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#### **ORIGINAL ARTICLE**

### The Association between Periodontal Conditions and Serum Lipids among Elderly Participants in Gadjah Mada Medical Centre, Yogyakarta

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#### ABSTRACT

Prevention of cardiovascular diseases by controlling risk factors at an early stage is very important. **Objective:** To determine the relationship between periodontal conditions with serum lipids among the elderly. **Methods:** Total of 78 participants (56 males and 32 females) who were in the age range of 60-76 years were selected for the current study. A logistic regression analysis was used to evaluate the association between periodontal conditions and serum lipid profile. Periodontal conditions was recorded as the maximum score of pocket depth (PD) and loss of attachment (LoA) score which presented in the participants, while levels of total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), and triglycerides (TG) were measured for the serum lipids profile. Age, gender, BMI, high blood pressure, pattern of dental visit, hypertension and cholesterol medication, number of teeth, PD, and LoA were included in the model as independent variable. TC, HDL, LDL, and TG were used as dependent variables. **Results:** According to the results of the logistic regression analysis, loss of attachment  $\geq 6$  mm was associated with TC (p<0.01; 5.295(1.710-16.391) and LDL (p<0.05; 2.87(1.118-7.405), while PD had no association with serum lipids (p>0.05). **Conclusion:** This study indicates that subjects with greater loss of attachment are potentially at risk of having serum lipid impairment.

Key words: elderly, loss of attachment, pocket depth, serum lipids

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#### **INTRODUCTION**

Indonesia is one of the Asian countries which has undergone a shifting population profile with a trend toward population ageing. By the year of 2035, Yogyakarta is estimated to be the one of aging province in Indonesia with more than 10% of the total population aged 65 years and over.<sup>1</sup> Moreover, in recent years, Indonesia is suffering from the double burden diseases which communicable diseases are now accompanied by non-communicable diseases (NCDs).<sup>2</sup> The disease patterns will shift concurrently with the demographic change and might possess tremendous challenges to health and social policy planners. Elderly is at a risk of having chronic diseases such as cardiovascular diseases (CVD), hypertension, cancer, and diabetes. In global population, CVD were found to be the major leading cause of non-communicable diseases in 2012.<sup>3</sup> In Europe, more than 4 million people died because of CVD every year.<sup>4</sup> Meanwhile CVD in Asia has become an important global health issue with the fact that half of the world population lives in Asia.<sup>5</sup> The national prevalence of coronary heart disease was found at 1.5% of the population and tend to increase by the age.<sup>6</sup> While 44.7% of the elderly in South of Jakarta, Indonesia were suffering from cardiovascular diseases.<sup>7</sup> In addition, the global burden of oral diseases is also relatively high in elderly, particularly periodontal disease, which was remained

at higher levels in Asia.<sup>8-12</sup> The chronic destruction of periodontal tissue which presented as the major cause of tooth loss was proven to have an association with  $\rm CVD.^{13-15}$ 

Periodontal pathogens were found to be the possible association between periodontal disease and atherosclerosis.<sup>16–19</sup> Atherosclerosis is a chronic inflammatory disease of artery vessels, starting from the endothelial injury and thrombus formation in the advanced plaque.<sup>20,21</sup> Atherogenesis development may be caused by multiple mechanism which induced by lipopolysaccharides (LPS) from periodontal pathogens in the formation of pro-atherogenic in lipid profile.<sup>22</sup> Associations between periodontal diseases and serum lipid levels was found in several studies.<sup>23,24</sup> On the hand, other studies found no relationship.<sup>25,26</sup> Review from Griffiths and Barbour suggests that periodontal diseases shifts the lipoprotein profile to be more proatherogenic.<sup>27</sup> The alteration of serum lipids profile may be resulted from the induction of changes in lipoprotein by cytokines. An increase in LDL and a decrease in HDL levels might be resulting in preatherosclerotic condition which might be a major risk factor for developing CVD.<sup>17</sup> In addition, greater loss of attachment >3mm was reported to have significant association with greater intima-media wall thickness as pre-atherosclerotic condition (OR=1.31, 95% CI=1.03-1.66).28

Periodontal disease is common among the elderly, while increased age may double the risk of having cardiovascular diseases. In elderly population, it is essential to prevent systemic disease, in particular cardiovascular diseases by controlling risk factors at an early stage. Unfortunately, the study of periodontal conditions and serum lipid profile among the elderly in Yogyakarta, Indonesia is limited. Therefore the aim of this study was to investigate the association between periodontal conditions and serum lipids profile among the elderly in order to raise the awareness of oral health as an essential factors in general health.

