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## CORRELATION OF ATHEROGENIC INDEX OF PLASMA WITH STENOSIS LEVEL OF CORONARY ARTERY IN ACUTE CORONARY SYNDROME

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### ABSTRACT

Atherogenic dyslipidemia is the main risk factor of Acute Coronary Syndrome (ACS), caused atherosclerosis plaque and stenosis of artery coronary. Lipid profile ratio used as a marker of cardiovascular disease severity. Atherogenic Index of Plasma (AIP) calculated as logarithm triglycerides/high-density lipoprotein cholesterol (TG/HDL-C) is a reflection of plasma atherogenicity degree and indicator of small dense low-density lipoprotein (LDL). Small dense LDL is the best predictor for cardiovascular disease, but expensive and difficult to examined. The aim of this study to determine the correlation of AIP with stenosis level of the coronary artery in ACS. This research was an analytical study with cross-sectional design in 24 ACS patients meet the inclusion and exclusion criteria and conduct blood tests at the Central Laboratory Installation of Dr. M. Djamil Hospital Padang in January 2017-September 2017. Triglycerides and HDL-C performed by an enzymatic colorimetric method and stenosis level determined by coronary angiography. Spearman correlation was used to analyze correlation of atherogenic plasma index with stenosis level of the coronary artery, significant if  $p < 0.05$ . The subjects of this study were 20 males (83.3%) and 4 females (16.6%) with mean age 57.6(7.9) years. The mean level of HDL cholesterol and triglycerides in ACS were 34.8 (8.7) mg/dL and 155.8 (51.8) mg/dL. The mean level of AIP in ACS was 0.28 (0.18). Median of stenosis level of coronary artery was 80% with range 50% - 95%. Spearman correlation test showed a moderate positive correlation between AIP with stenosis level of the coronary artery in ACS ( $r = 0.426$ ;  $p < 0.05$ ). There is a moderate positive correlation between AIP with stenosis level of the coronary artery in ACS.

**Key words:** Acute coronary syndrome, atherogenic index plasma, stenosis level

### INTRODUCTION

Cardiovascular disease is one of the diseases that threaten public health and become the main cause of death in the world. The World Health Organization (WHO) found in 2012 about more than 17.5 million people died from cardiovascular disease (31% of all deaths), and > 75% of them are in developing countries. Coronary Heart Disease (CHD) is the largest contributor to cardiovascular disease. The year 2020 is estimated to be the main cause of death is 36% of all deaths.<sup>1-3</sup>

The Acute Coronary Syndrome (ACS) is one of the major clinical manifestations of CHD and most often leads to death. An acute coronary syndrome is a set of manifestations or symptoms caused by a disturbance in the coronary arteries that cause oxygen supply to the heart muscle is reduced. The clinical spectrum of ACS varies from unstable angina pectoris, myocardial infarction without ST-elevation and myocardial infarction with ST-elevation.<sup>4,5</sup>

The ACS occurs due to the process of atherosclerosis that causes constriction of coronary vein lumen (stenosis of a coronary artery). Such narrowing disrupts blood flow so that the heart muscle cells lack the oxygen supply from the affected blood vessels.<sup>6,7</sup>

Atherosclerosis is the process of plaque formation in the intima tunica artery. Atherosclerosis is defined as progressive hardening and arterial constriction due to fat deposits with inflammation. This process of atherosclerosis occurs through 4 stages of endothelial damage, Low Density Lipoprotein (LDL) cholesterol migration to the intima tunica, inflammatory response, and fibrosis capsule formation.<sup>8,9</sup>

The image of the coronary artery in ACS can be known through invasive examination method ie coronary angiography (found in 1959). Coronary angiography is the first invasive method of screening performed by Sones, by inserting a catheter, injecting a contrast agent into a coronary artery, and

recording it with a radiographic image. Coronary angiography is helpful in determining the diagnosis, prognosis, and management of subsequent cardiovascular therapy. Coronary angiography is one of the most widely performed invasive procedures worldwide in the management of cardiovascular therapy today.<sup>10</sup>

Atherogenic dyslipidemia is a major risk factor for ACS. Atherogenic dyslipidemia can lead to the formation of atherosclerotic plaques in the coronary arteries. The ability of plasma lipids to migrate to intima tunica is an important stage for the development of atherosclerosis. Known atherogenic dyslipidemia include elevated triglycerides, increased free fatty acids, decreased HDL cholesterol, increased HDL cholesterol/ cholesterol ratio, and increased small dense LDL (sdLDL).<sup>11,12</sup>

