SURAT KETERANGAN

Nomor : /2 /UN2.R.3/SDM.0.2/2018

Yang bertanda-tangan dibawah ini:

Nama : Dr. agr. Taufiq Wisnu Priambodo, M.Sc
NUP. : 141 725 005
Jabatan : Direktur Inovasi dan Inkubator Bisnis Universitas Indonesia
          Direktorat Inovasi dan Inkubator Bisnis Universitas Indonesia

Dengan ini menerangkan kepada nama-nama yang tersebut di bawah:

1. drg. Nafisah Ibrahim Ahmad, Sp.Perio
2. Dr. drg. Sri Leliaty, SU., Sp.Perio(K)
3. drg. Robert Lessang, Sp.Perio(K)

adalah para pencipta atas karya tulis yang berjudul "Keterkaitan Kadar Loe Density Lipoprotein Dengan Status Periodontal Penderita Penyakit Jantung Korone", yang telah terdaftar dalam Daftar Umum Ciptaan No. 081779, Tahun 2016 di Direktorat Hak Cipta Dan Desain Industri, Direktorat Jenderal Kekayaan Intelektual, Kementerian Hukum dan HAM RI. (Salinan surat pencatatan ciptaan terlampir yang merupakan bagian yang tidak terpisahkan dari surat keterangan ini).

Demikian surat keterangan ini dibuat untuk dipergunakan sebagaimana mestinya.

Depok, 8 Januari 2018

Direktur Inovasi dan Inkubator Bisnis UI,

[Signature]

[Stamp]

Dr. agr. Taufiq Wisnu Priambodo, M.Sc
NUP. : 141 725 005
REPUKLIK INDONESIA
KEMENTERIAN HUKUM DAN HAK ASASI MANUSIA

SURAT PENCATATAN CIPTAAN

Menteri Hukum dan Hak Asasi Manusia Republik Indonesia, berdasarkan Undang-Undang Nomor 28 Tahun 2014 tentang Hak Cipta yaitu Undang-Undang tentang perlindungan ciptaan di bidang ilmu pengetahuan, seni dan sastra (tidak melindungi kekayaan intelektual lainnya), dengan ini menerangkan bahwa hal-hal tersebut di bawah ini telah tercatat dalam Daftar Umum Ciptaan:


II. Pencipta
Nama
Alamat
Kewarganegaraan
1. drg. NAFISAH IBRAHIM AHMAD, Sp.Perio.;
2. Dr. drg. SRI LELIYATI, S., Sp.Perio(K);,
Jalan P No.7 Rt.004 Rw.014
Indonesia

III. Pemegang Hak Cipta
Nama
Alamat
Kewarganegaraan
UNIVERSITAS INDONESIA
Gedung Pusat Administrasi, Lantai 2
Kampus UI, Depok, Jawa Barat 16242.

IV. Jenis Ciptaan
Karya Tulis

V. Judul Ciptaan
KETERKAITAN KADAR LOW DENSITY LIPOPROTEIN
DENGAN STATUS PERIODONTAL PENDERITA
PENYAKIT JANTUNG KORONER

VI. Tanggal dan tempat diumumkan untuk pertama kali di wilayah Indonesia atau di luar wilayah Indonesia : 04 Mei 2016, di Jakarta

VII. Jangka waktu perlindungan : Berlaku selama 50 (lima puluh) tahun sejak pertama kali diumumkan.

VIII. Nomor pencatatan : 081779

Pencatatan Ciptaan atau produk Hak Terkait dalam Daftar Umum Ciptaan bukan merupakan pengesahan atas isi, arti, maknud, atau bentuk dari Ciptaan atau produk Hak Terkait yang dicatat. Menteri tidak bertanggung jawab atas isi, arti, maksud, atau bentuk dari Ciptaan atau produk Hak Terkait yang terdaftar. (Pasal 72 dan Penjelasan Pasal 72 Undang-undang Nomor 28 Tahun 2014 Tentang Hak Cipta)

a.n. MENTERI HUKUM DAN HAK ASASI MANUSIA
REPUKLIK INDONESIA
DIREKTUR JENDERAL KEKAYAAN INTELEKTUAL
u.b.
DIREKTUR HAK CIPTA DAN DESAIN INDUSTRI

[signature]