#### **METHODS**

#### **Study Design and Participants**

Current cross sectional study was carried out in Yogyakarta, Indonesia. The subjects for this study was recruited from the elderly population whom the health condition was insured by primary health care center managed by Gadjah Mada Medical Centre, Universitas Gadjah Mada (UGM). Considering the availability of resources, examinations appointment could only be arranged for 100 individuals. Only 78 individuals aged 60 years and older were selected according to the inclusion and exclusion criteria. Elderly who were in good health were included in this study, while individuals who were suffering from severe infections, having active smoking habit, were hospitalized and edentulous were excluded from this study. Interview, anthropometric evaluation, blood pressure (BP) evaluation, clinical examination, and laboratory procedure analysis were used for data collection method in this study. All subjects were examined in Prof. Soedomo Dental Hospital, Faculty of Dentistry, UGM, Yogyakarta.

The Medical and Health Research Ethics Committee (MHERC), Faculty of Medicine, UGM and Dr. Sardjito Hospital approved this study protocols and protected the subjects' rights which complied with Declaration of Helsinki as revised in 2000 (KE/FK/052/EC/2015). All of the subjects agreed and signed informed consent form regarding the examination protocols.

#### **Clinical Procedures**

The intraoral examination were carried out by five trained dentist for the measurement of periodontal conditions and number of present teeth. Number of teeth was counted as all remaining teeth included third molar.<sup>29</sup> Periodontal conditions were determined by the measurement of PD and LoA score according to WHO's criteria.<sup>30</sup> Six sites of all remaining teeth (mesio-buccal, mid-bucal, disto-buccal, mesio-lingual, mid-lingual/ mid-palatal, and distolingual) were measured using mouth mirrors and specially designed WHO probe. LoA examination was done by measuring the distance between gingival margin relative to the cemento enamel junction (CEJ). The periodontal condition was defined as the maximum score of PD and LoA in the subjects. Furthermore, subject with PD score 0 and 1 grouped as PD <6mm, while subjects with PD score 2 was grouped in PD  $\geq$ 6mm. Group subjects with the LoA score of 2, 3 and 4 were grouped as individual who exhibited loss of attachment of  $\geq$ 6mm, while LoA score of 0 and 1 was categorized as loss of attachment <6mm. Before the examination, examiner calibration were done at Prof. Soedomo Dental Hospital, Faculty of Dentistry, UGM. Intra-and inter-examiner reliability for LoA score was confirmed using both percent agreement ranged from 70% to 100% and kappa statistic ranged from 0.62 to 1.00.

#### **Medical Examination and Interview**

In the present study, TG, HDL, LDL, and TC in the serum level at fasting condition were drawn for the measurement of serum lipids levels. This measurement was done by University Hospital laboratory of UGM. Subjects with normal TC, HDL, LDL, and TG were defined as favorable serum lipids, while high TC, LDL, TG and low HDL were defined as unfavorable serum lipids. Favorable and unfavorable serum lipids profile were defined according to the laboratory standard. High TC was defined as serum TC  $\geq$ 200mg/ dL, while <200mg/ dL define as normal TC. Low HDL was defined as serum HDL for the levels <40mg/dL in men and <50mg/dL in women, while normal HDL levels  $\geq$ 40mg/dL in men

and  $\geq$ 50mg/dL in women. Serum LDL levels  $\geq$ 130mg/dL was defined as high LDL levels, while <130mg/dL categorized as normal. High TG was defined as serum TG levels  $\geq$ 150mg/dL (elevated), while <150mg/dL grouped as normal.

