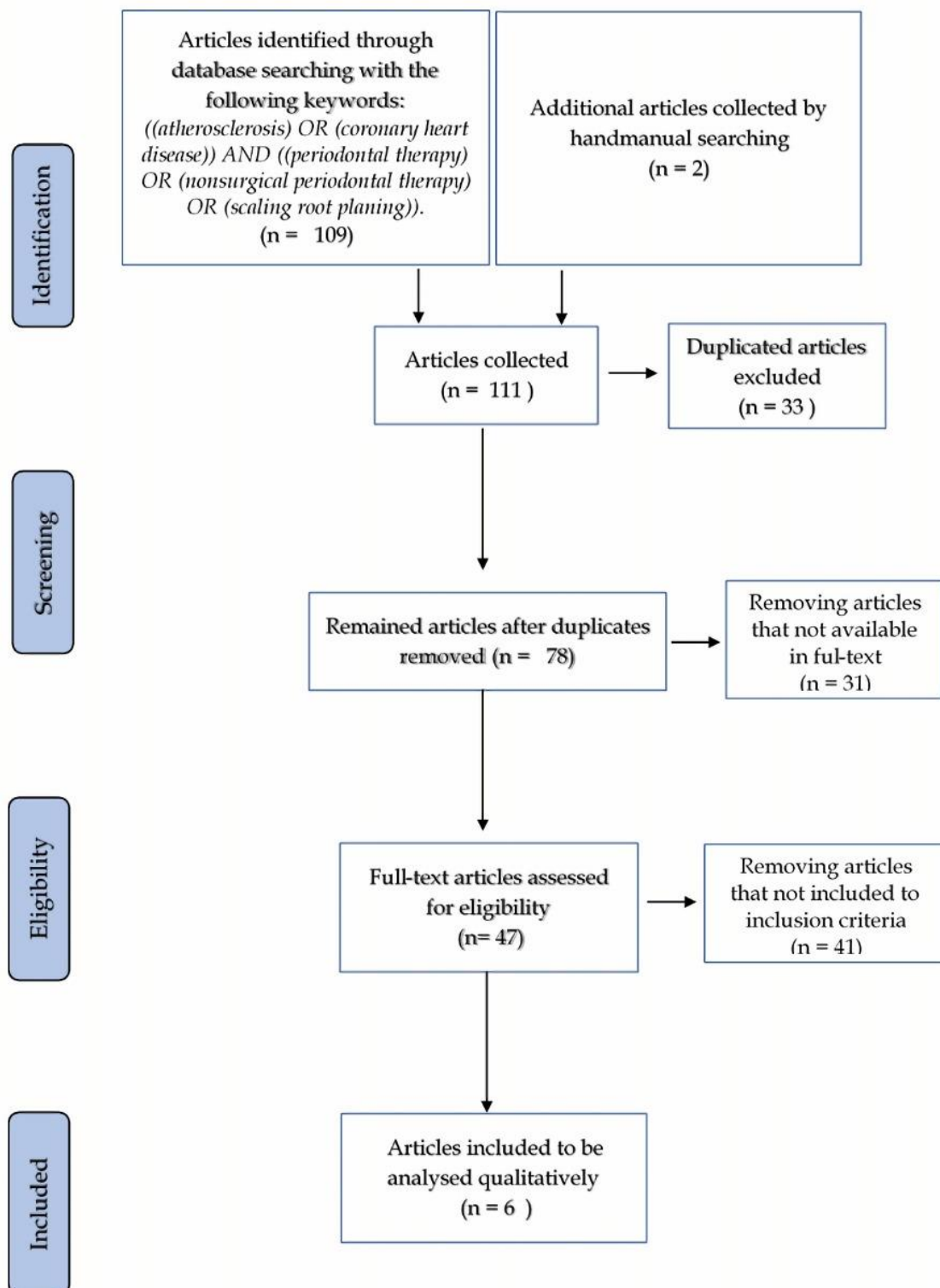


Figure 1. PRISMA flow diagram for search and selection process

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RESULTS

After searching and selecting articles, 6 articles were included in the inclusion criteria. Then, the results of data extraction from the six articles are summarized in **Table 2**.

