ISSN 2515-8260 Volume 07, Issue 08, 2020

The Comparison of AIRI values in Obese and Non Obese Acute Coronary Syndrome patients

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Abstract: Introduction : ***Insulin resistance (IR) has an important role in pancreatic β-cell dysfunction and incidence of type-2 Diabetes Mellitus (DM-2), and such resistance is also able to indicate the pathophysiological component of other endocrine metabolic disorders such as hypertension, obesity, dyslipidemia, and cardiovascular disease (CVD). Obesity is a major risk factor for endothelial dysfunction which develops as a result of abnormal regulation of vasoactive substances including nitric oxide, where endothelial dysfunction is the starting point in the pathogenesis of IR. This study's objective is to compare Admission Insulin Resistance Index (AIRI) values in Obese and Non-Obese Acute Coronary Syndrome patients.***

Methods: This was a cross sectional study with consecutive sampling method consisting of 60 subjects who were treated with Acute Coronary Syndrome at Dr. Wahidin Sudirohusodo Hospital Makassar, Indonesia from July-September 2020. Anthropometric examinations include measuring body weight and height to determine body mass index (BMI).
AIRI was measured insulin admission (μIU / ml) x plasma glucose admission (mg / dl) / 405. Statistical analyses used were Chi Square test and Spearman's Correlation test (significance p <0,01).

Results: Average age of the subjects was 54.9 ± 13.6 years old, with 76,7 % male. Based on the results of clinical, laboratory and ECG examination, the subjects had hypertension (48.3%), obesity (35%), decreased HDL (38.3%), increased triglycerides (28.3%), increased LDL (70%), increased RBG (76.7%), experienced IR (20%), diagnosed of STEMI (35%), NSTEMI (53.3%), and UAP (11.7%). There was a significant relationship between obesity and AIRI (p <0,001). Where in obese, it was found that the percentage of AIRI's tertile 3 (70%) was the highest compared to AIRI's tertile 2 (20%) and AIRI's tertile 1 (15%). Meanwhile, those who were not obese were found to have the highest level of 1 AIRI (85%) compared to 2 AIRI (80%) and 3 AIRI (30%).

Conclusion: Obesity in patients with ACS is related to the AIRI value.

Keywords: ACS, AIRI, Obesity.

ISSN 2515-8260 Volume 07, Issue 08, 2020

1. INTRODUCTION

Acute Coronary Syndrome (ACS) is an acute manifestation of a torn or ruptured coronary artery atheroma plaque. ACS is a major cardiovascular problem because it causes high hospital admissions and mortality rates.(1) Inpatients with ACS have a high incidence of impaired glycemic status with 33% being prediabetes and 33% Diabetes Mellitus type 2.(2) Insulin resistance plays a major role in both pathogenesis of type 2 diabetes mellitus, metabolic syndrome or in predicting the incidence of cardiovascular disease, so that the value of IR has a positive correlation with the incidence of ACS with or without previous diabetes.(3)

Insulin resistance is a condition in which there is a decrease in tissue sensitivity to insulin action resulting in an increase in insulin secretion as compensation for pancreatic beta cells.(4) Insulin resistance was first introduced in 1936 to describe the presence of metabolic disorders characterized by decreased cellular response to insulin.(5) Currently, IR is reported to be one of the main causes of death in adult populations worldwide and is projected to have a prevalence of around 33% in America in 2050.(6) In Asia, the prevalence of IR is reportedly increasing,(7) a survey in Jakarta reported that the prevalence of IR has reached 28.6% in 2006.(8)

Insulin resistance has an important role in pancreatic β-cell dysfunction and the incidence of type-2 Diabetes Mellitus (DM-2), and such resistance is also able to indicate the pathophysiological component of other endocrine metabolic disorders such as hypertension, obesity, dyslipidemia, and CVD.(6) Thaane et al (2019) explained that obesity (especially central obesity) is a major risk factor for endothelial dysfunction as a result of abnormal regulation of vasoactive substances including nitric oxide, where endothelial dysfunction is the starting point in the pathogenesis of IR.(9) Insulin resistance is also associated with an increased risk of CVD by 1.5-1.8 times higher.(10)

