The Correlation Between Cardiometabolic Risks and High-Sensitivity C Reactive Protein (Hs-CRP) Levels in Serum Among Young Adults with Overweight and Obesity

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Abstract. Introduction: The prevalence of overweight and obesity in young adults is increasing worldwide, including in Indonesia. Previous studies have shown that obesity increases inflammatory factors and is closely related to the incidence of metabolic and cardiovascular diseases. Cardiometabolic risk factors such as body mass index, waist circumference, dyslipidemia, fasting blood glucose levels, and blood pressure in young adults are thought to be associated with elevated serum Hs-CRP. Objective: This study aims to determine the correlation between cardiometabolic risks and serum High-Sensitivity C Reactive Protein (Hs-CRP) levels in young adults with overweight and obesity. Methods: This research was an analytical observational study with a cross-sectional design. The research subjects were young adults (20–40 years old) with overweight and obesity in Yogyakarta who met the inclusion and exclusion criteria. Cardiometabolic risks such as blood pressure, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, blood sugar, and serum levels of Hs-CRP were examined. The correlation between cardiometabolic risks and Hs-CRP levels was analyzed through the Pearson correlation test and declared significant if $p < 0.05$. Results: There was a significant positive correlation between the cardiometabolic risks of body mass index ($p = 0.001$; $r = 0.526$), fasting blood glucose levels ($p = 0.013$; $r = 0.414$), waist circumference ($p = 0.00$; $r = 0.816$), total cholesterol ($p = 0.10$; $r = 0.428$), LDL cholesterol ($p = 0.01$; $r = 0.521$), as well as HDL cholesterol ($p = 0.00$; $r = -0.747$) and serum Hs-CRP levels. No significant correlation was found between age, triglyceride levels, as well as blood pressure and serum Hs-CRP levels ($p > 0.05$). Conclusion: There is a significant positive correlation between the cardiometabolic risks of waist circumference, body mass index, total cholesterol, HDL cholesterols, LDL cholesterols, as well as fasting blood glucose levels and serum Hs-CRP levels.

Keywords: Cardiometabolic risk · Overweight · Obesity · Hs-CRP levels · Young adults

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1 Introduction

The incidence of obesity in young adults is increasing worldwide, including in Indonesia. Based on data from the World Health Organization (WHO), global obesity has grown quite rapidly to more than double since 1980. In 2016, more than 1.9 billion adults aged 18 years were overweight, and more than 600 million people in the world were obese [1]. Mortality among obese individuals is also high. This obesity condition increases inflammatory factors. Previous studies have also shown that obesity is closely related to type-2 diabetes and the incidence of cardiovascular diseases [1][2].

A number of studies have shown that obesity occurs in adipose hypertrophy. Excess adipocytes are associated with greater systemic inflammation. The relationship between subcutaneous adipose tissue and visceral adipose tissue with markers of inflammation and circulating oxidative stress is positive and associated with C-reactive protein [3][4]. Adipose tissue regulates molecular and cellular changes that impact systemic metabolism. Accumulation of macrophages in adipose tissue will trigger inflammation, while several proinflammatory factors (such as TNF- and IL-6) are produced by adipose tissue. Local inflammation and accumulation of macrophages result in various metabolic dysfunctions, including systemic inflammation and atherosclerosis. Proinflammatory and pro-thrombotic states contribute to endothelial dysfunction and are common in obese individuals. In addition, inflammation has a key role in the pathophysiology of atherosclerosis and cardiovascular diseases [2][5][6].

One of the biomarkers of endothelial dysfunction and inflammation is C-reactive protein (CRP). However, CRP examination using conventional methods is inadequately sensitive to detect cardiovascular risks, leading to the use of high-sensitivity C-Reactive Protein (Hs-CRP) instead. High-sensitivity C-Reactive Protein (Hs-CRP) is the main acute phase protein in humans which acts as a sensitive marker of systemic inflammation. Hs-CRP is also one of the important inflammatory markers in cardiovascular diseases [4][7]. It is an inflammatory marker closely associated with central obesity, metabolic syndrome, and cardiovascular diseases [2].

Examination of high-sensitivity c-reactive protein (Hs-CRP) in serum can measure the CRP of individuals who physically look healthy. In addition to Hs-CRP, another marker that is also closely related to the risk of cardiovascular disease is interleukin-6 (IL-6). However, clinical measurement of IL-6 is more difficult than Hs-CRP due to various factors such as circadian variation, short half-life, post-prandial effects, and assay stability as well as unstandardized methods and references for IL6 measurement. Meanwhile, Hs-CRP has a longer half-life than that of IL6 which is only 19 h [8][9].

