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Correlation between Lipid Accumulation Product with Fasting Blood Glucose and CRP in Obese Females

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ABSTRACT

Obesity is an excessive fat accumulation due to an imbalance between energy intake and consumption. Central obesity, represented by an increase in Waist Circumference (WC) and waist-to-hip ratio, is a predictor for obesity-related metabolic disorders and has replaced BMI to determine the clinical diagnosis of metabolic syndrome. Lipid accumulation product calculated from WC and fasting triglyceride concentration is presumed to be an alternative to measure excessive lipid accumulation and a marker to predict diabetes or cardiovascular risk. Lipid accumulation product is related to cardiovascular disease, diabetes, and metabolic syndrome and is preferable to BMI to identify diseases. It has been established that obesity and increased visceral adipocytes contribute to increased levels of some inflammatory proteins such as CRP. This study aimed to determine the correlation between LAP with FBG and CRP in obese females. This cross-sectional study involved female with obesity aged 35-50 years at Diponegoro National Hospital, Semarang, carried out from February to May 2021. Lipid accumulation product was calculated using LAP=(WC[cm]–58)×(TG[mmol/L]), TG and FBG levels were measured with the colorimetric enzymatic method, and CRP levels were analyzed with an immunoturbidimetric method using the chemical analyzer. The correlation between variables was analyzed using Pearson and Spearman correlation tests ($p < 0.05$). CRP and FBG average levels were 3.546±2.6554 mg/dL and 83.1±11.363 mg/dL, respectively. There was a weak positive correlation between LAP with FBG ($p=0.033$; $r=0.262$) and LAP with CRP ($p=0.04$; $r=0.251$). Therefore, lipid accumulation products might influence FBG and CRP levels in the obese population.

Keywords: LAP, FBG, CRP, obesity

INTRODUCTION

Obesity is the excessive accumulation of fat resulting from an imbalance between energy intake and energy consumption for a long time.[1] Obesity has reached epidemic proportions globally, with more than 1 billion adults classified as overweight. At least 300 million are clinically obese and a significant contributor to the global burden of chronic disease and disability. Obesity is a complex condition with severe social and psychological problems and affects almost all ages and socioeconomic groups.[2]

The definition of obesity, according to the American College of Cardiology/American Heart Association (ACA/AHA), is a state at which a Body Mass Index (BMI) >30 kg/m^2.[3] The Asia Pacific standard for obesity is BMI > 25 kg/m^2.[4] In addition, according to the Riskesdas 2013) a BMI >27 kg/m^2 is categorized as obese.[5] Riskesdas 2013 also found that obesity was higher in females compared to males in all regions. Although BMI is the most common measure of obesity, it is not very specific in its anatomical or physiological implications. The International Diabetes Federation (IDF) recognizes that central obesity, an essential determinant of metabolic syndrome, has a strong relationship with Waist Circumference (WC), cardiovascular disease (CVD), and other components of the metabolic syndrome. Therefore, central obesity is placed in an important position of the new definition and essential elements.[6]

High WC and elevated fasting triglyceride levels indicate the relative inability of the individual to manage and store extra energy in the subcutaneous fat depot. Increased WC with high fasting triglyceride levels are suggested to indicate visceral obesity and are associated with various metabolic disorders.[7]

It is emphasized that the effect of obesity on glucose is not only related to fat content and the distribution of excess adiposity.[8] Management of obesity has been studied extensively in the last decade; obesity is related to appetite management, affecting homeostasis, mainly due to impaired lipid and glucose metabolism balance.[9]

Lipid accumulation product calculated from WC and fasting triglyceride levels has been proposed as an alternative test to measure excessive lipid accumulation and as a better marker to identify diabetes or cardiovascular risk in several studies.[7] Previous studies have shown that Lipid Accumulation Product (LAP) was positively associated with total serum cholesterol, fasting plasma glucose, and insulin levels. In addition, it was also negatively associated with High Density Lipoprotein (HDL).[8]

Impaired glucose tolerance and hyperglycemia can cause functional changes in various target tissues. However, without clinical symptoms, they can appear for a long time before diabetes is detected.[10]

Lipid accumulation product is associated with abnormal glucose homeostasis, Insulin Resistance (IR), and increased alanine aminotransferase in healthy individuals.[11]

Obesity and increased visceral adipocytes contribute to increased levels of several inflammatory proteins such as C-Reactive Protein (CRP), Interleukin 6 (IL-6), and Plasminogen Activator Inhibitor (PAI). [10,12] Low-grade inflammation causing increased production of inflammatory proteins will eventually lead to type 2 diabetes mellitus. C-reactive protein levels are regulated by IL-6 and TNF-, which are produced by adipocytes.[12]

This study analyzed the relationship between lipid accumulation product, fasting blood sugar, and c-reactive protein in obese females using bivariate and multivariate analyses. These parameters are known to play an essential role as inflammatory markers in obese females. However, there has yet to be any previous research that connected both parameters.