Anthropometric evaluation was calculated through body mass index (BMI) by measuring the height and weight of respondents. Serum lipid, BMI, and blood pressure were grouped based on National Cholesterol Education Program's Adult Treatment Panel III.<sup>31</sup> BMI  $\geq$ 25 kg/m<sup>2</sup> was categorized as obesity, while <25 kg/ m<sup>2</sup> grouped as normal. BP recordings were obtained from the right arm of the participants in a sitting position after 5 minutes of rest. High BP was defined as systolic/diastolic BP of ≥130/85 mmHg. Personal interview was performed to obtain several information including the years of school attendance, pattern of dental visit, hypertension medication (yes or no), and cholesterol medication (yes or no). Data of years of school attendance then grouped as lower and higher education. School attendance <9 years was defined as lower education, whereas higher education defined as  $\geq 9$  years of school attendance.

#### **Statistical Analyses**

The data which were recorded in clinical forms and questionnaires were entered into a computer. The participant's variables were described using the frequency distribution for categorical variables and the mean + standard deviation (SD) for continuous variables. Initially, the relationship between periodontal conditions, age, gender, BMI, number of teeth, elevated blood pressure, dental visit, hypertension and cholesterol medication and serum lipids variables were evaluated using Spearman correlations coefficients. Finally, logistic regression analysis was used to estimate the independent effect of periodontal conditions while controlling for confounding factors. Serum lipids components were used as dependent variables, whereas those that showed significant relationship with serum lipids in the second analysis were selected as independent variables (p<0.05). Data analysis was performed using the statistical software package version 22 (SPSS; Chicago, IL, USA, College Station).

#### RESULT

The characteristic of the subjects are shown in Table 1. Our sample was 59% male and 41% females with mean number of remaining teeth was  $25.22 \pm 4.86$ . The average BMI of respondents was  $25.57 \pm 2.74$ , while systole and diastole were  $134.41 \pm 21.35$  and  $85.34 \pm 12.22$ , respectively. The mean  $\pm$  SD for TC was 197.15  $\pm 32.20$ mg/dl, HDL was  $49.95 \pm 12.67$ mg/dl, LDL was  $142.81 \pm 34.19$ mg/dl, and TG was  $143.51 \pm 65.51$ mg/dl. Mostly, they brushed their teeth twice a day, while none of them used dental floss for cleaning the interdental site of teeth.

Characteristic	Moon ±SD					
Characteristic	Mean <u>+</u> SD					
Age (years)	64.26 <u>+</u> 3.69					
Sex						
Females	32 (41 %)					
Males	46 (59 %)					
Number of present teeth	25.22 <u>+</u> 4.86					
Education status	16.72 <u>+</u> 2.93					
Higher education	76 (97.40 %)					
Lower education	2 (2.60 %)					
Dental visit						
Frequently	13 (16.70 %)					
Occasionally	65 (85.30 %)					
Tooth brushing $\geq 2$ times/day	77 (98.70 %)					
Dental floss	0 (0.00 %)					
Current use of hypertension medication	40 (51.30 %)					
Current use of cholesterol medication	6 (7.70 %)					
Systole BP (mm Hg)	135.14 <u>+</u> 21.35					
Diastole BP (mm Hg)	85.34 <u>+</u> 12.22					
BMI (kg/m <sup>2</sup> )	25.57 <u>+</u> 2.74					
TC (mg/dL)	197.15 <u>+</u> 32.20					
HDL (mg/dL)	49.95 <u>+</u> 12.67					
LDL (mg/dL)	142.81 <u>+</u> 34.19					
TG (mg/dL)	143.51 <u>+</u> 65.51					

BMI = body mass index; BP = blood pressure; TG = triglycerides; TC = total cholesterol

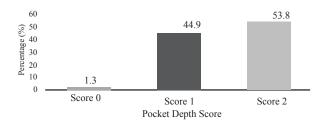
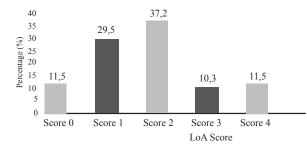


Figure 1. Percentage of subjects based on maximum score of pocket depth (Score 0 = absence of condition; Score 1 = pocket depth 4-5 mm; Score 2 = pocket depth 6 mm or more)

Pocket depth score data on Figure 1 shows that majority of subjects had pocket depth score 2 (53.8 %), while only 1.3 % with score 0. More than half of the respondents having pocket depth 6 mm or more.

Figure 2 presents that majority of subjects exhibited loss of attachment score 2 (37.2%), but only a few numbers of subjects had LoA score 0 (11.5%). Data shown that 59% of subjects having loss of attachment 6 mm or more (score 2-4).

