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RESEARCH

APO B/APO A-I RATIO IN PATIENTS WITH STENOSIS CORONARY HEART DISEASE GREATER OR LESS THAN 70%

(Rasio Apo B/Apo A-I di Pasien Penyakit Jantung Koroner dengan Stenosis Lebih Besar atau Kecil 70%)

Dedi Ansyari¹, Tapisari Tambunan¹, Harris Hasan²

ABSTRAK

Penyakit kardiovaskular adalah salah satu penyebab terbesar kematian di dunia, termasuk di Indonesia. Salah satunya adalah penyakit jantung koroner yang disebabkan adanya aterosklerosis. Perlu adanya petanda pengganti proses aterosklerosis sebagai faktor bahaya dan sebagai peramal aterosklerosis dan PJK. Apo B dan rasio Apo B/Apo A-I dianggap sebagai petanda yang terbaik. Tujuan penelitian untuk mengetahui rasio Apo B/Apo A-I di pasien PJK dengan stenosis lebih besar atau sama dengan 70% dan lebih kecil 70%. Metode penelitian dengan potong lintang di 69 pasien PJK, yaitu 46 pasien PJK dengan stenosis lebih besar atau sama dengan 70% dan 23 pasien PJK dengan stenosis lebih kecil 70% di Departemen Kardiologi FK. USU/RSUP H. Adam Malik Medan bekerja sama dengan Departemen Patologi Klinik FK. USU/RSUP. H Adam Malik Medan masa waktu Juli 2015 sampai dengan November 2015. Hasil telitian didapatkan kadar Apo B di pasien PJK dengan stenosis lebih besar atau sama dengan 70% adalah $115,63 \pm 30,96$ dan pasien PJK dengan stenosis lebih kecil 70% adalah $96,43 \pm 25,62$ dengan nilai $p=0,013$. Kadar Apo A-I di pasien PJK dengan stenosis lebih besar atau sama dengan 70% adalah $148,30 \pm 26,80$ dan pasien PJK dengan stenosis lebih kecil 70% adalah $173,74 \pm 32,33$ dengan nilai $p=0,001$. Rasio Apo B/Apo A-I di pasien PJK dengan stenosis lebih besar atau sama dengan 70% adalah $0,79 \pm 0,20$, rasio Apo B/Apo A-I di pasien PJK dengan stenosis lebih kecil 70% adalah $0,55 \pm 0,14$ dengan nilai $p=0,0001$. Dari hasil telitian dapat disimpulkan, bahwa terdapat perbedaan bermakna kadar Apo B, Apo A-I serta rasio Apo B/Apo A-I di pasien PJK dengan stenosis lebih besar atau sama dengan 70% dan pasien PJK dengan stenosis lebih kecil 70%.

Kata kunci: Apo B, Apo A-I, rasio Apo B/Apo A-I, penyakit jantung koroner, stenosis lebih besar atau sama dengan 70%, stenosis lebih kecil 70%

ABSTRACT

Cardiovascular disease is one of the main causes of death in the world, including in Indonesia. One is coronary heart disease caused by atherosclerosis. It needs a surrogate marker of atherosclerosis as a risk factor and as a predictor factor of atherosclerosis and CHD. Apo B and ratio of Apo B/Apo A-I is regarded as the best marker. The aim of this research was to determine Apo B/Apo A-I ratio in CHD patients with stenosis greater or less than 70%. The method of the study was conducted by cross-sectional method in 69 patients with CHD, 46 CHD patients with stenosis greater or equal to 70% and 23 CHD patients with stenosis less than 70% in the Department of Cardiology, Medical Faculty Sumatera Utara University/H. Adam Malik General Hospital in collaboration with the Department of Clinical Pathology, Medical Faculty Sumatera Utara University/H. Adam Malik General Hospital, during July 2015 until November 2015. Results showed that, Apo B levels in CHD patients with stenosis greater or equal to 70% were 115.63 ± 30.96 and CHD patients with stenosis less than 70% was 96.43 ± 25.62 with $p=0.013$. Apo A-I levels in CHD patients with stenosis greater or equal to 70% were 148.30 ± 26.80 and CHD patients with stenosis less than 70% was 173.74 ± 32.33 , with $p=0.001$. Apo B/Apo A-I ratio in CHD patients with stenosis greater or equal to 70% were 0.79 ± 0.20 , Apo B/Apo A-I ratio in CHD patients with stenosis less than 70% is 0.55 ± 0.14 with a value of $p=0.0001$. Based on this research it can concluded that there were significant differences in the levels of Apo B, Apo A-I as well as Apo B/Apo A-I ratio in CHD patients with stenosis greater or equal to 70% and less than 70%.

