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Original Research Article

Correlation between insulin resistance and metabolic syndrome in obesity adolescents

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Abstract: The prevalence of obesity and the metabolic syndrome increased significantly in developing countries. Insulin resistance is considered to be the central pathophysiologic factor in development of the metabolic syndrome. Several factors are known to increase insulin sensitivity, namely obesity, gender, perinatal factors, puberty, sedentary lifestyle and diet. The aim of this study was to determine the correlation between component of metabolic syndrome and insulin resistance in obesity adolescents. This study was a cross-sectional design conducted in adolescents in Tondano city Minahasa distric, on February - April 2013, involving a total 160 adolescents with obesity. Anthropometric measurements including height measurement (HM), body weight (BW), waist circumference (WC) and blood pressure and laboratory tests such as lipid profile, plasma glucose level and HOMA-IR. Determination of metabolic syndrome using the IDF criteria, 2007. Data analyzed using univariate, bivariate and Pearson correlation test. Data was analyzed with SPSS software version 22, p value <0.05 was considered significant. There were 160 subjects collected in this study who have met the inclusion criteria. All subjects had experienced abdominal obesity as much as 26.9% among males with WC ≥ 90 cm and 73.1% females with WC ≥ 80 cm.A total of 14.4% of the subjects had TG ≥150 mg / dL, and 100% subjects had HDL < 40 mg / dL for males and females<50 mg / dL. A total of 4.4% of the subjects who already had a FBS ≥100 mg / dL, 29.4% had had a blood pressure systolic≥ 130 mmHg and 21.9% blood pressure diastolic ≥ 85 mmHg. In addition, as many as 2.4% of the subjects had insulin resistance (IR). Multiple regression analysis showed, among the components of metabolic syndrome, waist circumference (p = 0.006), triglycerides (p = 0.013), and FBS (p= 0.000) are the MS component that contributes to the HOMA-IR. The high prevalence of the metabolic syndrome and their correlation with insulin resistance in obese adolescents provides evidence for prevention against the risk morbidity and mortality of degenerative diseases, especially type II diabetes and cardiovascular disease.
Keywords: insulin resistance, metabolic syndrome, adolescent.

INTRODUCTION

The prevalence of obesity and the metabolic syndrome increased significantly in developing countries that cause increased morbidity and mortality rates of type II diabetes and cardiovascular disease [1, 2]. Increasing obesity, cardiovascular disease and type II diabetes in adulthood has become a serious problem in children and adolescents. The National Health and Nutrition Examination Survey III (NHANES III) indicated that the prevalence of the metabolic syndrome in 12-19 y-old in obese adolecents in USA is 30% [3]. These data same as with the results of research in Semarang, the prevalence of metabolic syndrome in obese adolescents was 31.6% [4]. It has been reported that the prevalence of the metabolic syndrome has increased rapidly among children and adolescents and increases directly with the degree of obesity [2].

Insulin resistance is considered to be the central pathophysiologic factor in development of the metabolic syndrome; however the underlying is not clear [5]. Components of the metabolic syndrome such as hypertension, hyperglycemia, dyslipidemia and hypertriglyceride. Insulin resistance illustrates the complications of diabetes during childhood and adolescence. When in childhood and adolescence has experienced it will affect insulin resistance in adulthood. Several factors are known to increase insulin sensitivity, namely obesity, gender, perinatal factors, puberty, sedentary lifestyle and diet [6]. Insulin resistance or insulin sensitivity levels can be determined by HOMA-IR index (Homeostasis Model Assessment - Insulin Resistance) [7, 8].

HOMA index had the best sensitivity and specificity for the detection of insulin resistance in children and adolescents [8]. The level of insulin

resistance is directly proportional to the magnitude of the HOMA index, the higher the value the higher the degree of HOMA index of insulin resistance. The reference value used to determine insulin resistance in adolescents is 3.29 and 3.16, 3.29 is the upper quartile values for determining insulin resistance in the whole population of adolescents [9]. While the value of 3.16 is a benchmark for determining insulin resistance in obese adolescent population [8]. The purpose of this study was to determine the correlation between insulin resistance and metabolic syndrome in obesity adolescent in Minahasa district.