Penalva *et al.* conducted a study in Brazil, in patients with ACS who had performed angiographic examinations to determine the relationship of lipid profiles (total cholesterol, HDL cholesterol, LDL cholesterol, and total cholesterol/HDL cholesterol ratio) to the severity of coronary artery disease in patients ACS. The results showed that the ratio of total cholesterol/ HDL cholesterol was a marker of the severity of coronary artery disease better than a lipid profile alone.<sup>13</sup>

The lipid profile ratio was developed as a marker of cardiovascular disease severity. This lipid ratio illustrates the balance between proatherogenic lipids and antiatherogenic lipids. Khazaal compares several lipid ratios as a predictor of incidence of ACS, the ratio of total cholesterol and HDL cholesterol, the ratio of LDL cholesterol and HDL cholesterol, and the Atherogenic Index of Plasma (AIP). The results of the study obtained AIP is the index with the highest sensitivity to predict the incidence of ACS.<sup>14</sup>

The atherogenic index of plasma is defined as the logarithm (TG/HDL-C) in a molar. The AIP is a reflection of the degree of plasma atherogenicity. The AIP is proposed as a marker of plasma atherogenicity as its value increases in individuals with a high risk of CHD occurrence.<sup>15</sup> Dobiasova *et al.* obtaining AIP is a predictor of cardiovascular disease risk and therapeutic effectiveness.<sup>16</sup> Bhardwaj *et al.* studied 60 patients with coronary artery disease as evidenced by coronary angiography compared with controls, obtaining AIP significantly predicted coronary artery disease.<sup>17</sup>

The AIP correlates well with LDL particle size and may be an indicator of the atherogenic lipoprotein phenotype. The AIP is an sdLDL indicator. Small

dense LDL is a small and dense LDL particle, which is proatherogenic in that it has the greater atherogenic ability because it is susceptible to oxidation. High sdLDL concentrations correlated with CHD risk 3-7 times, regardless of LDL cholesterol levels in circulation. High sdLDL concentrations were found in patients with elevated triglycerides and low HDL cholesterol levels.<sup>18</sup>

Kwon *et al.* found that small LDL particle size in CHD patients has a relationship with the severity of CHD and ACS. Koba *et al.* obtained a strongly correlated coronary artery stenosis with small LDL particle size. Ghassab *et al.* also found a significant difference in the increase in sdLDL in patients with coronary stenosis compared with non-stenotic.<sup>11</sup>

Examination of sdLDL is expensive and uses complex procedures such as ultracentrifugation, electrophoresis, and nuclear magnetic resonance. This limits the use of sdLDL as a risk factor for cardiovascular disease.<sup>19</sup>

This study aimed to identify the correlation of AIP with stenosis level of the coronary artery at ACS in the Cardiovascular Care Unit (CVCU) M. Djamil Hospital Padang.

## METHODS

This research is an analytic study with a cross-sectional design. The study was conducted at the Central Laboratory Installation of M. Djamil Hospital Padang and CVCU M. Djamil Hospital Padang from January 2017 to September 2017. The population is a patient who has been diagnosed with acute coronary syndrome by a clinician and has performed coronary angiography. The sample is part of the population that meets the inclusion and exclusion criteria. The inclusion criteria are willing to take the study, while the exclusion criterion is the patient with a history of dyslipidemia treatment. Tests of triglycerides and HDL cholesterol with enzymatic colorimetric methods used clinical chemistry analyzer, whereas the stenosis level was determined using coronary angiography examination. Spearman's correlation test was used to analyze the correlation of AIP with stenosis level of the coronary artery, meaning if  $p < 0.05$ .

## RESULTS AND DISCUSSION

Cross-sectional analytic studies of 24 ACS patients treated at the CVCU M. Djamil Hospital Padang. The sample of the study is that meet the

criteria of inclusion and exclusion, and perform blood tests at the Central Laboratory Installation of the M. Djamil Hospital Padang from January 2017 to September 2017. The parameters examined included HDL cholesterol and triglycerides. The data obtained were analyzed using a computer program.

Basic characteristics of subjects can be seen in Table 1. The subject of males research is more than females. The age range of the study subjects was 42-74 years.