Key words: Apo B, Apo A-I, Ratio Apo B/Apo A-I, coronary heart disease, stenosis greater or equal to 70%, stenosis less than 70%

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INTRODUCTION

Cardiovascular disease is one of the main causes of death in the world,^{1,2} including in Indonesia.^{3,4} In 2004, World Health Organization (WHO) reported that Coronary Heart Disease (CHD) is the main cause of death as many as 7.2 million people constituting 12.2% of all causes of death⁵ and estimated that cardiovascular disease will remain the most common number first killer in 2020.⁶ In Indonesia, since the 1990's based on the Survey Kesehatan Rumah Tangga (Household Health Survey) and Riset Kesehatan Dasar (Health Research Association), cardiovascular disease became a major cause of death, while in 2008, CHD became the second leading cause after stroke.⁷

Coronary heart disease is the result of an imbalance between myocardial oxygen supply and demand and is most often caused by the inability of atherosclerotic coronary arteries to perfuse the heart due to total or partial occlusion of the coronary arteries.⁸⁻¹⁰ One of the major risk factors for Coronary Heart Disease is a disorder of lipid-lipoproteinemia. Many studies have examined various lipid-lipoprotein parameters to obtain a surrogate marker of atherosclerosis process as a risk factor and as a predictor factor of atherosclerosis and CHD. The National Cholesterol Education Program – Adult Treatment Panel III (NCEP – ATP III) reported an increase in cholesterol – LDL as the major risk factor and also recommended total cholesterol, HDL and triglycerides as a risk factor for CHD.¹¹ However, recent studies have shown that levels of Apo B, Apo B/Apo A-I ratio are a better predictor of risk of coronary heart disease.

Several studies, such as by Sarah Parish *et al.*¹², concluded that Apo B/Apo A-I ratio provided more informative information about the risk of myocardial infarction compared to fraction of other lipids such as LDL and HDL.¹² Fei Huang *et al.*¹³, conducted a research about association between apolipoproteins and Carotid Intima-Media Thickness (CIMT) in patients with normal glucose tolerance, they concluded that there was a significant association between Apo B and Apo B/Apo A-I ratio in patients with normal glucose tolerance with elevated CIMT.¹³

Coronary angiography is defined as the radiographic visualization of the coronary vessels after the injection of radiopaque contrast media. The purpose of coronary angiography is to define coronary anatomy and the degree of luminal obstruction of the coronary arteries.¹⁴ This present study was to assess whether there was a difference in Apo B/Apo A-I ratio

in CHD patients with stenosis greater or equal to 70% and stenosis less than 70%.

METHODS

Ethical Clearance was obtained from the Institutional Review Board of the Medical Faculty Sumatera Utara University/H. Adam Malik General Hospital (Number: 391/KOMET/FK USU/2015). Written informed consent was obtained from each participant before data collection.

The study was conducted by cross-sectional method. Coronary heart disease patients aged 40 years and older were invited to participate. The subjects of the research underwent history taking and recording of sex, age, history of diabetes mellitus, hypertension and smoking, the use of antilipid drug and family history suffering from CHD. Based on the inclusion and exclusion criteria eventually 69 CHD patients, were obtained 46 patients with stenosis greater or equal to 70% and 23 patients with stenosis less than 70% from the Department of Cardiology, Medical Faculty Sumatera Utara University/H. Adam Malik General Hospital in collaboration with the Department of Clinical Pathology Medical Faculty Sumatera Utara University/H. Adam Malik General Hospital, from July until November 2015.