METHODS

This study was an observational analytic study with cross-sectional design, conducted in high school students in Minahasa District in February - April 2013. A total of 1282 students consisting of 483 males and 812 females aged 13-18 years old. The prevalence of obesity was 21.3% (274 students). Inclusion criteria were obese students aged between 13-18 years. Willing to be a research participant by signed an agreement (informed concent). Exculision criteria were: being or have had kidney disease, lung disease, heart disease, blood disorders, skin disease and hormonal disorders. Current or past use of diuretic drugs, aspirin, uricosuric, and pyrazinamide acid, pregnan women, unwilling to do blood sampling. A total 0f 160 people consisting of 54 males and 106 females. Subjects requested to fill the informed concent after receiving concent from the parents. This study approved by the research ethics committee of the medical faculty of Sam Ratulangi University. In this study anthropometric measurement includes measurement of height (HM) using microtoise, body weight (BW) using electric scale, waist circumference (WC) using the meter gauge. The presence of metabolic syndrome among the studied was defined as those patients having ≥ 3 of the following 5 items:

1. Waist circumference ≥ 90 for males and ≥ 80 for females;
2. Serum triglyceride levels ≥ 150 mg/dl;
3. Serum HDL levels <50 mg/dl;
4. Systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg;
5. Fasting serum glucose ≥100 mg/dl.

Blood pressure measurement performed when the patient seated quietly for 5 minutes, the upper arm placed on the table. Blood pressure measured 2 times and the average taken as the value of the subject's blood pressure. Laboratory tests are only performed on 160 students for lipid profile (LDL, HDL, total cholesterol, triglycerides) and blood pressure measurement using Nova® mercury sphygromanometer tool. Blood sampling performed after fasting subjects between 10-12 hours. Blood samples were analyzed in clinical laboratory in Manado. Glucose levels of total cholesterol, triglycerides, HDL and LDL were measured by the COBAS Mira autoanalyzer. HOMA-IR to determine insulin sensitivity obtained with insulin formula (μ U / ml) X glucose (mmol / L) / 22.5, cut off of points in adolescents was 3.16.[8] Data were analyzed using SPSS for Windows version 22 for univariate test and multiple regression analysis.

RESULTS

Table 1 show that a sample of adolescents is most often in middle-adolescent age category (78.1%), only 9.4% late adolescent and early adolescent 12.5%. All subjects had experienced abdominalobesity as much as 26.9% among males with WC ≥ 90 cm and 73.1% females with WC ≥ 80 cm. A to tal of 14.4% of the subjects had TG ≥150 mg / dL, and most 72.5% subjects were composed of males with HDL < 40 mg / dL and 27.5% females <50 mg / dL. A total of 4.4% of the subjects who already had a FBS ≥100 mg / dL, 29.4% had had a blood pressure systolic≥ 130 mmHg and 21.9% blood pressure diastolic ≥ 85 mmHg. In addition, as many as 2.4% of the subjects had insulin resistance (IR), and 41.85 % of subjects had three or more components of metabolic syndrome.

Table 2 shows the role of each component of MS with HOMA-IR, analyzed with multiple linear regression analysis. The results of linear regression analysis. The results of the components of metabolic syndrome, waist circumference (p = 0.006), triglycerides (p = 0.013), and FBS (p= 0.000) are the MS components that contributes to the HOMA-IR. The components of HDL (p = 0.189), systolic (p = 0.646) and diastolic (p = 0.276) did not contribute significantly to the HOMA-IR. From the three of the components that play a role, the role is the most powerful component is the FBS, followed by the WC component, and Triglycerides (seen from the p-value, the smaller the p-value (sig), the stronger role).

Table 1: Sample distribution by age, insulin resistance and metabolic syndrome components

Variable	Criteria	Sum (n)	Percentage (%)
	Early adolescent	20	12.5%
Age	Middle adolescent	125	78.1%
	Late adolescent	15	9.4%
WC	Male ≥ 90 cm	43	26.9%
	Female ≥ 80 cm	117	73.1%
TG	≥150 mg/dL	23	14.4%
	<150 mg/dL	137	85.6%
HDL	Male<40 mg/dL,	160	100%
	Female<50mg/dL		
	Male≥40 mg/dL,	-	-
	Female ≥ 50 mg/dL		
FBS	≥100 mg/dL	7	4.4%
	<100 mg/dL	153	95.6%
BP	SYST ≥ 130 mmHg	47	29.4%
	< 130 mmHg	113	70.6%
	DIAST ≥ 85 mmHg	35	21.9%
	< 85 mmHg	125	78.1%
HOMA-IR	≤ 3.16	156	97.5%
	> 3.16	4	2.5%
MS components	> 1	93	58.125 %
	> 2*	56	35 %
	> 3	9	5.625 %
	> 4	2	1.25 %