METHODS

This study was analytical observational research with a cross-sectional approach conducted at the Diponegoro National Hospital, Semarang, from February to May 2021. The research subjects were females aged 35-50 with obesity in the Faculty of Medicine/Diponegoro National Hospital. Females aged 35-50 years with a BMI of 27 kg/m^2 with average body temperature and who had not reached menopause were included in this study. Pregnant females and those taking hormonal therapy were excluded from this study. Research permission was obtained with ethical approval from the Health Research Ethics Committee of the Diponegoro University Medical School No. 81/EC/KEPK/FK-UNDIP/III/2021.

The data collected in this study were as follows: The LAP value obtained from the calculation of the formula LAP=(WC [cm]–58)×(TG [mmol/L]); Fasting blood sugar levels and; CRP levels. Data were then processed using IBM's SPSS Statistics program version 25. Data normality was analyzed using the Kolmogorov-Smirnov test. The LAP and FBG data were normally distributed, while the CRP data were not normally distributed. Therefore, the correlation between LAP and FBG in obese females was determined using the Pearson test, and the correlation between CRP and LAP was determined using the Spearman Rank test. $p < 0.05$ was significant.

RESULTS AND DISCUSSIONS

A total of 67 females with obesity were involved in this study. The characteristics of subjects in this are presented in Table 1.

Measurement results of LAP, FBG, and CRP levels were then analyzed. There was a weak positive correlation between LAP and FBG levels (p=0.04; and r=0.251). The distribution of LAP data with FBG can be seen in Figure 1. There was a weak positive correlation between LAP and CRP levels (p=0.033; and r=0.262). The distribution of LAP data with CRP can be seen in Figure 2.

Statistical tests results in this study showed that there was a weak positive correlation between LAP, FBG, and CRP levels in the obese female population in Indonesia, following a study by Chawla *et al*., which also found a relationship between LAP and CRP and confirmed the fact that adipocytes produce inflammatory proteins such as CRP, IL-6, P-selectin contributing to the underlying inflammation that might be the cause of insulin resistance.[12] Sun *et al*. also found a relatively stronger correlation of LAP compared to other adiposity parameters with increased measures of insulin resistance and diabetes mellitus.[12] The weak positive correlation in this study was probably because the study's average blood glucose and triglyceride levels were 83 mg/dL and 106 mg/dL, respectively, indicating that these levels were still within normal limits.

Mahwati *et al*. found that all indicators of obesity were associated with hs-CRP levels. Expansion of adipose tissue causes changes in the production of proinflammatory molecules and results in low-grade inflammation. An increase in hs-CRP levels indicates a low-grade inflammatory state in the obese group.[13] The mean hs-CRP levels in this study were 3 mg/L, indicating moderate inflammation. According to a

Table 1. Characteristics of research subjects

Variable (n=67)	Mean±SD	Median (min-max)
Age (years)*		33 (26–48)
Systolic blood pressure (mmHg)*		110 (90–170)
Diastolic blood pressure (mmHg)*		70 (60–100)
Body weight (Kg)*		72.3 (58–108)
Body height (cm)	155.87±5.285	
BMI (Kg/m^2)	30.6910±3.71029	
WC (cm)*		89 (80–109)
Hip circumference (cm)*		109 (91–133)
SGOT (U/L)*		21 (15–75)
SGPT (U/L)*		19 (6–57)
Ureum (mg/dL)*		21 (8–53)
Creatinine (mg/dL)*		0.8 (0.6–1.3)
Total cholesterol (mg/dL)	186.55±33.327	
HDL-C (mg/dL)	112.78±30.822	
LDL-C (mg/dL)	52.97±13.067	
Triglyceride (mg/dL)	111,24±44,432	
Triglyceride (mmol/L)	1,2561±0,50205	
LAP *		36.28 (15.24–96.29)
FBG (mg/dL)	83.1±11.363	
CRP (mg/L)*		3 (0.2–10)

