The Correlation between Apolipoprotein B Levels and Inflammatory Markers in Obese Individuals

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Abstract: Apolipoprotein B (ApoB) levels reflect the total number of potentially atherogenic particles that can predict cardiovascular risk. The purpose of this study was to assess if the ApoB in obese subjects is associated with inflammatory markers. This cross-sectional study was conducted in 80 obese patients at Haji Adam Malik Hospital, Medan, Indonesia. Of the 80 patients studied, the average age was 38.95 ± 8.13 years old. There was a strong positive correlation between ApoB and triglycerides (r=0.44, *P*<0.001), low-density lipoprotein cholesterol (r=0.74, *P*<0.001), and HOMA-IR (r=0.31, *P*=0.005). However, no strong correlation with the inflammatory markers were seen; adiponectin (r=-0.23, *P*=0.41) and Chemerin (r=0.021, *P*=0.851). In obesity, ApoB is significantly associated with lipid and insulin resistance, as a risk factor for cardiovascular disease.

1 INTRODUCTION

Obesity, characterized by the excess amount of abnormal fat, may interfere in an optimal state of health. It may increase the mortality risk through chronic diseases, such as cardiovascular disease, type 2 diabetes, and cancer (Tobias and Hu, 2018). The increment of cardiovascular disease risk is due to inflammation, hyperlipidemia, high blood glucose, elevated insulin levels and high blood pressure (Adams et al., 2006; Klop et al., 2013).

In obese individuals, the risk for atherosclerotic disease is still high even after adjustment for established risk factors. It is thought that there are abnormalities in lipoprotein metabolism that do not cause hyperlipidemia and yet accelerate atherosclerosis (Egusa et al., 1985). Low-density lipoprotein (LDL) are atherogenic; however, when triglyceride concentration is high, LDL values are often not available. Therefore, other markers of lipoprotein-related to cardiovascular disease are needed. The measurement of lipoprotein particle such as apolipoprotein B (ApoB) may enhance the prediction of the risk of cardiovascular disease (Holme et al., 2007; Khadem-Ansari et al., 2009).

As part of metabolic syndrome, chronic inflammation has also been associated with obesity. Larger adipocytes in abdominal obesity alter the ability to suppress lipolysis. Fat tissue releases adipocytokines that may cause insulin resistance and increased risk of cardiovascular disease. There are two types of adipocytokines; classical adipocytokines (adiponectin, resistin, and leptin) and new adipocytokines (chemerin, omentin, and omentin) (Ellulu et al., 2015; Gateva et al., 2018).

Several studies have examined the association between plasma lipid and inflammatory markers. However, the evaluation of ApoB is rarely included. Therefore, we aim to examine the association between ApoB and inflammatory markers such as adiponectin and chemerin in obesity.

2 MATERIALS AND METHODS

This cross-sectional study was conducted in Haji Adam Malik Hospital, Medan, Indonesia. Obese nurses (BMI > 25 kg/m2) aged 30-55 were recruited. Eighty subjects agreed to participate. Informed consent was obtained from each subject, following ethical approval from the Health Research Ethical Committee of Universitas Sumatera Utara, Indonesia. Subjects with a secondary illness such as acute inflammation, anemia, menopause, diabetes, cardiovascular disease, chronic kidney disease, liver

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dysfunction and subjects with secondary obesity such as pregnancy, smoking cessation, patients treated with corticosteroid, estrogen, beta-adrenergic receptor agonists, nitrates, or other vasodilator agents were excluded.

Blood samples were collected from the subjects in the morning after 10-12 hours of fasting combined with ethylenediaminetetraacetate (EDTA) containing heparin, and then centrifuged.

2.1 Biochemical Analysis

Serum HDL cholesterol (HDL-C) and triglycerides (TG) were analyzed by the enzymatic colorimetric method, while Apo-B levels were assessed by the immunoassay method with Hitachi Modular analyzer using the Roche Diagnostic kit. Insulin levels were determined by the chemiluminescence immunoassay method using the DPC Immulite-I analyzer (Diagnostic Products Corp, Los Angeles, CA, USA) kit.

HOMA-IR formula (Matthews et al., 1985) was used to determine the index of insulin resistance using the following formula:

HOMA-IR = [(fasting glucose serum (mmol / l) x fasting insulin (μU / ml) / 22,5]

2.2 Statistical Analysis

Data are presented as mean ± standard deviation. All data were summarized as descriptive statistics. To determine whether a variable was normally distributed, we used the Shapiro-Wilk test. The parametric analysis was performed on variables with normal distribution, whereas the nonparametric test was performed on variables with the abnormal distribution. Furthermore, the Pearson and Spearman test were used to evaluate the correlation between variables according to the variable distribution. A value of $P < 0.05$ was accepted as an indication of statistical significance. SPSS for Windows 22.0 was used for the statistical analysis.