Table.2

Data extraction from 6 articles about the efficacy of scaling root planing on periodontitis patients with atherosclerosis

N o	Authors (Year)	Participants	Research time	Interventions	Inflammatory Biomarker Parameters	Research result	Conclusion
1	Montenegro <i>et al.</i> ¹⁷ (2019)	A total of 82 patients, stable CAD and chronic Periodontitis: 1. Test Group: 39 2. Control Group: 43	3 months, with a follow-up time: 1. Baseline 2. 1 month 3. 3 months	1. Test Group: OHI is continued by 4 subgingival SRP sessions per quadrant 2. Control Group: 1 dental prophylaxis session	1. CRP 2. Profil lipid 3. Cytokines (IL-1, IL-6, IL-8, IL-10, and TNF- α) 4. Glycated Hb	After 3 months: 1. There was a significant decrease in biomarker concentrations in the test group, namely: • CRP: 11.3 ± 12.8 mg / L to 5.7 ± 4.1 mg / L • IL-10: 1.50 ± 31.28 pg / ml to 6.31 ± 8.35 pg / ml • IL-8: 14.18 ± 18.20 pg / ml to 11.12 ± 11.86 pg / ml • IL-6: 6.20 ± 17.90 pg / ml to 4.11 ± 11.50 pg / ml • TNF- α : 9.59 ± 5.83 pg / ml to 9.58 ± 5.75 pg / ml 2. There was no significant difference in the levels of glycated Hb. 3. More than 80% of patients in the test and control groups had LDL and total cholesterol under control and HDL under control. 4. After 3 months, there was significant periodontal tissue improvement in the test group. There was a significant decrease in the number of plaques, the PPD value and CAL value in the test group, as well as a significant decrease in the BOP value in both groups.	Standard nonsurgical periodontal treatment has been shown to reduce levels of CRP, IL-6, and IL-8 as indicators of systemic inflammation in cardiovascular disease patients as well as to reduce local periodontal tissue inflammation.
2	Bozoglan <i>et al.</i> ¹⁸ (2017)	A Total of 40 patients: 1. Test group: 20 patients	6 months, with a follow-up time: 1. Baseline	1. Nonsurgical periodontal treatment	1. CRP 2. Lipid profile 3. PLT 4. WBC	After 6 months: 1. There was a significant decrease in levels of CRP, LDL, PLT, fibrinogen, and	An association between decreased microorganism

	with Periodontitis and atherosclerosis	2. 6 m		5. Fibrinogen	WBC which was also in line with the decrease in the number of periodontal pathogens: • CRP: 5.01 ± 2.71 mg / L to 1.14 ± 0.57 mg / L • WBC: 9.3 ± 1.4 103 / ml to 6.8 ± 1.6 103 / ml • PLT: 264.4 ± 74.6 103 / ml to 222.5 ± 64.6 103 / ml • Fibrinogen: 356.4 ± 86.3 mg / dl to 296 ± 64.5 mg / dl • LDL: 223.5 ± 42.2 mg / dl to 162.5 ± 28.2 mg / dl 2. There was a significant decrease in the clinical parameters of periodontal disease, include PI, GI, PPD, and CAL in the test and control groups	ms and inflammatory biomarkers after nonsurgical periodontal treatment may indicate that nonsurgical periodontal treatment has the potential to reduce the risk of atherosclerosis.
3	Hada <i>et al.</i> ¹⁹ (2015)	A total of 55 CHD patients with mild to moderate chronic Periodontitis: 1. Test Group: 30 2. Control Group: 25	6 months, with a follow-up time: 1. Baseline 2. 1 month 3. 3 m 4. 6 m	1. SRP 2. OHI in 1, 3, and 6 months 3. WBC	1. CRP 2. Lipid profile 3. WBC After 6 months: 1. There was an increase in CRP levels that was not significant in the test group and significant in the control group • Test Group: 5.10 ± 2.00 mg / L to 6.30 ± 7.53 mg / L • Control Group: 3.62 ± 2.31 mg / L to 4.94 ± 2.04 mg / L (p < 0.05) 2. There was a decrease in levels of LDL, TGL, and total WBC in the test group • TGL: 161.97 ± 105.32 mg / dL to 147.00 ± 90.70 mg / dL • VLDL: 37.55 ± 23.20 mg / dL to 32.39 ± 18.43 mg / dL • WBC: 7660.00 ± 2821.79 / cumm to 7553.33 ± 1634.91 / cumm 3. There is a significant decrease in the BOP, PPD, and GI parameters, but not significant in the CAL value.	Nonsurgical periodontal treatment has a positive effect in reducing risk markers in patients with CHD