Abbrev: BMI, Body Mass Index; SGOT, Serum Glutamic Oxaloacetic Transaminase; SGPT, Serum Glutamic Pyruvic Transaminase; HDL, High Density Lipoprotein-Cholesterol; LDL, Low Density Lipoprotein-Cholesterol; LAP, Lipid Accumulation Product; FBG, Fasting Blood Glucose; hs-CRP, high-sensitivity C-reactive protein; SD, Standard Deviation; min (minimum); max (maximum); *Abnormal data distribution

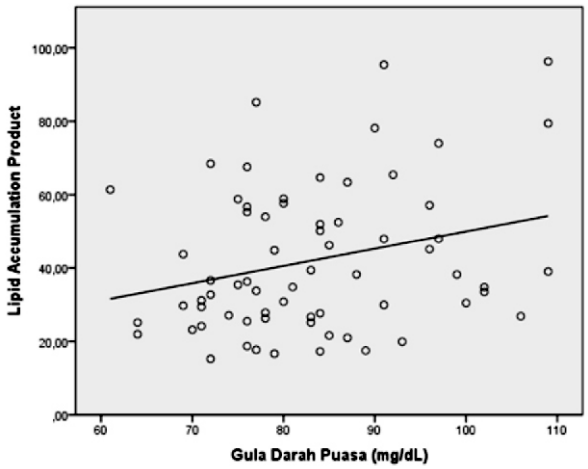

Figure 1. Correlation between LAP and FBG in obese females (p=0.04; and r=0.251)

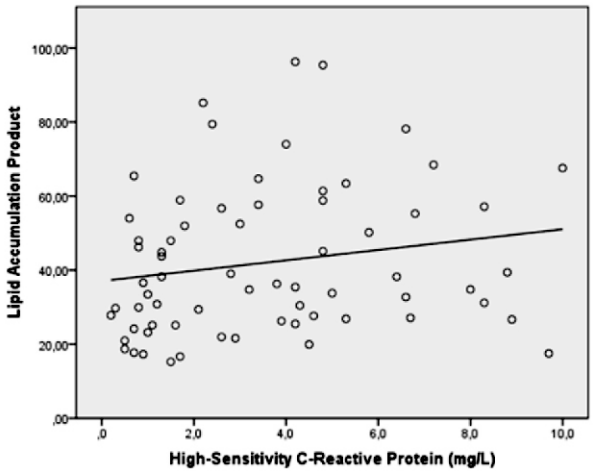

Figure 2. Correlation between LAP and CRP levels in obese females (p=0.033; and r=0.262)

previous survey by Nirmitha *et al.,* 70% of the subjects had hs-CRP levels of 3 mg/L, indicating ongoing inflammation.[13] In general, people whose smoking habits, high blood pressure, overweight state, and those unable to be physically active tend to have high hsCRP levels. Contrastingly, thin and athletic people tend to have low hsCRP levels.[14]

Telles *et al.* found a significant relationship between FBG and WC. Lipid accumulation product is a combination of two measures: WC as a proxy for visceral fat and fasting triglyceride (TG) concentration.[15] The increase in blood triglycerides or hypertriglyceridemia is influenced by genetic factors and food consumption such as carbohydrates, fats, and alcohol.[16] Previous studies have found that fasting serum glucose increased significantly in obese males and females.[17] Boku *et al.* suggested that physical activity was associated with blood sugar levels compared to other variables such as age, gender, and stress levels.[18]

Lipid accumulation product was suggested as a robust marker indicating visceral fat accumulation. A previous study by Song *et al*. aimed to analyze the predictive performance of LAP in identifying impaired FBG in China and explore the potential interaction effect between LAP and other factors on the risk of impaired fasting blood glucose tolerance. Individuals with LAP levels in the fourth quartile had a significantly higher chance of impaired FBG than those in the lowest quartile. In addition, ROC curve analysis showed that LAP had a better performance in differentiating the risk of IFG compared to BMI in males and females. It was found that LAP had higher predictability compared to WC in females only, not males.[8]

This study showed a weak positive correlation between the LAP value and FBG levels with p-value = 0.04; and r=0.251; there was a weak positive correlation between the LAP value and CRP levels with p=0.033; and r=0.262. This finding indicated that increasing LAP values would affect FBG levels and CRP levels in obese females. However, no further analysis of the degree of increase in LAP value remained one of the limitations in this study due to its potential to cause selection bias.

CONCLUSIONS AND SUGGESTIONS

This study found a weak positive correlation between LAP, FBG, and CRP levels in obese females. It was suggested to perform further research to consider other factors that can affect LAP values, FBG levels, and CRP levels. It was expected that the subsequent research could expand the characteristics of the sample, analyze the sample in another character range by comparing obese males and females, narrow the age gap and obtain a more representative sample size.

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