Dr. Dra. Erni Widhyastari, Apt., M.Si.
NIP. 196003181991032001
Low Density Lipoprotein Levels Linkage with The Periodontal Status Patients of Coronary Heart Disease

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3Staff of Harapan Kita, Cardiovascular Hospital, Jakarta, Indonesia

Abstract

Background: Studies found an association between periodontitis and coronary heart disease (CHD), but relationship between periodontal status CHD patients with LDL (Low Density Lipoprotein) levels, as risk factors for atherosclerosis, has not been studied. Objective: To analyze relationship between LDL and periodontal status CHD. Methods: Periodontal status of 60 CHD, 40 controls was examined (PBI, PPD, CAL) and their blood was taken to assess levels of LDL. Result: Found significant differences LDL (p=0.005), correlation between LDL with PPD (p=0.003) and CAL CHD (p=0.013), and PPD (p=0.001), CAL (p=0.008) non-CHD, but no significant correlation between LDL with PBI CAD (p=0.689) and PBI non-CHD (p=0.320). Conclusion: There is a correlation between the LDL level with periodontal status.

Keywords: Levels of LDL, periodontal status, coronary heart disease

1. Introduction

Periodontal disease is an inflammatory disease caused by bacteria. Periodontal inflammation can develop into destructive periodontal tissue damage. Subgingival microorganisms in periodontitis dominated by Gram-negative bacteria and its products such as lipopolysaccharide that can fit into the periodontal tissues and blood circulation through the epithelium of the sulcus. These bacteria and their products cause changes in inflammatory responses and systemic changes that induce vascular response. The body’s response to explain the mechanism of how the relationship between periodontal infection with a variety of systemic disorders, especially coronary heart disease (CHD).[1]–[3]

LDL cholesterol (low density lipoprotein) in the blood can cause a buildup of cholesterol in the walls of blood vessels, resulting in the formation of atherosclerotic lesion or atheroma.[3]–[5] Atherosclerosis that occurs in the coronary arteries can lead to CHD.[6] The research that has been done suggests periodontitis associated with an increased risk of cardiovascular disease, it was found that 25-50% increased risk of cardiovascular disease for patients with periodontitis compared with no or minimal periodontitis.[8]

2. The Object of the Study

Increased levels of LDL are a major risk factor of developing CHD. Some studies linking periodontal status with atherosclerosis, but whether the role of periodontal status on atherosclerosis related to the mechanism of change in LDL levels in patients with CHD, it is not yet clear. Therefore, this study aimed to evaluate the relationship of periodontal status with LDL in patients with CHD.

3. Methods

A consecutive sampling of clinical study were taken from 60 patients with CHD patients conducted at Harapan Kita, the Cardiovascular Hospital, and 40 control of non-CHD patients conducted at the Dental Hospital, Faculty of Dentistry, University of Indonesia. The subjects were male and female, aged 40-74 years, diagnosed with stable angina pectoris (coronary heart disease) with stenosis ≥ 50% will be taken bypass and diagnosis with coronary angiography procedures. Additional checks are being made to control for non CHD patients is a treadmill examination and electrocardiography (ECG). Patients with other systemic diseases and had a history of professional oral prophylaxis within the last 3 months is not included in the sample criteria.

Examination of periodontal status made by examining the papilla bleeding index (Figure 1), pocket depth and clinical attachment loss (Figure 2), were taken from six sides per teeth, excepted teeth number 8. The level of LDL in the blood is sent to the pathology laboratory clinic. Collection of 5 ml of blood was done in serum separator tube (SST) that contain with cloth activator gel, then centrifuged in 2000 rpm for 10 minutes. The level of LDL measured and analyzed by enzymatic with reagent from Daichising Abbot Architect ci4100 Abbot (Figure 3).
4. Result and Discussion

The study was conducted on 60 CHD subject, and 40 non-CHD, from November 2015 to February 2016. The age range of this study were 40-74 years of CHD subjects and 41-73 years of non CHD subjects. The age range is considered period allows the occurrence of heart disease. Research that has been carried explained that periodontal disease is associated with disease occur cardiovascular 15% at age 21-50 years, and 30% over age 50 years. Distribution of the gender and age of the subjects are shown in Table 1, while distribution of the results are shown in Table 2.