Information: WC=waist circumference, FBS=fasting blood sugar, HDL= High Density Lipoprotein, TG=triglycerides, SYST=systole, DIAST=diastole, MS=metabolic syndrome

Table 2: Relationship of metabolic syndrome components with HOMA-IR

Independent	B	SE	Coefficient	T	P
Variables			**B**		
WC	0.016	0.006	0.171	2.768	0.006
TG	- 0.002	0.001	- 0.155	- 2.526	0.013
HDL	0.019	0.014	0.082	1.318	0.189
FBS	0.038	0.003	0.773	14.072	0.000
SYST	0.002	0.005	0.037	0.460	0.646
DIAS	- 0.008	0.008	- 0.089	- 1.093	0.276

Information: WC=waist circumference, FBS=fasting blood sugar, HDL= High Density Lipoprotein, TG=triglycerides, SYST=systole, DIAST=diastole

DISCUSSION

Metabolic syndrome is a combination of various cardio metabolic risk are: abdominal obesity, insulin resistance, glucose intolerance, dyslipidemia, hypertension, and nonalcoholic fatty liver disease (NAFLD) [10]. This opinion sustain statement of Grundy *et al.* [11]who said that the metabolic syndrome is a combination of various cardiovascular risk factors such as obesity, glucose intolerance, insulin resistance, dyslipidemia (hypertriglyceridemia), the increase in FFA, decreased HDL, hypertension, proinflammatory state, oxidative stress and NAFLD .

The results of this study indicate that the components of metabolic syndrome is a risk factor for insulin resistance ($p>1$). But only fasting blood sugar (FBS) components are statistically significant ($p<0.05$). The results of this study are in line with result published by Pinho who conducted a cross sectional study in adolescents aged 12-18 years in Sao Paulo, Brazil on biochemical and physiological variables in adolescents with overweight/obese and assess the components of metabolic syndrome. These results showed that subjects had higher levels of TG, blood sugar, high uric acid and low HDL levels found in subjects with insulin resistance [12].

Insulin resistance reflect that its usually found in patients with abnormal metabolic components. Insulin is secreted by pancreatic β cells led to the cells take up glucose from the blood circulation. When these cells decreased sensitivity to stimulate glucose uptake or a state of insulin in normal or increased glucose levels, the condition is referred to as insulin resistance. Insulin resistance occurs when the pancreas to produce more insulin and cause hyperinsulinemia resulting in hyperglycemia and glucose intolerance and type 2 diabetes [13, 14]. Marotta in the research stated, insulin resistance was also an influence on the metabolism of lipoproteins and is associated with increased levels of triglycerides and stressed of HDL level. TG-HDL ratio has been widely used as a marker to predict whether someone has insulin resistance [15]. Yamauchi suggest the obese with hypertriglyceridemia and increased free fatty acids can contribute to insulin resistance. Triglycerides will undergo hydrolysis by the enzyme lipoprotein lipase from endothelial then be an increase in free fatty acids (Free Fatty Acid / FFA) in plasma resulting in increased hepatic gluconeogenesis; decrease in muscle glucose uptake causes insulin resistance in muscle, liver and pancreas [16]. Moran in his study with the euglycemic insulin clamps showed that insulin resistance increases at the beginning of puberty, reaching a peak in mid-puberty and decreased at the end of puberty. This is in accordance with the subjects in this study is the largest age in the mid puberty (16-17 years) [17].

According Caprio [18] lipid disorders, especially hypertriglyceride, low levels of HDL is highly correlated with insulin resistance. The results of this study support this statement, because the whole subject had HDL levels below normal. Research conducted on more than 3000 teenagers in Iran by using the modified ATP III criteria showed that TG and WC was significantly associated with a group of metabolic disorders that are characteristic of the metabolic syndrome [19]. The high prevalence of the metabolic syndrome and their correlation with insulin resistance in obese adolescents require attention to minimize morbidity and mortality from degenerative diseases, especially diseases of type II diabetes and cardiovascular disease.

Limitations of this study because it uses a cross-sectional design. This design cannot explain the causal relationship of a disease.

Our conclusion is the high prevalence of the metabolic syndrome and their correlation with insulin resistance in obese adolescents provides evidence for prevention against the risk morbidity and mortality of degenerative diseases, especially type II diabetes and cardiovascular disease.

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