Venous blood samples were collected after angiography. Coronary angiography was performed by an experienced cardiologist. Apo B and Apo A-I were measured with Immunoturbidimetry method by Cobas 6000 Analyzer.

To compare Apo B/Apo A-I ratio between CHD patients with stenosis greater than or equal to 70% and less than 70% independent t test was used, if the data in the two groups were normally distributed, otherwise Mann-Whitney was used. A p value <0.05 was considered statistically significant.

RESULT AND DISCUSSION

Based on the inclusion and exclusion criteria, 69 patients were found, with the number of males 46 (66.7%) and females 23 (33.3%). 36 (78.3%) of males with stenosis greater than or equal to 70% and 10 (21.7%) male patients with stenosis less than 70%. 10 (43.5%) of female patients with stenosis greater than or equal to 70% and 13 (56.5%) female patients with stenosis less than 70% with p value=0.004 (Table 1).

Table 1. Sex characteristics of study population

Variable	Angiography		P
	<70% (n=23)	≥ 70% (n=46)	
Sex (n,%)			
Male	10 (21.7%)	36 (78.3%)	0.004*
Female	13 (56.5%)	10 (43.5%)	

* p value <0.05 = significant

There was no significant difference in age of CHD patients with stenosis greater than or equal to 70% and CHD patients with stenosis less than 70% (p=0.849). Age of CHD patients with stenosis greater than or equal to 70% was 56.96±6.15 ($\bar{x}\pm SD$), while CHD patients with stenosis less than 70% was 56.52±9.91 ($\bar{x}\pm SD$) (Table 2).

In this study, risk factors to CHD were recorded such as diabetes mellitus, hypertension, smoking, family history of CHD, history of anti-lipid used. It was found that patients who have risk factors tended to have a more severe degrees of stenosis (≥70%) (Table 3).

There was a significant difference in the level of Apo B in CHD patients with stenosis greater than or equal to 70% and patients with stenosis less than 70% (p=0.013). Apo B levels in CHD patients with stenosis greater than or equal to 70% were 115.63±30.96 and CHD patients with stenosis less than 70% were 96.43±25.62. Apo A-I levels in CHD patients with stenosis greater than or equal to 70% were 148.30±26.80 and CHD patients with stenosis less than 70% were 173.74±32.33 with a significant difference (p=0.001) (Table 4).

Table 2. Age characteristics of study population

Variable	Angiography	N	($\bar{x}\pm SD$)	P
Age (years)	<70%	23	56.52±9.91	0.849
	≥70%	46	56.96±6.15	

* p<0.05=significant

Table 3. Characteristics of study population

Variable	Angiography	
	<70%	≥70%
Hypertension (n,%)	9 (36%)	16 (64%)
Diabetes mellitus (n,%)	5 (26.3%)	14 (73.7%)
Antilipid used (n,%)	7 (36.8%)	12 (63.2%)
Smoking (n,%)	9 (22.5%)	31 (77.5%)
Family history (n,%)	6 (28.6%)	15 (71.4%)

Table 4. Apo B and Apo A-I level of study population

Variable	Angiography		p
	<70%	≥70%	
Apo B (mg/dL)	96.43±25.62	115.63±30.96	0.013*
Apo A-I (mg/dL)	173.74±32.33	148.30±26.80	0.001*

Data in Mean ± SD

* p < 0.05 = significant

Table 5. Apo B/Apo A-I ratio of study population

Variable	Angiography		P
	<70% (n=23)	≥70% (n=46)	
Apo B/Apo A-I ratio ($\bar{x}\pm SD$)	0.55±0.14	0.79±0.20	0.0001*

* p<0.05 = significant

A significant difference was also found between Apo B/Apo A-I ratio in CHD patients with stenosis greater than or equal to 70% and CHD patients with stenosis less than 70% (p=0.0001). Apo B/Apo A-I ratio in CHD patients with stenosis greater than or equal to 70% is 0.79 ± 0.20 and in CHD patients with stenosis less than 70% is 0.55 ± 0.14 (Table 5).