### Table 1. Distribution Subjects

<table>
<thead>
<tr>
<th>Subjects</th>
<th>CHD (N=60)</th>
<th>Non CHD (N=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>53</td>
<td>26</td>
</tr>
<tr>
<td>Female</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>Pocket depths</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td>Moderate</td>
<td>43</td>
<td>21</td>
</tr>
<tr>
<td>Severe</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Clinical attachment loss</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Moderate</td>
<td>35</td>
<td>15</td>
</tr>
<tr>
<td>Severe</td>
<td>22</td>
<td>21</td>
</tr>
</tbody>
</table>

### Table 2. Distribution of Mean, Standard Deviation, Minimum and Maximum of Age, and Papilla Bleeding Index levels of Coronary Heart Disease

<table>
<thead>
<tr>
<th>Subjects</th>
<th>N</th>
<th>Mean(SD)</th>
<th>Min - Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHD</td>
<td>60</td>
<td>58.33 (8.410)</td>
<td>40-74</td>
</tr>
<tr>
<td>Non CHD</td>
<td>40</td>
<td>52.37 (8.992)</td>
<td>41-73</td>
</tr>
<tr>
<td>Papilla bleeding index</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHD</td>
<td>40</td>
<td>0.815 (0.607)</td>
<td>0.00-2.38</td>
</tr>
<tr>
<td>Non CHD</td>
<td>60</td>
<td>1.095 (0.718)</td>
<td>0.00-3.14</td>
</tr>
</tbody>
</table>

SD = Standard Deviations, Min = Minimum, Max = Maximum
The result of this study are shown in Table 3, Table 4 and Table 5. High LDL levels in the blood can cause a buildup of cholesterol in the walls of blood vessels, resulting in the formation of atherosclerotic lesion or atheroma. [3]–[5] Atherosclerosis, which occurs in the coronary arteries can lead to coronary heart disease. [6],[7]. Periodontal status associated with this inflammation in a long period of time could make LDL levels increase, so is proatherogenik. [5] Table 3 showed that there was significant difference (p=0.005) in LDL cholesterol between CHD patients with non-CHD The mean levels of LDL in patients with CHD (109.73 mg/dl) is lower than non CHD (130.83 mg/dl). The whole subject of CHD have been taking statins. Statins are the most effective lipid-lowering drugs to lower LDL cholesterol and proven to be safe with no significant side effects. Statins reduce the incidence of cardiovascular disease, because it is relative effective and fewer side effects and is the first drug of choice. Different types of statins can reduce LDL cholesterol levels up to 18-55%. This class of drugs known as inhibitors of HMG-CoA reductase. HMG-CoA reductase is an enzyme that controls cholesterol biosynthesis. With the denial of cholesterol synthesis in the liver, it will lower LDL and total cholesterol and to increase HDL plasma. The studies have been published confirming the relationship between dyslipidemia and CHD. Research also shows a decrease in fat or cholesterol aggressively by statins is very helpful in suppressing or reducing acute coronary events. Statins also can improve the endothelial function, stabilize plaque, reduce thrombus formation, are anti-inflammatory, and reduced lipid oxidation.[9],[10]

**Table 3. The mean value, standard deviation, and the significance of Low Density Lipoprotein Levels of Patients and Non Patients Coronary Heart Disease**

<table>
<thead>
<tr>
<th>CHD</th>
<th>N</th>
<th>LDL Levels (mg/dl) Mean(SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>60</td>
<td>109.73 (40.851)</td>
<td>0.005*</td>
</tr>
<tr>
<td>No</td>
<td>40</td>
<td>130.83 (32.226)</td>
<td></td>
</tr>
</tbody>
</table>

Unpaired T-test; * p<0.05 significantly different

Gingival inflammation has early signs of increased gingiva crevicular fluid and gingival bleeding on probing. Gingival bleeding is a clinical indicator of inflammation in the epithelial and connective tissue, where there is a change in the form of dilated capillaries and thin epithelium sulcus. Thin epithelial surface and width of capillaries resulting in gingival bleeding on mild stimuli.[1] Table 4 Pearson correlation test showed no significant correlation between the levels of LDL with papilla bleeding in patients with CHD (0.689) and non CHD (0.302). These results are possible because papilla bleeding can result from inflammation of gingivitis and periodontitis. Several studies have been conducted regarding the association of periodontitis with LDL as a risk factor for heart disease is concerned with loss of attachment, where bacteria and inflammation product can be easily related to systemic factors on the condition of periodontal tissues lost the support of bone and connective tissue gingiva. Research on the association of periodontitis with LDL in the blood do Nugraha et al., Which found that periodontitis increases LDL levels in the blood.[4] Research conducted by Akkaloori et al., drew the conclusion that patients with chronic periodontitis at high risk for cardiovascular disease with elevated levels of LDL as a major risk factor for heart disease.[11]