4	Cauala <i>et al.</i> ²⁰ (2014)	A total of 64 chronic periodontitis patients: 1. Test Group: 32 2. Control group: 32	6 months, with a follow-up time: 1. Baseline 2. 2 months 3. 6 months	1. SRP 2. OHI instruction and monitoring	1. CRP 2. Lipid profile 3. ESR	After 6 months: 1. Decrease in the median CRP, ESR, total cholesterol, LDL, and TGL values after 6 months in the test group: • CRP: 1.0 to 0.5 • ESR: 12 to 7 • Total cholesterol: 200.5 to 180 • LDL: 116.5 to 114 • TGL: 139 to 115.5 2. There was a significant decrease in the parameters of periodontal disease, namely CAL, BOP, PPD, and PI in the test and control groups	Nonsurgical periodontal treatment is effective in reducing levels of systemic inflammatory biomarkers of cardiovascular disease in patients with advanced chronic Periodontitis.
5	Koppolu <i>et al.</i> ²¹ (2013)	A total of 39 periodontitis patients with myocardial infarction 1. Test Group: 20 2. Control Group: 19	2 months, with a follow-up time: 1. Baseline 2. 2 months	1. SRP	1. CRP 2. TNF- α	After 2 months: 1. CRP and TNF- α levels were significantly reduced in the test group ($p < 0.05$) • CRP: $0.45 \pm 0.12 \mu\text{g} / \text{dl}$ to $0.29 \pm 0.12 \mu\text{g} / \text{dl}$ • TNF- α : $22.15 \pm 1.46 \text{ pg} / \text{ml}$ to $20.20 \pm 1.61 \text{ pg} / \text{ml}$ 2. There is an increase in both the OHI index and a significant decrease in the PPD value in the test group	Clinically, successful nonsurgical periodontal treatment can reduce the concentration of pro-inflammatory cytokines that are essential in the development of cardiovascular disease.
6	Bokhari <i>et al.</i> ²² (2012)	A total of 246 patients with CHD and Periodontitis: 1. Test group: 161 2. Control Group: 85	2 months, with a follow-up time: 1. Baseline 2. 1 month 3. 2 months	1. Supragingival and subgingival SRP 2. OHI	1. CRP 2. Fibrinogen 3. WBC	After 2 months: 1. Significant changes in levels of CRP, WBC, and fibrinogen ($p < 0.001$) in the test group: • CRP: $4.4 \pm 0.2 \text{ mg} / \text{L}$ to $3.1 \pm 0.2 \text{ mg} / \text{L}$ • WBC: $7.8 \pm 0.1 \times 10^9 / \text{L}$ to $6.7 \pm 0.1 \times 10^9 / \text{L}$ • Fibrinogen: $367.1 \pm 10.4 \text{ mg} / \text{L}$ to $299.3 \pm 8.0 \text{ mg} / \text{L}$ 2. In the control group there was no change in CRP levels ($p > 0.8$) 3. There was a significant decrease in the parameters of periodontal disease, namely BOP, PPD, and CAL in the test and control groups	In CHD patients with Periodontitis, nonsurgical periodontal treatment significantly decreased CRP, fibrinogen, and WBC levels systemically within 2 months of follow-up and without systemic changes in medication regimen.