The gold standard for assessing IR is the Hyperinsulinemic Euglycemic Clamp (HEC), which has a sensitivity of 95.7% and a specificity of 84.4%, but the implementation of such test is very cost and time consuming. Another test that has a simpler method and is relatively inexpensive is the Homeostasis Model Assessment-Insulin Resistance (HOMA-IR), which has a sensitivity of 56% and a specificity of 86%, by taking fasting insulin and plasma glucose, then entering these values into the formula: insulin fasting (μIU / ml) x plasma glucose (mg / dl) / 405.(11–13) Although the HOMA-IR test is relatively inexpensive, it takes a relatively long time to examine fasting insulin and glucose. Another examination alternative that has relatively low cost and fast results is the AIRI, by taking insulin and plasma glucose at admission then entering these values into the formula: insulin volume at admission (μIU / ml) x plasma glucose at time admission (mg / dl) / 405. Although sensitivity and specificity are still unknown, AIRI has a significant correlation with HOMA-IR and insulin resistance syndrome.(14,15)

This study's objective is to comparison of AIRI values between Obese and Non-Obese ACS patients.

2. METHODS

2.1. Research Design

This study was a cross sectional at Dr. Wahidin Sudirohusodo Hospital in Makassar, South Sulawesi Indonesia.

2.2. Research Subjects

The study population was all patients who entered Emergency Room Wahidin Sudirohusodo Hospital Makassar, who were included into the inclusion criteria. The inclusion criteria was > 30 years old and having Acute Coronary Syndrome. All subjects sign an informed consent form.

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2.3. Research Data Collection

All subjects who had ACS were categorized as STEMI, NSTEMI, and UAP. All subjects were measured with AIRI. Admission Insulin Resistance Index classified into 3 tertiles. Tertile 1 (3,5-6,8), Tertile 2 (6,9-13,5), Tertile 3 (13,6-26,3). Body mass index of the subjects was categorized obese (IMT > 25 kg/m2) and non obese.

2.5. Research Data Analysis

Statistical analysis was performed with SPSS version 22. The statistical analysis performed was descriptive statistical calculation and frequency distribution as well as Chi-Square test and Spearman Correlation test. Significant if p<0,01.

2.6. Ethical Clearance

This study protocol was approved by the Health Research Ethics Commission of Universitas Hasanuddin, Medical Faculty, following the ethical recommendations with approval letter number 1155 / UN4.6.4.5.31 / PP36 / 2019.

3. RESULTS

The study was conducted at Wahidin Sudirohusodo hospital from July 2020-September 2020. This study involved 60 research subjects who met the inclusion criteria. Data analysis was performed using SPSS version 22. The statistical analysis carried out was the frequency distribution and Chi Square test and Spearman Correlation test. Significant p <0,01.

The analysis was carried out on 60 subjects with Acute Coronary Syndrome patients with an age range of 30-80 years with a mean of 54.9 $\pm$ 13.6 years. Descriptive statistical values of the variable and AIRI can be seen in Table 1.

Table 2 shows the distribution of the research variable categories consisting of male (76.7%) and female (23.3%) research subjects. Based on the results of clinical, laboratory and EKG examinations, the subjects had hypertension (48.3%), obesity (35%), decreased HDL (38.3%), increased triglycerides (28.3%), increased LDL (70%), increased RBG (76.7%), experienced IR (20%),diagnosed of STEMI (35%), NSTEMI (53.3%), and UAP (11.7%).

Table 3 shows there was a significant relationship between obesity and AIRI (p <0,001). Where in obese patients, it was found that the percentage of AIRI's tertile 3 (70%) was the highest compared to AIRI's tertile 2 (20%) and AIRI's tertile 1 (15%). Meanwhile, those who were not obese were found to have the highest level of 1 AIRI (85%) compared to 2 AIRI (80%) and 3 AIRI (30%).