Table 2 lists the categorical serum lipids components among the subjects. Majority of the subjects had normal TG, TC and HDL levels. On the other hand, majority subjects were in high LDLgroup.



**Figure 2.** Percentage of subjects based on maximum score of LoA (Score 0 = 0.3 mm; Score 1 = 4.5 mm; Score 2 = 6.8 mm; Score 3 = 9.11 mm; Score  $4 = \ge 12$  mm)

Table 2. Serum Lipids Profile (N=78)							
Serum Lipid	n	%					
TG							
Normal	45	57.69					
High	33	42.31					
HDL							
Normal	57	73.07					
Low	21	26.92					
TC							
Normal	43	55.10					
High	35	44.90					
LDL							
Normal	30	38.46					
High	48	61.54					

TG = triglycerides; TC = total cholesterol

Table 3. Correlation coefficients between variables

	Age	Gender	Education Status	BMI	Elevated BP	Cholesterol Medication	Hypertension Medication	Dental Visit	NOP	PD	LoA	TC	HDL	LDL	TG
Age	1.00	-0.27*	-0.47*	-0.22*	0.25*	0.05	0.11	0.01	-0.25*	-0.07	0.06	-0.10	-0.09	-0.04	-0.31*
Gender		1.00	0.22*	-0.10	-0.14	-0.15	0.07	-0.04	0.11	0.06	-0.06	-0.25*	0.11	-0.12	0.08
Education status			1.00	0.18	-0.23*	-0.08	-0.11	0.26*	0.14	-0.07	-0.16	-0.01	0.17	-0.06	0.07
BMI (normal; obesity)				1.00	-0.02	0.02	-0.01	-0.06	0.05	-0.07	0.01	0.20*	0.17	0.21	0.28*
High BP (no; yes)					1.00	0.27*	0.13	0.05	-0.17	0.02	0.01	0.31*	-0.14	0.17	0.01
Cholesterol medication (no; yes)						1.00	0.09	0.18	-0.05	-0.02	-0.15	0.11	-0.11	0.03	0.04
Hypertension medication (no; yes)							1.00	0.00	-0.03	0.08	0.07	-0.05	0.01	-0.09	0.11
Dental Visit (frequently; occasionally)								1.00	0.04	-0.02	-0.07	-0.08	0.02	-0.13	-0.16
NOP									1.00	-0.09	-0.22*	-0.06	0.18	0.04	0.07
PD (<6 mm; ≥6 mm)										1.00	0.53*	0.11	0.13	-0.04	0.17
LoA (<6 mm; ≥6 mm)											1.00	0.32*	-0.11	0.25*	0.08
TC (normal; high)												1.00	-0.26*	0.75*	0.23*
HDL(normal; low)													1.00	-0.20	0.41*
LDL (normal; high)														1.00	0.20
TG (normal; high)															1.00

BMI= body mass index; BP = blood pressure; NOP = number of present teeth; LoA = loss of attachment; PD = pocket depth; TC = total cholesterol; TG = triglycerides Pearson correlation coefficients; \*Statistically significant (p< 0.05)

Table 4. Relationship between Periodontal Condition and Serum Lipids

	Dependent Variables								
Independent Variable	TC LDL								
	β	p-value	OR (95% CI)	β	p-value	OR (95% CI)			
Loss of attachment <6mm	Refere	nce group		Reference group					
Loss of attachment ≥6mm	1.667	0.004	5.295 (1.710 - 16.391)	1.06	0.028	2.87 (1.118-7.405)			

Adjusted for age, gender, BMI and elevated BP

 $\beta$ =coefficients; OR=Odds Ratio; CI = confidence internal; p<0.05

Correlations among periodontal conditions, serum lipids, and other relevant factors such as age, gender, number of teeth, and pattern of dental visit, elevated blood pressure, BMI, anti-hypertensive, cholesterol medication are shown in Table 3. Loss of attachment 6 mm and more showed a significant associations with TC and LDL (p<0.05), whereas no significant correlation was showed on HDL and TG (p>0.05).