DISCUSSION

The relationship between periodontal disease and cardiovascular disease, especially in atherosclerotic conditions, has been quite widely studied.^{1,23-24} The formation of atherosclerotic plaques depends on several factors, systemic infections and local factors.⁶ The presence of chronic inflammation also contributes to the progression of the disease.^{1,5} The formation of atherosclerotic plaques is influenced by several inflammatory mediators, often used as inflammatory biomarkers to assess cardiovascular disease risk.^{9,25} The primary biomarker in cardiovascular disease risk assessment is CRP.²⁶ Meanwhile, several biomarkers are often used as parameters for risk assessment of cardiovascular diseases, such as cytokines, fibrinogens, WBC, and molecules that describe lipid profiles such as LDL, HDL, total cholesterol, and triglycerides.¹⁷⁻¹⁹

The association that suggests that patients with Periodontitis have an increased risk of the progressive cardiovascular disease shows a question mark whether periodontal disease treatment can be performed as an action that has a positive effect on the level of risk of cardiovascular disease.²⁷⁻²⁸ Standard periodontal treatment in the form of scaling root planing is considered effective in eliminating plaque and reducing the risk of cardiovascular disease level of inflammation.^{1,29-30} This was then investigated further to determine the effect of these treatments on the risk of cardiovascular disease.

Research Montenegro et al. (2019) revealed that nonsurgical periodontal treatment positively affected reducing CRP levels.¹⁷ Participants who took part in the study were CAD patients in stable conditions accompanied by Periodontitis.¹⁷ Examinations were carried out on CAD patients and showed stable cardiovascular disease conditions and found HDL and CRP levels that were uncontrolled in some patients in both the test and control groups.¹⁷ This indicates that even though the patient has received cardiovascular treatment so that his condition is stable, there is still systemic inflammation characterized by abnormal levels of CRP biomarkers. CRP, which is a sensitive molecule, is known as the gold standard biomarker that measures systemic inflammation in cardiovascular disease, so it is often used as the primary outcome.^{5,26,31} Periodontal treatment in the form of SRP and OHI carried out in the test group resulted in a significant reduction in CRP levels after 3 months, thus indicating a decrease in systemic inflammation.¹⁷ Decreased inflammatory biomarkers

are also found in the cytokines IL-6 and IL-8 as inflammatory mediators that play a role in atherosclerotic plaque formation.^{17,32} IL-6 is known to have a role in the process of atherosclerotic plaque erosion that triggers thrombogenesis.⁹ IL-8 is known to have a role in monocyte infiltration as the initiation of atherosclerotic plaque formation.⁶ Decreased levels of TNF- α cytokines were also mentioned in the study of Koppolu et al. (2013) after SRP in 2 months.²¹ TNF- α is a type of inflammatory mediator produced by monocytes and neutrophils.³³ TNF- α plays a role in causing endothelial cell dysfunction in the pathogenesis of atherosclerosis.^{6,34} The decrease in cytokine levels occurs due to the reduction in the degree of inflammation post-scaling root planing treatment.^{1,35} Decreased cytokine levels will also affect CRP levels that decrease due to one of the effects caused by cytokines, excretion of CRP levels.²⁶ Another parameter that was also assessed in the study of Montenegro et al. (2019) are levels of lipid profile components (HDL, LDL, TGL, and total cholesterol) which are finally in control.¹⁷ In addition, it was also found that the level of glycated Hb had decreased even though it was not significant.¹⁷ Glycated Hb is an indicator of the stability of diabetes, which is one of the risk factors for atherosclerosis.⁹

The positive effect of nonsurgical periodontal treatment on the reduction of CRP levels was also revealed in the study of Bozoglan et al. (2017), Caula et al. (2014), and Bokhari et al. (2012).^{18,20,22} Research by Bozoglan et al. (2017) associated decreased levels of CRP along with other parameters of cardiovascular disease such as fibrinogen, WBC, and LDL with the number of periodontal pathogenic microorganisms such as *Porphyromonas gingivalis* (Pg), *Aggregatibacter actinomycetemcomitans* (Aa), and several other periodontal pathogens that cause Periodontitis in atherosclerotic plaques.¹⁸ *Porphyromonas gingivalis* are known to be the primary pathogens in chronic Periodontitis, which contribute to the pathogenesis of atherosclerosis through endotoxin in the form of LPS and the ability of bacteria to translocate into systemic blood vessels.^{3,36-37} The presence of microorganisms such as Pg and Aa plays a role as triggers LDL oxidation in the formation of foam cells, including at the stage of atherosclerotic plaque formation.¹⁸ Bozoglan et al. (2017) revealed a positive correlation between a decrease in the number of microorganisms accompanied by a decrease in CRP levels, fibrinogen, WBC, and LDL as essential indicators of cardiovascular disease after SRP.¹⁸ This strongly