Cardiometabolic risk is a condition which leads to an increase in the incidence of cardiovascular or metabolic diseases such as coronary heart disease and diabetes mellitus. Previous research suggested that some factors significantly related to the risk of cardiometabolic diseases include age, gender, body mass index, waist circumference, total cholesterol levels, LDL cholesterol levels, HDL cholesterol levels, triglyceride levels, blood pressure, and fasting blood glucose levels [2][10][11][12]. The increased prevalence of cardiometabolic risk factors in individuals with elevated central adipocytes can result from the inflammatory process of adiposopathy by producing inflammatory cytokines. Adiposopathy is a pathological, anatomical, and functional disorder of adipose tissue triggered by a positive caloric balance, resulting in impaired endocrine and immune

responses as well as triggering cardiovascular diseases. It is more likely to occur in conditions of excessive central or visceral adiposity [5][13][14].

Research by Gelaye B et al. (2010) found that an increase in hs-CRP levels is significantly associated with an increase in fasting blood glucose levels and HOMA-IR concentrations in adults in Peru. The study concluded that chronic systemic inflammation characterized by elevated levels of hs-CRP may become the main cause of insulin resistance in type-2 DM [15][16]. Based on the aforementioned background, this study aims to determine the correlation between cardiometabolic risks (body mass index, waist circumference, total cholesterol levels, LDL cholesterol levels, HDL cholesterol levels, triglyceride levels, blood pressure, and fasting blood glucose levels) and Hs-CRP levels in young adults with overweight and obesity.

2 Method

2.1 Study Design

This research was conducted with a descriptive-analytical approach and a cross-sectional research design. The study was conducted in Yogyakarta through screening in the community. The research target population was young adults with overweight and obesity. The population covered by the study was the young adults with overweight and obesity obtained from the community data in Posbindu of Kotagede sub-district and Turi sub-district. The inclusion criteria were those aged 18–40 years old, overweight and obese with BMI > 23, and having agreed and signed the informed consent. The exclusion criteria were individuals suffering from acute infectious diseases, trauma, radiotherapy, and acute complications of diabetes mellitus as well as malignancy.

2.2 Sample

The calculation of the research sample size employed the correlative formula.

$$N = \frac{(Z\alpha + Z\beta)^2}{0.5\, In\, (1+r)/(1-r)} + 3$$

with type 1 error = 5%, one-way hypothesis, Zα (alpha standard deviation) = 1.64, and type 2 error = 10%, Zβ (beta standard deviation) = 1.28, and r from previous research = 0.370 [17], thereby yielding N = 15.99 people. In this study, 35 people were involved.

2.3 Variable

The independent variable was the cardiometabolic risks (body mass index, waist circumference, blood pressure, total cholesterol, HDL cholesterol, LDL cholesterol, triglyceride levels, and fasting blood glucose levels). The dependent variable was the serum Hs-CRP level/concentration.

Measurement of Hs-CRP was carried out in a lean laboratory in Yogyakarta. Fasting blood glucose levels were measured through the enzymatic colorimetric method with mg/dl unit. Examination of the fasting blood glucose levels was carried out in Prodia Laboratory, Yogyakarta. On the pre-determined day, the patients who have signed the informed consent came in a state of fasting for 10 h for the examination of height, weight, waist circumference, and blood to obtain the fasting blood glucose levels, cholesterol levels (total, LDL, HDL), triglyceride levels, and Hs-CRP levels.

2.4 Analysis

All of the examination results were recorded and further analyzed. Analysis of the correlation between cardiometabolic risks and Hs-CRP levels was performed using the Pearson correlation test with $p < 0.05$ being considered significant. All of the statistical analyses were carried out on computer programs.

2.5 Ethics

This study was approved by the ethics committee for biomedical research in humans and through patients' consent. The subjects were asked to fill out and sign an informed consent to agree to participate in the study. The approval from the Ethics Committee of the Faculty of Medicine UII was obtained with the number 16/Ka.Kom.Et/70/KE/VI/2020.

3 Result and Discussion

This study was conducted on 35 research subjects, consisting of 24 women and 11 men. The age range of the research subjects was from 21 years to 49 years. The body mass index consisting of overweight and obesity criteria recorded the lowest body mass index of 23.03 kg/m2 and the highest of 30.8 kg/m2. The basic characteristics of the research subjects can be seen in Table 1.

To determine the correlation between cardiometabolic risks (body mass index, waist circumference, blood pressure, total cholesterol levels, LDL cholesterol, and HDL cholesterol, fasting blood glucose levels, triglyceride levels) and serum Hs-CRP levels, a statistical analysis was performed using the Pearson correlation test. The results of each cardiometabolic risk correlation test with Hs-CRP levels can be seen in Table 2.

