
ASSOCIATION BETWEEN HIGH DENSITY LIPOPROTEIN LEVEL WITH DEGREE OF STENOSIS IN CORONARY ARTERY DISEASE**Arrizki Azka Pratama¹, Saugi Abduh², Siti Thomas Zulaikhah^{3*}**¹Program Pascasarjana, Fakultas Kedokteran (UNISSULA), Semarang²Departemen Penyakit Dalam, Fakultas Kedokteran (UNISSULA), Semarang³Departemen Kesehatan Masyarakat, Fakultas Kedokteran (UNISSULA), Semarang*Corresponding authors, email: sitithomas@unissula.ac.id

ABSTRACT

Coronary Artery Disease (CAD) can be prevented by early detection and control of risk factors. This study aimed to determine the relationship of High Density Lipoprotein (HDL) levels with stenosis levels based on Significant Non-Significant angiography in CAD patients. Observational research method with cross-sectional design from secondary data at RSI Sultan Agung Semarang in January 2016 - October 2018, 363 respondents met the inclusion and exclusion criteria. Data were analyzed by Spearman test and logistic regression. In low HDL, significant stenosis was found to be 80.5% and non-significant 19.5%, significant HDL was found with significant stenosis 67.0% and non-significant 33.0%, whereas in high HDL, all (100%) with significant stenosis. The results with the Spearman test obtained $p = 0.022$. In the multivariate analysis of sex as the predominant variable ($p=0,000$; $PR=4.743$; $95\%CI=1.496-4.109$). age ($p = 0.013$; $PR = 3.48$; $95\% CI = 1.24- 6.13$), hypertension ($p = 0.044$; $PR = 1.79$; $95\% CI = 1.10-3.17$). There was a significant relationship between HDL levels and significant stenosis levels based on significant non-angiography in CAD patients and after being analyzed together with the disrupting variables as sex the most influential factors.

Keywords: HDL Level; Coronary Artery Disease; Degree of Stenosis; Significant-Non Significant score.

INTRODUCTION

Coronary Artery Disease (CAD) is the leading cause of death with a prevalence rate of 45.1% in developed countries, followed by stroke, heart failure, hypertension, and other arterial diseases.¹ One-third of all deaths in individuals above 35 years were caused by CAD, with half and one-third of all middle-aged men and women in the USA developing manifestations of CAD, respectively.² Developing countries (specifically Indonesia) showed CAD as one of the diseases with the highest prevalence rate among cardiovascular diseases based on The Riskesdas.³ The prevalence rate of CAD in Indonesia is 1.5% (2,650,340 people), dominating East Java and least in West Papua.⁴

CAD is a disease characterized by the formation of plaques in the coronary artery. The coronary artery carries oxygen-rich blood to the heart muscles. Atherosclerosis is a condition caused by narrowing the artery due

to the accumulation of extracellular lipids and the formation of foam cells, leading to the thickening and stiffening of the affected artery.⁵ High-Density Lipoproteins (HDL) are blood cholesterol synthesized and excreted from the liver and intestines. High blood cholesterol levels compromise 56% of the risk factors that contribute to the incidence of CAD.⁶ Blood cholesterol is distributed by mainly two lipoproteins, which are Low Density Lipoprotein (LDL) dan High Density Lipoprotein (HDL).⁷ A high HDL level is known to have protective effects on the deposition of atherosclerotic plaques. Research showed high HDL levels in the blood contribute to preventing CAD.⁸

Current interventions aimed to improve lipid profile include administering anti-lipidemic agents to reduce CAD risk. Anti-lipidemic agents are synthetic drugs that have potential side effects. Therefore, further

research is required that focuses on the role of HDL in the prevention of CAD. The degree of severity or classification of CAD can be determined through a scoring system, for example, using the significant and non-significant grouping method, *one vessel disease, two vessels disease three vessel disease*, or by calculating the Gensini Score.⁹ The significant and non-significant angiography grouping method is a simple classification method by observing the narrowing of the artery lumen $\geq 50\%$ or $< 50\%$.¹⁰ This research needs to be done because there have been no previous studies that are similar. This study aimed to determine the association between HDL levels and degree of stenosis based on a significant-non significant angiography score in CAD patients.