**Table 1.** Basic characteristics of subjects

Variable	f (%)	Mean (SD)
Male	20 (83.3)	
Female	4 (16.7)	
Age (years )		57.6 (7.9)

Subjects of this study were 24 patients with ACS males (83,7%) more than females (16.3%). These results are consistent with the research of Penalva *et al.* in Brazil that examined the lipid profile and severity of atherosclerotic disease in the ACS patients receiving 88% of men. The study of Samsuria & Adninta in Semarang who studied sdLDL and stenosis level in ACS patients also found as many as 81.5% of males. Sex is one of the risk factors for ACS. Acute coronary syndromes are more common in men than in females. Female have the hormone estrogen that serves as antiatherogenic, so it can prevent the process of atherosclerosis in the blood vessels. The risk increases in postmenopause females but remains lower than males of the same age.<sup>20</sup>

The mean age of patients with ACS in this patient is 57.6 (7.9) years with the age range 42-74 years. This result is similar to the research of Sutamti *et al.* and Samsuria & Adninta in Semarang which had found 57.35 (10.96) years of ACS patients with age range 37-76 years and 55.5 (9.55) years with the age range 34-73 years. The most powerful independent predictor of ACS is age. The risk increases every ten years in the male. Male over 45 and female over 55 are the conventional risk of ACS.<sup>21</sup>

The clinical characteristics of subjects included HDL cholesterol and triglyceride levels divided according to NCEP ATP III guidelines, AIP, and coronary artery stenosis levels as shown in Table 2. More than half of the subjects had low HDL levels and normal triglyceride levels based on NCEP ATP III. A total of 5 people (21.8%) of the study subjects had HDL cholesterol levels > 40 mg/dL but <60 mg/dL. More than half of the study subjects had AIP with high cardiovascular risk and most had a stenosis level

**Table 2.** Clinical characteristics of subjects

Variable	f (%)
HDL (NCEP ATP III)	
Low (<40mg/dL)	19(79.2)
High (>60mg/dL)	0(0)
Triglycerides (NCEP ATP III)	
Normal (<150mg/dL)	14(58.3)
Borderline high(150-199mg/dL)	6(25.0)
High (200-400mg/dL)	4(16.7)
Atherogenic index of plasma	
>0.24	13(54.2)
0.11-0.24	9(37.5)
< 0.11	2(8.3)
Stenosis degree	
≥70%	23(95.8)
<70%	1(4.2)

with a significant clinical disorder.

Clinical characteristics of subjects obtained half of the subjects had low HDL cholesterol levels and normal triglyceride levels. Luz *et al.* studied the ratio of TG/HDL cholesterol as a predictor of the extent of coronary artery disease in ACS patients getting most of the study subjects had low HDL cholesterol and high triglyceride levels. More than half of the study subjects had an AIP with high cardiovascular risk, and most of the study subjects had a stenosis level with a significant clinical disorder.

Low HDL cholesterol and high triglyceride levels are part of atherogenic dyslipidemia, accompanied by high AIP scores can trigger the formation of atherosclerotic plaques resulting in coronary artery stenosis, causing a significant clinical hemodynamic disturbance in ACS patients.

The mean HDL cholesterol, triglyceride levels, and AIP levels were seen in Table 3. The mean HDL cholesterol levels of the study subjects included low HDL criteria, and mean triglyceride levels including high-triglyceride borderline criteria based on NCEP ATP III. The subjects had AIP with high cardiovascular risk.

**Table 3.** HDL cholesterol levels, triglycerides, and AIP

Variable	Mean (SD)
HDL cholesterol (mg/dL)	34.8 (8.6)
Triglycerides (mg/dL)	155.8 (51.8)
Atherogenic index of plasma	0.28 (0.18)

The mean HDL cholesterol level of the study subjects was 34.8 (8.7) mg/dL (low HDL) similar to that of Sharma *et al.* in India that investigated clinical



and angiographic characteristics in ACS patients getting HDL cholesterol 38.39 (8.401) mg/dL. The results of this study differ from Penalva *et al.* who examined lipid profiles in ACS patients receiving HDL cholesterol levels of 50.2 (21.8) mg/dL.