In this study it was found that sex in CHD patients with stenosis greater than or equal to 70% and CHD patients with stenosis less than 70% was statistically significant. Sex was a risk factor that cannot be modified (non-modifiable) for CHD.^{15,16} This study also showed that the degree of stenosis is more severe (≥70%) in CHD patients with diabetes mellitus, hypertension, smoking and family history of CHD. This was according to a research conducted by Fei Huang *et al.*¹³ where it was also found that gender, age, diabetes mellitus, hypertension, smoking, and family history of CHD had a statistically significant association with increased CIMT.¹³

Increased blood pressure was associated with the risk of CHD. It was associated with the occurrence of progressive vasculopathy and stiffness of the aorta and blood vessel elasticity.¹⁷ Nitric Oxide (NO), a free radical, was primarily responsible for the vasodilatory function of the endothelium. Cigarette smoking was associated with decreased NO availability, as well as the expression and activity of the endothelial NO synthase enzyme. Nitric oxide also helped to regulate inflammation, leukocyte adhesion, platelet activation and thrombosis.¹⁸ Clinical studies suggested that, in diabetes mellitus, atherosclerotic lesions have a tendency to be heavier and in the small vessels, so the higher mortality. The pathogenesis of cardiovascular disease in diabetes was associated with abnormalities of macrovascular occurring through multiple pathways mechanisms: hyperglycemia, insulin resistance, changes in lipid and lipoprotein, increased production of Apo B, impaired clearance of Apo B VLDL, activation of cytokines and vasoactive hormones, which in the end led to an increase in oxidative stress to cells and tissues. Oxidative stress will continue to damage the endothelium and activation of cytokines and hemostasis disorders.¹⁹

Apo B level was significantly higher in CHD patients with stenosis greater than or equal to 70% compared with CHD patients with stenosis less than 70%. Levels of Apo B showed the total number of atherogenic lipoproteins, reflecting the amount of cholesterol and the amount of particles containing triglycerides. In most conditions, 90% or more Apo B in the blood was found in LDL. Apo A-I levels were lower in CHD patients with stenosis greater than or equal to 70% compared with stenosis less than 70%. Apo A-I was the main apolipoprotein associated with HDL and considered as an indicator for anti-atherogenic lipid particle. Apo A-I not only to initiated the reverse cholesterol transport by activating LCAT, but also acted as an antioxidant and anti-inflammation.^{20,21}

There were significant differences in Apo B/Apo A-I ratio in CHD patients with stenosis greater than or equal to 70% compared with stenosis less than 70%. This indicated the occurrence of an imbalance between atherogenic lipoproteins with anti-atherogenic lipoproteins. This was according to research conducted by Sachu *et al.*²² who found that Apo B/Apo A-I ratio was significantly increased in patients with CHD both diabetes mellitus and without diabetes mellitus compared with normal controls. They also found that levels of Apo B were significantly higher and levels of Apo AI were significantly lower in CHD patients compared to normal control.²² Fei Huang *et al.*¹³ in their study concluded that Apo B/Apo A-I ratio and Apo B levels were associated with increased CIMT in patients middle age and older with NGT.¹³

CONCLUSION AND SUGGESTION

From this research it can be summarized as follows: Sex in CHD patients with stenosis greater than or equal to 70% and less than 70% showed a statistically significant difference; The degree of stenosis was more severe (≥70%) in CHD patients with risk factors such as diabetes mellitus, hypertension, smoking and having a family history of CHD; Apo B levels were significantly higher in CHD patients with stenosis greater than or equal to 70% compared with stenosis less than

70%; Apo A-I levels were lower in CHD patients with stenosis greater than or equal to 70% compared with CHD patients with stenosis less than 70%; There were significant differences in the ratio of Apo B/Apo A-I in CHD patients with stenosis greater than or equal to 70% compared with CHD patients with stenosis less than 70%.

Some limitations of our present study were of concern. Firstly, the cross-sectional design of this study did not provide information as to whether apolipoproteins predicted the progression of stenosis. Secondly, the population maybe included the subjects with dislipidemia, they might have been treated, but adjustment was not made for the drug using history to control the bias. Further studies in a large population are required to establish a cut-off value to be utilized in the clinical analysis.

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