Based on the correlation analysis using the Pearson correlation test between cardiometabolic risks (body mass index, waist circumference, blood pressure, total cholesterol levels, LDL cholesterol and HDL cholesterol, fasting blood glucose levels, triglyceride levels) and serum Hs-CRP levels, a significant correlation was found in the body mass index ($p = 0.001$; $r = 0.526$), fasting blood glucose levels ($p = 0.013$; $r = 0.414$), waist circumference ($p = 0.00$; $r = 0.816$), total cholesterol level ($p = 0.10$; $r = 0.428$), LDL cholesterol levels ($p = 0.01$; $r = 0.521$), HDL cholesterol levels ($p = 0.00$; $r = -0.747$). There was no significant correlation between triglyceride levels ($p = 0.752$; $r = 0.050$), systolic blood pressure ($p = 0.306$; $r = -1.780$), as well as diastolic blood pressure ($p = 0.0471$; $r = 1,260$) and serum Hs-CRP levels.

Table 1. Characteristics of Research Population

Research variable	mean + SD
Gender n (%)	
Male	11 (31.4%)
Female	24 (68.6%)
Age (years)	29,43 ± 6.54
Body Mass Index (BMI) (kg/m^2)	24.22 ± 1.65
Waist Circumference (cm)	81.04 ± 8.56
Systolic blood pressure (mmHg)	126.57 ± 13.27
Diastolic blood pressure (mmHg)	80.57 ± 9.68
Total Cholesterol	205.57 ± 35.67
LDL Cholesterol	135.34 ± 29.23
HDL Cholesterol	61.77 ± 19.48
fasting blood glucose levels	132.0 ± 64.84
Triglycerides	135.77 ± 35.32
Hs-CRP levels	5.16 ± 4.01

Table 2. Cardiometabolic risk with Hs-CRP levels

Variable	Hs-CRP	
	P	r
Body Mass Index (BMI)	p = 0.001	r = 0.526
Waist Circumference	p = 0.000	r = 0.816
Systolic blood pressure	p = 0.306	r = - 1.780
Diastolic blood pressure	p = 0.471	r = 1.260
Total Cholesterol	p = 0.010	r = 0.428
LDL Cholesterol	p = 0.010	r = 0.521
HDL Cholesterol	p = 0.000	r = -0.747
fasting blood glucose levels	p = 0.013	r = 0.414
Triglycerides	p = 0.752	r = 0.05

4 Discussion

Obesity is a chronic inflammatory process characterized by increased concentrations of C-reactive protein, Interleukin-6 (IL-6), and Plasminogen activator inhibitor-1 (PAI-1). Overweight is a state before obesity, where there is also an excess of adiposity cells and metabolic deterioration while inflammatory processes begin to take place.

In overweight and obese conditions, other cardiometabolic risks (body mass index, waist circumference, blood pressure, total cholesterol levels, LDL cholesterol, and HDL cholesterol, fasting blood glucose levels, and triglyceride levels) can further increase the levels of High-Sensitivity C-reactive protein (Hs-CRP) in serum [7][18][19].

In our study, there was a significant correlation between body mass index ($p = 0.001$; $r = 0.526$) and serum Hs-CRP levels in overweight and obese individuals. This is in line with the research by Mulyamin et al. (2021) which stated that body mass index is a factor that affects serum Hs-CRP levels in overweight and obese individuals and in non-diabetic adults [2][11][20]. Research by Rattu et al. [21] in Manado also found a significant positive relationship between body mass index and serum Hs-CRP levels in obese students and no significant relationship between BMI and Hs-CRP levels in non-obese students [21][22]. This increase in body mass index and Hs-CRP can become a risk factor for atherosclerosis to develop into a heart disease [8].

The results of this study indicated that fasting blood glucose levels had a significant correlation with serum Hs-CRP levels with $p = 0.013$; $r = 0.414$. This is in line with the research which found a positive and significant correlation between Hs-CRP and HOMA-IR ($r = 0.380$, $p < 0.023$), where a high HOMA IR indicates a condition of insulin resistance, thus meaning that there is a high blood glucose level. Increased Hs-CRP in a condition of high fasting blood glucose levels (hyperglycemia) occurs in patients with acute myocardial infarction [23][24].