**Table 4. Correlation and significance Value of Low Density Lipoprotein Levels of Patients and Non Patients with Coronary Heart Disease**

<table>
<thead>
<tr>
<th>LDL levels with papilla bleeding index</th>
<th>N</th>
<th>r</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD</td>
<td>60</td>
<td>-0.051</td>
<td>0.689</td>
</tr>
<tr>
<td>Non CHD</td>
<td>40</td>
<td>0.167</td>
<td>0.302</td>
</tr>
</tbody>
</table>

Pearson correlation test; p <0.05 significant correlation

Periodontal pocket is a deepening of the gingival sulcus that can occur due to movement toward the coronal gingival margin, decreased adhesion of the gingival epithelium apical direction, or a combination of both. Pockets of periodontal pockets can be divided into relative and absolute pocket. Relative pocket is a pocket formed from gingival enlargement in the absence of periodontal tissue destruction. Absolute pockets are pockets that are caused due to destruction of periodontal tissues and is characterized by the movement of the attachment of epithelial apical direction.[1]

Table 5 Spearman correlation test between LDL cholesterol levels and pocket depth of coronary heart disease patients (0.376) showed a positive correlation with the strength of the correlation was, with the clinical attachment loss CHD patients (0.318) showed a positive correlation with the strength of the correlation is weak, with the level of pocket depth non CHD (0.490) showed a positive correlation with the strength of the correlation was, and with the level of non-CHD clinical attachment loss (0.412) showed a positive correlation with the strength of the correlation was. Levels of LDL had a significant correlation with the pocket depth and clinical attachment loss in patients with CHD and non CHD. This can happen because of pocket depth and clinical attachment loss is an indicator of periodontitis and correlated directly with the severity of periodontal disease. The inflammatory response can have a profound effect on the movement of lipoproteins in the artery. Inflammatory mediators such as TNF-α, IL-1, which increases the time of periodontitis increases LDL adhesion to the endothelium and smooth muscles, and increases the transcription of the LDL receptor gene.[5]
The results are consistent with research conducted by Joseph et al., which showed a significant positive relationship between LDL levels with parameters of periodontal disease on the increase in pocket depths higher LDL levels. However, in contrast to the results of research that has been done Ekaputri, which found that there was no correlation between clinical attachment loss with LDL in patients with coronary heart disease.

The strength of the correlation non CHD is higher than CHD, both of pocket depth and clinical attachment loss. The results of this correlation may be because the patient a sample of CHD, is the patient who will undergo bypass surgery, so it has been done extractions on mobile teeth and big caries, so that the teeth are examined only teeth by dentists previously considered has a focal infection for the operation to be performed.

<table>
<thead>
<tr>
<th>Subjects</th>
<th>N</th>
<th>r</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL levels with pocket depths</td>
<td>60</td>
<td>0.376</td>
<td>0.003*</td>
</tr>
<tr>
<td>LDL levels with clinical attachment loss</td>
<td>60</td>
<td>0.318</td>
<td>0.013*</td>
</tr>
<tr>
<td>Non CHD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL levels with pocket depths</td>
<td>40</td>
<td>0.490</td>
<td>0.001*</td>
</tr>
<tr>
<td>LDL levels with clinical attachment loss</td>
<td>40</td>
<td>0.412</td>
<td>0.008*</td>
</tr>
</tbody>
</table>

Spearman correlation test; * p <0.05 significant correlation

5. Conclusion

There is a difference of LDL levels between CHD and non CHD patients. There is a correlation between LDL levels with periodontal status pocket depths and clinical attachment loss of CHD and non CHD patients, and no correlation between LDL levels and papilla bleeding index of CHD and non CHD patients.

Acknowledgements

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References