Table 4 presents the results from the logistic regression analysis of having serum lipids alteration. Variables which showed a significant associations with serum lipids in bivariate analysis were included in the multivariate analysis. Loss of attachment 6mm and more was associated significantly with an increased risk of having higher levels of TC and LDL. It remained significantly associated with higher risk of having unfavorable TC and LDL levels after simultaneously adjusting for other covariates. In the multivariate model, the adjusted OR for participants with loss of attachment 6mm and more was 5.295 (95% CI = 1.710-1.6931) for developing unfavorable TC levels, while 2.87 (1.118-7.405) for having elevated LDL (Table 4).

#### DISCUSSION

In the present study, associations between the periodontal disease and serum lipid were evaluated in healthy elderly aged 60 years. Logistic regression analysis, after adjusting confounders, showed that only loss of attachment  $\geq$  6 mm have a significant relationship with TC and LDL (Table 4). This could reflect an increased risk for CVD in poor periodontal conditions.

We demonstrated that participants with poor periodontal conditions had a significantly increased of TC and LDL, whereas HDL and TG showed no significant difference. It should be highlighted that recent cross-sectional studies, which investigated the relationship between periodontal disease and serum lipid have obtained similar findings to the present study.<sup>32,33</sup> Previous study reported that chronic inflammation in periodontal tissue significantly correlated with TC and LDL, while it showed no relationship with TG and HDL. Greater loss of attachment  $\geq$ 3 mm was reported previously to have 1.31 times greater in intima-media wall thickness as pre-atherosclerotic condition.<sup>28</sup> Lipid profile involving LDL and TG had a significant relationship in those conditions.

Some scholars reported that bacterial infection from periodontal lesions was the cause of the changes in systemic markers. A possible mechanism of this connection had been reported through the inflammatory reactions which caused by the progression of periodontitis, bacteria and their endotoxin, and other products.<sup>22</sup> Periodontal tissues destruction caused by chronic inflammation was presented by loss of attachment, bleeding on probing, and periodontal pocket.<sup>27,34</sup> A greater loss of attachment among the subjects might reflect a chronic inflammation caused by periodontal pathogen bacteria. Ostoeclastic bone resorption which degrades the alveolar bone supporting teeth in the infected area was influenced by inflammatory reactions.35 Inflammatory cytokines indirectly activated by periodopathogens might produce reactive oxygen species (ROS).<sup>36</sup> Remarkable study suggest that oxidative stress plays an essential role in the periodontal and alveolar bone destruction.<sup>37</sup> Previous study also reported the connection between clinical attachment level with the escalation of reactive oxygen metabolites (ROM).<sup>38</sup> Moreover, mitochondria as the major producer of ROS in cells causes a chronic over production which leads to increased oxidation of LDL in atherosclerosis development.<sup>39</sup> Another study reported that Porphyromonas gingivalis infection might increase the LDL levels and induces hypercholesterolemia.40

HDL has anti-inflammatory and anti-atherogenic properties and decreased of HDL levels have also been considered to be a risk factor for CVD. HDL plays an important role as anti-atherogenic lipoprotein by neutralizing LPS in circulation<sup>41,42</sup> and protecting LDL against oxidation as well as its role in reverse cholesterol transport.<sup>43,44</sup> In the present study, lower HDL had an association with higher TG, but showed no significant association withn LDL, TC and periodontal conditions. Similar findings also reported from previous study which stated that HDL was not found significantly decreasing in subjects with chronic periodontal infection.<sup>32,45</sup> Gufran et al also found no significant association between HDL and periodontal disease.<sup>46</sup> A possible explanation which underlying differences in results are the various cut off and methods in determining the serum lipid levels which had been used among studies.

Finally, they are some limitations of our study that should be taken into consideration. Since this study was a cross sectional, the exact mechanism of this relationship was not clarified in this study and it needs to be further explored in longitudinal studies. This was conducted on modest sample size of 78 subjects, study with larger sample sizes needs to be carried out in the future to endorse the results observed in our study.

#### CONCLUSSION

The findings of the present study suggest that loss of attachment ≥6mm may be a risk factor of impairment of serum lipid profile among the elderly. Future work with larger, more diverse populations and more complete information would be essential to complete our findings. More studies, including prospective trials, are necessary to understand the exact nature of the relationship of periodontal conditions and serum lipids.

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#### **CONFLICT OF INTEREST**

The authors report no conflict of interests related to this study.

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