METHODS

This study used an observational analytic method with a cross-sectional design from secondary data at Sultan Agung Islamic Hospital Semarang, using 363 samples retrieved from medical records at Sultan Agung Islamic Hospital Semarang from Januari 2016 – Oktober 2018. The independent variable in this study was HDL level, and the dependent variable was the degree of stenosis based on significant and non-significant scores. Confounding variables in this study were smoking, nutritional status (BMI), diabetes mellitus, hypertension, age, sex, and dyslipidemia. Confounding variables were controlled by multivariate analysis. Inclusion criteria were: Patients that have undergone angiography examination, a complete medical record consisting of: patient administration code, age, sex, smoking, history of diabetes mellitus, angiography results, and laboratory results compromising HDL level, total cholesterol level, and hypertension. HDL level data was categorized into low: HDL level < 40 mg/dL; normal: HDL level 40-59 mg/dL; high: HDL level ≥ 60 mg/dL¹⁰ Degree of

stenosis was categorized into non-significant: if coronary artery stenosis was $< 50\%$ and significant: if coronary artery stenosis was $\geq 50\%$.¹¹ Data were analyzed with univariate analysis using frequency distribution, bivariate analysis using Spearman test, and multivariate analysis using logistic regression. The hypothesis was accepted or rejected based on an α value of 5%.¹²

RESULT

Table 1. Respondent characteristics.

Characteristic	Total	Percentage (%)
Sex		
- Male	245	87.9%
- Female	123	21.1%
Age group		
- ≥ 45 years	324	89,3%
- < 45 years	39	10.7%
HDL level		
- Low	251	69.1%
- Normal	106	29.2%
- High	6	1.7%
Total cholesterol		
- < 200	282	75.2%
- ≥ 200	90	24.8%
Hypertension		
- Yes	214	59.0%
- No	149	41.0%
Smoking		
- Yes	145	39.9%
- No	218	60.1%
Nutritional status		
- Overweight	209	57.6%
- Normoweight	145	39.9%
- Underweight	9	2.5%
DM		
- Yes	126	34.7%
- No	237	65.3%
Degree of Stenosis		
- Significant	279	76.9%
- Non-significant	84	23.1%

Table 2. Correlation between HDL level and degree of stenosis based on a significant-non significant score in patients with CAD

HDL level	Degree of stenosis		Total	<i>p-value</i>	<i>r</i>
	Significant	Non-Significant			
Low	202 (80.5%)	49 (19.5%)	251 (100%)	0.022	0.120
Normal	71 (67%)	35 (33%)	106 (100%)		
High	6 (100%)	0 (0%)	6 (100%)		

Table 2 showed that patients with low HDL levels were found with significant stenosis (80.5%) and non-significant stenosis (19.5%), patients with normal HDL levels were found with significant stenosis (67.0%) and non-significant stenosis (33.0%). In contrast, patients with high HDL levels were found with significant stenosis (100%).

Spearman test analysis obtained a *p*-value = 0.022, which indicated a significant correlation between HDL level and degree of stenosis based on a significant-non significant angiography score in patients with CAD at Sultan Agung Islamic Hospital Semarang. However, the correlation strength between variables was low ($r=0.120$).

Table 3. Bivariate analysis of confounding variables with the degree of stenosis based on a significant-non significant angiography in patients with CAD

Variable	<i>p-value</i>
Total cholesterol	0.417*
Sex	0.000**
Age	0.005**
Hypertension	0.163*
DM	0.008**
Smoking	0.000**
Nutritional status	0.646*

* $p>0,05$ no significant correlation

** $p\leq 0,05$ significant correlation

Analysis results with the Spearman test (see Table 3) showed two variables with a *p*-value $>0,25$, total cholesterol and nutritional

status, statistically indicating that the two variables mentioned were ineligible to be included in the multivariate analysis.