4. DISCUSSION

This study included 60 subjects aged 30-80 years with the research subjects consisting of men (76.7%) and women (23.3%). Based on the results of clinical, laboratory and EKG examinations, it showed that subjects had hypertension (48.3%), obesity (35%), decreased HDL (38.3%), increased triglycerides (28.3%), increased LDL (70%), increased RBG (76.7%), experienced IR (20%), a diagnosis of STEMI (35%), NSTEMI (53.3%), and UAP (11.7%).

In this study, it was found that most of the subjects were male, namely 76.7%. This is in accordance with a study conducted by Stubbs et al. It showed that men more common experienced ACS than non-ACS, namely 70% vs 66% with p <0,001.(15) Ormazabal et al reported that the association of IR with cardiovascular risk was found common in middle-aged men than in women.(16)

In this study, subjects who experienced hypertension were 48.3%. This result is in accordance with the study by Refaie Wael et al. the AIRI value was higher in hypertensive subjects than in non hypertensive subjects, 98.2 $\pm$ 16.4 (66-130) vs 86.2 $\pm$ 10.8 (66-106) with p <0,001.(14) Likewise, Scherrer et al found that almost 50% of individuals with IR can

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develop hypertension.(17) DeFronso et al. explained that in theory IR can lead to hypertension by increasing sodium reabsorption, disrupting ion transport to the transmembrane, activating the sympathetic nervous system and increasing the regulation of angiotensin receptors II.(18)

In this study, it was found that the percentage obese subjects was 35%. These results are in accordance with the study by Refaie Wael et al which shows that the AIRI value in obese patients is higher in ACS patients than the one found in non-ACS patients, 30.4 ± 1.9 (26-34) vs 25, 1 ± 2.2 (21-29) with p <0,001.(14). A study by Facchini et al showed that IR was higher in obese than non-obese patients, namely 25.6 ± 0.3 vs 23.1 ± 0.3 with p <0,0001.(19) This is consistent with a study by Thaane et al explaining that obesity (especially central obesity) is a major risk factor for endothelial dysfunction as a result of abnormal regulation of vasoactive substances including nitric oxide, where endothelial dysfunction is the starting point in the pathogenesis of IR.(9)

The next characteristic also found was increase of TG 28.3% with a low HDL level 38.3%. This study is in accordance with the study conducted by Tenenbaum et al showing higher IR values in subjects with a higher TG increase than without increases in TG, namely 156 ± 53 vs 136 ± 49 with p <0,0001 and higher IR in subjects with a higher HDL reduction than the ones without any decrease in HDL with 33.8 ± 5.5 vs 35.3 ± 3,4 with p <0,0001.(20) This is in accordance with the results obtained by Reaven et al, explaining individuals that individuals who experience IR can cause excess adipose tissue lipoprotein lipase and increase the activity of hepatic triglyceride lipases so as to have an effect on low HDL values.(21), in this study is the subject who experienced an increase in RBG by 76.7% and the incidence of STEMI (35%) and NSTEMI (53.3%) was greater than UAP (11.7%). This study is in accordance with the study by Refaie Wael et al. (2012) in a study of 120 non-diabetic patients who entered with complaints of chest pain and divided the patients into 3 groups (myocardial infarction, unstable angina pectoris, and control), it was found that AIRI was significantly highest in patients with myocardial infarction, followed by unstable angina pectoris and a control group.(14) and showed that the increase in RBG was higher in ACS patients than non-ACS patients, 6.0 ± 0.01 (5.98-6.02) vs 5 ± 0.3 (4.4-5, 6) with p <0,001.(14) Tenenbaum et al explained that IR was higher in patients with hyperglycemia than non-hyperglycemic patients 110 ± 19 vs 94 ± 14 with p <0,0001.(20) Karrowni et al, conducted a study on 1073 non-diabetic patients with myocardial infarction, showed an independent relationship between IR and coronary artery disease in patients with post myocardial infarction and non-diabetes mellitus.(22)