3 RESULTS

This analysis included 80 obese individuals with no previous history of cardiovascular disease. The mean age was 38.95 + 8.13 years. The risk factors for cardiovascular disease and inflammatory markers (adiponectin and chemerin) measured in this study are presented in Table 1.

Pearson correlation of Apo-B with all traditional risk factors is presented in Table 2. In general, apoB correlated positively with LDL-C, TG, HOMA-IR and negatively with HDL-C. Apo-B also has a strong correlation with HOMA-IR. However, there is no correlation between Apo-B and inflammatory markers.

Table 1: Baseline Characteristic of Obese Individuals.

Parameters		Total (mean±SD); *n*=80
Age	(years)	38.95 ± 8.13
Body weight	(Kg)	75.35 ±13.49
WC	(cm)	91.95 ± 9.59
LDL-C	(mg/dL)	138.12 ± 32,40
HDL-C	(mg/dL)	53.72 ± 16.73
TG	(mg/dL)	131.30 ± 75.92
Adiponectin		4.42 ± 2.40
Chemerin	(ng/mL)	408.64 ± 118.41
ApoB	(g/L)	98..43 ± 20.27
HOMA-IR		2.36 ± 3.02

Abbreviations: WC, waist circumference; HOMA-IR: homeostasis model assessment of insulin resistance; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; ApoB: apolipoprotein B.

Table 2: Association between ApoB, Traditional Risk Factors of Cardiovascular Disease and Inflammatory Markers in Obese Individuals.

Parameter		r	*P*
Age	(year)	0.209	0.063
Body weight	(Kg)	0.90	0.420
WC	(cm)	0.173	0.124
LDL-C	(mg/dl)	0.74	0.000**
HDL-C	(mg/dl)	-0.33	0.001**
TG	(mg/dl)	0.44	0.000**
HOMA-IR		0.31	0.005**
Adiponectin		-0.23	0.410
Chemerin	(ng/dl)	0.021	0.851

Abbreviations: BMI, body mass index; WC, waist circumference; HOMA-IR: homeostasis model assessment of insulin resistance; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; ApoB: apolipoprotein B.
*P<0.05, ** P <0.01

4 DISCUSSION

This study demonstrated that in obese individuals, plasma ApoB is positively correlated with several traditional risk factors for cardiovascular disease and type 2 diabetes (insulin resistance, LDL-C, and TG).

ApoB is a better atherogenic parameter compared to the traditional lipid parameters (LDL-C and TG) because ApoB levels indicate the number of atherogenic lipoprotein particles, such as LDL, VLDL, and intermediate-density lipoprotein. One cross-sectional study examined the correlation of ApoB and the risk of coronary heart disease (n=13,523), ApoB was found to be independently related to the risk of CHD using Framingham risk score (FRS) (Ryoo et al., 2011). Moreover, the elevation of ApoB levels is also found in normolipidemic patients with the early coronary arterial disease even when the total and LDL-C levels are normal (Dati and Tate, 2001).

Insulin resistance, measured with the homeostasis index (HOMA-IR), is correlated with ApoB as shown in this study supports the association of insulin resistance with lipoprotein transport. The results of the present study are in agreement with the previous study on 476 subjects demonstrating that ApoB was correlated with insulin resistance (HOMA-IR) (Wang et al., 2017)

Earlier studies have shown that the increment of plasma ApoB was associated with inflammatory markers (hsTNF-α, IL-6, hsCRP, and orosomucoid) (Faraj et al., 2006). Lipoprotein thought to have triggered inflammation in humans. However, contradicting to our findings, we did not find the correlation between ApoB and inflammatory markers (adiponectin and chemerin). Schlitt et al. also found that there is no correlation between ApoB and C-Reactive Protein (Schlitt et al., 2005).

Our study has some limitations. Since this study used a cross-sectional method, we could not reflect causality. This study also did not exclude patients who used lipid-lowering medication that could affect the results.

5 CONCLUSION

The association between ApoB and increased cardiovascular disease risks were related to lipid, and insulin resistance. Thus, further prospective studies should be used to investigate the causality between ApoB and inflammatory markers.

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