Table 4. Multivariate Analysis Results

Variable	P-value	PR	95% CI	
			Lower	Upper
DM	0.131	2.752	0.899	2.258
Hypertension	0.044	1.796	1.107	3.171
Smoking	0.068	2.012	0.949	4.268
Sex	0.000	4.743	1.496	4.109
Age	0.013	3.482	1.240	6.135

Logistic regression analysis (see Table 4) showed a significant correlation in hypertension, sex and age with the degree of stenosis in CAD patients, with sex being the predominant variable (PR=4.743; 95%CI=1.496-4.109), indicating that male patients with significant stenosis were at risk 4.743 times higher compared to female patients.

DISCUSSION

This study showed that 69.1% CAD patients had HDL levels <40 mg/dL, 29.2% had HDL levels between 40-59 mg/dL and 1.7% had HDL levels \geq 60 mg/dL. Spearman test obtained a significant correlation between HDL level and degree of stenosis based on significant-non significant angiography score with a p -value = 0.022; however, the correlation strength was low ($r=0.120$). Incidence of CAD was much more common in male patients (87.9%) rather than females (21.1%), indicating a significant correlation between sex and degree of stenosis ($p = 0.022$). The result obtained in this study was similar to Suherwin's study¹³ showed that the incidence of CAD in female patients was less common (36.8%) than in male patients (63.2%). Multivariate analysis results showed that sex was the predominant variable correlating to the degree of stenosis (PR=4.743; 95%CI=1.496-4.109), indicating that men with CAD have a 4.743 times higher risk of significant stenosis compared to women with CAD.

In this study, the age group of CAD patients was 89.3% \geq 45 years and 10.7% <45 years. Spearman test obtained a significant p -value of 0,005 between age groups. The difference in population found in this study was due to the age restriction of respondents between 35-81 years since the tool of diagnosis used was based on a significant-non significant score, and respondent data was obtained from medical records at Sultan Agung Islamic Hospital Semarang.

Spearman test results showed a significant correlation between CAD patients and diabetes mellitus ($p = 0.008$). This result

was relevant to Suherwin's study (2018) that found 41 respondents without a history of diabetes mellitus (30.1%) and 95 with a history of diabetes mellitus (69.9%). The significant correlation obtained between diabetes and the degree of stenosis in CAD patients was based on the theory stating that diabetes can cause progressive damage to the microvasculature, leading to an increased risk of CAD.

No significant correlation was found between nutritional status and incidence of stenosis in CAD patients ($p = 0.987$). This result was similar to a study that obtained a p -value = 0.197¹⁴. Although no statistical significance was found, theoretically, an obese adult will experience an increase in cholesterol levels that may trigger the incidence of CAD. The difference found in this study was due to the discrepancy in the criteria for nutritional status used.

Smoking and obesity are risk factors for the occurrence of atherosclerosis. This study found that 39.9% of respondents had a smoking history, and 60.1% of respondents were non-smokers. Total respondents with an overweight status were 57.6%. Spearman's analysis obtained a significant correlation between smoking and the incidence of stenosis in CAD patients with p -value = 0.000, whereas obesity had no significant correlation with p -value = 0.646. This result was not relevant to Ridwan's study that showed smoking intensity had no significant correlation with the degree of severity in CAD ($p = 0.156$).¹⁵ This can be seen from the results obtained that showed ten people (33%) with stenosis in all three coronary arteries were mild smokers. In contrast, two people (6%) with stenosis of only one coronary artery were heavy smokers.

CONCLUSION

HDL level was associated with the degree of stenosis in CAD patients based on a significant-nonsignificant score. After HDL level was analyzed with confounding factors (sex, age, hypertension, DM, and

smoking) with the degree of stenosis, it was found that hypertension, sex, and age were associated with the degree of stenosis in CAD patients, with sex as the predominant variable (PR=4.743; 95%CI=1.496-4.109).

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