The correlation between waist circumference and Hs-CRP levels in overweight and obese individuals in Yogyakarta was also found to be positive ($p = 0.00$; $r = 0.816$). This result is consistent with a previous study which found that waist circumference is significantly related to the increase in serum Hs-CRP levels in overweight and obese patients [11]. The anthropometric parameters significantly associated with Hs-CRP are the body mass index and waist circumference [20]. Waist circumference is a parameter of abdominal obesity with a waist circumference > 80 cm for women and > 90 cm for men indicating abdominal obesity or central obesity. The risk of cardiometabolic diseases due to abdominal obesity is associated with an increase in visceral adipocyte tissue (VAT). Obesity is characterized by adipose tissue hyperplasia and adipocyte hypertrophy. Adipose tissue is an endocrine organ that produces adipokines and inflammatory cytokines. Compared to subcutaneous fat, visceral fat is more sensitive to lipolysis and secretes more inflammatory cytokines. Thus, there is an increase in the production of the proinflammatory cytokine IL-6, producing Hs-CRP, which is a sensitive marker of systemic inflammation [17].

Dyslipidemia is a risk factor for cardiometabolic diseases. Arellano et al. (2020) stated that there is a strong relationship between hypercholesterolemia and hypertriglyceridemia and elevated Hs-CRP levels in young adult subjects [2]. The results of our study showed that there was a positive correlation between serum Hs-CRP levels and total cholesterol levels ($p = 0.10$; $r = 0.428$), a positive correlation with LDL cholesterol levels ($p = 0.01$; $r = 0.521$), and a negative correlation with HDL cholesterol levels ($p = 0.00$; $r = -0.747$). Meanwhile, there was no significant correlation between triglyceride levels and Hs-CRP levels. This result is similar to that of Pratinidhi's study (2019), which stated that there is a significant correlation between lipid profile and Hs-CRP levels [25]. Total cholesterol, LDL cholesterol, HDL cholesterol, and triglyceride levels

are strongly associated with an increase in serum Hs-CRP levels. However, in this study, there was no significant correlation between HDL cholesterol and Hs-CRP levels [11]. Research in Medan by Pasaribu gave the results of the Pearson correlation test showing a significant relationship between Hs-CRP and total cholesterol ($r = 0.326$; $p = 0.02$), Hs-CRP and LDL ($r = 0.327$; $p = 0.02$), as well as triglycerides and Hs-CRP ($r = 0.468$; $p = 0.01$). However, in contrast to our results in this study, no significant correlation between Hs-CRP and HDL ($r = -0.093$; $p = 0.58$) was found [25][26].

Increased blood pressure or hypertension in patients with such disease is one of the factors that can cause a systemic inflammatory process, which starts in the blood vessels. Hypertension can become a risk factor for atherosclerosis and the development of cardiometabolic diseases. This is supported by several studies which found a strong, significant relationship between increased blood pressure, especially hypertension, and an increase in Hs-CRP as an inflammatory mediator [11][26]. In our study, no correlation was found between either systolic blood pressure or diastolic blood pressure and increased Hs CRP levels in overweight and obese young adults. These results are in line with Lee's study in Korea which stated that there is no significant relationship between hypertension and Hs-CRP levels [27]. In addition, it can be influenced by other cardiometabolic risk factors. Hs-CRP levels as an inflammatory cytokine are also influenced by conditions that can create systemic inflammation in the body, such as diabetes mellitus and dyslipidemia.

Elevated CRP levels can trigger atherosclerosis, which is a pathological process and is responsible for coronary heart disease. The role of CRP in the process of atherosclerosis appears through several mechanisms, including when CRP is able to increase the uptake of LDL into macrophages and trigger the formation of foam cells. In addition, CRP also inhibits the expression of endothelial NO synthase in endothelial cells. Another study conducted in 2009 on non-obese adults in Italy also showed that abdominal obesity is associated with increased C-reactive Protein (CRP). High-sensitivity C-Reactive Protein (Hs-CRP) significantly increases in people with abdominal obesity compared to people with general obesity alone even though they have the same BMI [28].

Some of the limitations of our study are the number of samples that should be expanded, the research design which can be improved, and the bias factors that can affect the research results.

5 Conclusion

In this study, there was a significant positive correlation between body mass index, waist circumference, total cholesterol levels, LDL cholesterol levels, as well as fasting blood glucose levels and Hs-CRP levels, and there was a significant negative correlation between HDL cholesterol levels and serum Hs-CRP levels in young adults with overweight and obesity. However, there was no correlation between triglyceride levels, systolic blood pressure, as well as diastolic blood pressure and serum Hs-CRP levels.

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Author's Contribution. EM conceived and designed the work, contributed to data acquisition, analyzed, and interpreted the data. EM and EA drafted the manuscript and revised the manuscript critically for important intellectual content.

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