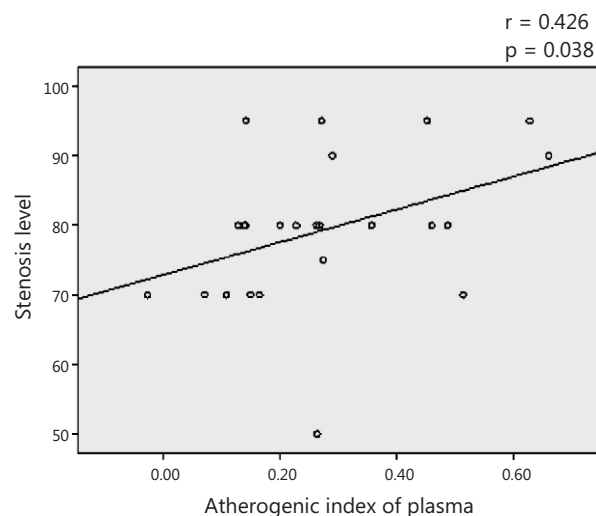
The mean of triglyceride level of the subjects was 155.8 (51.8) mg/dL (borderline high triglyceride). The results of this study were similar to Luz *et al.* (2014) receiving triglyceride levels of 167.9 (91.7) mg/dL. Different results obtained Bhardwaj *et al.* in India who examined the association of AIP with coronary artery stenosis in patients with ACS received triglyceride levels of 140.6 (6.3) mg/dL (generally based on NCEP ATP III).

The mean AIP in this study was 0.28 (0.18). Bhardwaj *et al.* obtained AIP values with high cardiovascular risk (0.39). Different results were obtained by Frohlich & Dobiasova in Canada who examined FerHDL and AIP as a predictor of coronary artery disease in CHD to obtain AIP < 0.24. Research conducted by Dobiasova in 2005 reported that AIP values < 0.11 were associated with a lower risk of cardiovascular disease, AIP values 0.11-0.24 were associated with intermittent cardiovascular risk and AIP values > 0.24 were associated with high cardiovascular risk.<sup>22</sup>

The stenosis level of the study subjects based on Knudtson, the study subjects had median stenosis level with a significant clinical disorder ( $\geq 70\%$  stenosis). The median stenosis level of the study subjects was 80% with a 50% -95% range. This result is similar to that of Sutamti *et al.* in Semarang who studied the stenosis level in patients with ACS receiving a median of 80% stenosis with a range of 30% - 90%. A slowly progressing process of atherosclerosis caused coronary artery stenosis with thickening of the intima tunica due to fibrous buildup which will gradually narrow the lumen of the coronary arteries.

Normality test is performed on AIP value and stenosis level of the coronary artery. Normality test results using Saphiro-Wilk obtained abnormal distribution in stenosis level of the coronary artery. Furthermore, log transformation was obtained, the abnormal distribution of coronary artery stenosis

degree, so that AIP correlation test with the degree of coronary artery stenosis on ACS, was done by Spearman correlation test based on Table 4.



**Figure 1.** The linear curve of the AIP and stenosis level of the coronary artery in ACS

Based on Spearman correlation test, the results of this study obtained a moderate and significant positive correlation between AIP with the stenosis level of the coronary artery in patients with ACS ( $r = 0.426$ ,  $p < 0.05$ ) (Figure 1). The Bhardwaj *et al.* also found a moderate and significant positive correlation between AIP and stenosis of the coronary artery ( $r = 0.56$ ,  $p < 0.001$ ).

The AIP is a reliable marker for predict the risk of atherosclerosis and CHD. The AIP represents the relationship between protective lipoproteins and atherogenic lipoproteins. The AIP corresponds to the size of the atherogenic lipoprotein particles, the more AIP increases, the smaller the atherogenic lipoprotein particles. The ability of plasma lipids to migrate to tunica intima is an essential stage for the development of atherosclerosis. The smaller the particles of atherogenic lipoproteins, the more easily the particles migrate and oxidize, there by accelerating the process of atherosclerosis that causes the increasing stenosis level of coronary artery.<sup>23</sup>

Limitations of this study do not distinguish patients based on risk factors ACS. The ACS is a multifactorial disease, which is influenced by many

**Table 4.** Analysis of AIP correlation plasma with stenosis level of the coronary artery by Spearman correlation test

	Stenosis level of the coronary artery (%)	
	r	P
Atherogenic index of plasma	0.426	0.038

factors, such as hypertension, diabetes mellitus, and smoking.

## CONCLUSION AND SUGGESTION

Atherogenic index plasma has a moderate positive correlation with the stenosis level of the coronary artery in patients with ACS in the M. Djamil Hospital Padang. Further studies are required to prove the correlation of AIP with the stenosis level of the coronary artery in patients with ACS based on the grouping of many risk factors.

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