In this study, there was a significant relationship between obesity and AIRI (p <0,001), where in obese it was found that the percentage of AIRI's 3rd tertile was the highest compared to tertile 2 and 1(70%). Meanwhile, those who were not obese were found to have the highest level of AIRI 1 (85%) compared to 2 and 3. Thaane et al explained that lack of physical exercise and bad habits are major risk factors for IR accompanied by a poor diet. Obesity (particularly central obesity) is a major risk factor for endothelial dysfunction as a result of abnormal regulation of vasoactive substances including nitric oxide, where endothelial dysfunction is the starting point in the pathogenesis of IR. In the development of obesity, macrophages infiltrate adipose tissue which produce abnormal adipokines and cytokines (leptin and IL-6) and cause systemic inflammation, then decrease the response of liver, muscle and adipose tissue to insulin action in cells resulting in IR.(9)

Another study by Qatanani et al found that the link between obesity and IR is an increase in FFA and inflammatory factors that inhibit insulin signaling, interfere with insulin sensitivity and directly trigger IR.(23) In theory, one of the major risk factors for IR is obesity(24) as a result of lifestyle modification including high calorie intake as well as low physical activity and prolonged sitting habits.(25–27)

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In obese individuals, adipose tissue will produce several factors, including unsaturated FFAs, neurotransmitters and inflammatory cytokines in large amounts that will affect the development of IR.(28) In the development of obesity, macrophages will infiltrate adipose tissue and produce adipokines and abnormal cytokines, causing inflammation. systemic. This reaction will decrease the response of muscle, liver and adipose tissue to insulin action and cause IR. The failure of insulin to suppress lipolysis in adipose tissue that is insulin resistant, especially the visceral adipose tissue will increase circulating FFA which directly affects metabolism in the liver and muscles and aggravates IR. Obesity also plays a role in IR, suppresses insulin signaling through serine kinase activation by activating endoplasmic reticulum stress.(29)

5. CONCLUSION

Obesity in patients with Acute Coronary Syndrome is related to the Admission Insulin Resistance Index value.

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Table 1.Descriptive Statistics of Research Variables (n = 60)

Variabel	Minimum	Maximum	Mean	SD
Age	30	80	54,9	13,6
IMT	16,7	36,4	24,0	3,5
GDP	74,0	151,0	108,2	14,4
TG	58,0	330,0	138,1	46,9
LDL	16,0	193,0	114,2	30,9
HDL	9,0	71,0	43,3	14,0
AIRI	3,5	26,3	11,3	6,4

Table 2. Distribution of Research Variable Categories (n = 60)

Variable		N	%
Gender	Men	46	76,7
	Women	14	23,3
Hypertension	Yes	29	48,3
	No	31	51,7
Obese	Yes	21	35,0
	No	39	65,0
HDL	Low	23	38,3
	Normal	37	61,7
TG	High	17	28,3
	Normal	43	71,7
LDL	High	42	70,0
	Normal	18	30,0
RBG	High	46	76,7
	Normal	14	23,3
AIRI	Tertil 1 (3,5 – 6,8)	20	33,3
	Tertil 2 (6,9 – 13,5)	20	33,3
	Tertil 3 (13,6 – 26,3)	20	33,3
Diagnosis	STEMI	21	35,0
	NSTEMI	32	53,3
	UAP	7	11,7

Table 3.Correlation between Obesity and AIRI

Obese			Tertil AIRI			Total
			Tertil 1	Tertil 2	Tertil 3	
	Yes	N	3	4	14	21
		%	15,0%	20,0%	70,0%	35,0%

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	No	N	17	16	6	39
		%	85,0%	80,0%	30,0%	65,0%
Total		N	20	20	20	60
		%	100,0%	100,0%	100,0%	100,0%

p<0,001