suggests that nonsurgical periodontal treatment has a positive effect on the prognosis of atherosclerosis.

Research by Caula et al. (2014) also assessed other parameters to determine the association of the efficacy of nonsurgical periodontal treatment on the risk of cardiovascular disease.²⁰ One of the parameters evaluated was ESR as an indicator of red blood cell aggregation, indicating the level of blood viscosity.²⁰ ESR is also known as an indicator of coronary heart disease.²⁰ Research by Caula et al. (2014) revealed that the ESR value decreased significantly after six months along with several other biochemical parameters of cardiovascular disease, namely CRP and lipid profile components.²⁰ Based on these findings, it can be said that nonsurgical periodontal treatment is considered effective in reducing levels of systemic inflammatory biomarkers of cardiovascular disease in patients with chronic Periodontitis.

The results of other studies that were also reviewed were the research of Hada et al. (2015).¹⁹ In contrast to other studies that have shown decreased CRP levels, Hada et al. (2015) revealed an increase in CRP levels after the intervention of nonsurgical periodontal treatment.¹⁹ The study found an increase in CRP levels that were not significant in the test group and significant in the control group within six months of the SRP intervention.¹⁹ As we know, CRP is a sensitive molecule that changed during the systemic process in the body. Still, the systemic inflammatory condition in the test group was better than the control group by looking at the insignificant increase in CRP in the test group. In

addition to CRP, other parameters such as levels of lipid profile components and WBC were also assessed.¹⁹ The lipid profile in the test group showed a decrease in TGL and VLDL levels.¹⁹ The number of WBC in 6 months also decreased in the test group and increased in the control group.¹⁹ Periodontal disease causes the WBC levels to increase frequently.³ After eliminating periodontal infection with nonsurgical periodontal treatment, the decreased level of inflammation may be indicated by a decreased WBC count.^{1,34} Therefore, the management of Periodontitis as a chronic periodontal disease has positively reduced the risk of cardiovascular disease.

Evidence on the effectiveness of nonsurgical periodontal treatment in reducing levels of inflammatory biomarkers of cardiovascular disease is also supported by the results of the study by Bokhari et al. (2012).²² A significant reduction in CRP levels, WBC, and fibrinogen within three months in the test group indicates a reduced risk of cardiovascular disease.²² Fibrinogen and CRP are molecules produced by the liver in response to inflammation or infectious stimuli, and these biomarkers will increase when inflammation in the atherogenesis process continues.^{9,31} A limitation in this study is that there is a need to review other RCTs with a longer and more sustained follow-up period. Furthermore, RCT research can be carried out with the consistency of the number of participants at the beginning to the end of the study to be maintained to be carried out with a larger number of samples.

CONCLUSIONS

Based on the analysis results qualitatively, scaling root planing treatment was considered effective in reducing the levels of atherosclerotic inflammatory biomarkers in periodontitis patients with atherosclerosis. This could strengthen the potential for nonsurgical periodontal therapy to

reduce the risk of atherosclerosis which plays a dominant role in cardiovascular disease. Reviews of experimental and observational studies with more extended follow-up periods are needed for more reliable results

ACKNOWLEDGEMENT

We want to thank you for the advice that has been given to this manuscript. Drg. Erna Herawati, M. Kes (Department of Oral Medicine Faculty of Dentistry Universitas Padjadjaran) also drg. Jamas Ari Anggraini, M. Kes and drg. Felisha

Febriane Balafif, M. Kes (Department of Oral Biology Faculty of Dentistry Universitas Padjadjaran).

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