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High waist-to-height ratio worsens inflammatory and adiposity profiles in adult women with abdominal obesity

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ABSTRAK

Latar Belakang: Wanita lebih mudah mengalami kenaikan berat badan karena faktor hormonal. Obesitas abdominal lebih berisiko terkena penyakit metabolik daripada obesitas umum. Peradangan dalam tubuh berkaitan erat dengan obesitas. Adipositokin merupakan leptin dan adiponektin, sedangkan IL-6 adalah sitokin pro-inflamasi. Ketiga biomarker ini sering digunakan untuk menggambarkan individu dengan obesitas abdominal.
Tujuan: Penelitian ini bertujuan untuk menganalisis hubungan antara Waist-to-Height Ratio (WHtR) dengan profil inflamasi dan adipositas pada wanita dewasa dengan obesitas abdominal.
Metode: Penelitian ini merupakan penelitian cross sectional dengan jumlah 88 wanita dewasa dengan obesitas abdominal berusia 25-45 tahun yang bekerja di lingkungan Universitas Diponegoro Semarang. Sampel diambil dengan teknik consecutive sampling. Profil peradangan serum diukur menggunakan metode enzyme-linked immunosorbent assay (ELISA).
Hasil: Rerata lingkar pinggang subjek penelitian adalah 93,82 ± 10,64. Rerata WHtR, adiponektin, leptin dan IL-6 adalah 0,61 ± 0,07; 14,15 ± 9,71; 4,64 ± 0,79; 6,49 ± 3,19. Hasil uji korelasi antara WHtR dengan adiponektin, leptin dan IL-6 adalah (r=-0,279; p=0,005), (r=0,233; p=0,029) dan (r=0,271; p=0,011). Dibandingkan dengan pengukuran antropometri menggunakan BMI, lemak visceral, dan WC, WHtR secara statistik lebih tinggi (p<0,05).
Kesimpulan: WHtR secara signifikan berkorelasi negatif dengan adiponektin dan berkorelasi positif dengan leptin dan IL-6

KATA KUNCI: *Obesitas Abdominal; WHtR; Adiponektin; Leptin; Interleukin 6*

ABSTRACT

Background*: Women gain weight more easily due to hormonal factors. Abdominal obesity is more at risk for metabolic disease than general obesity. Inflammation in the body is intimately linked to obesity. Adipocytokines are leptin and adiponectin, while IL-6 is a pro-inflammatory cytokine. These three biomarkers are frequently used to describe abdominal obesity individuals.*
Objectives*: This study aimed to analyze between Waist-to-Height Ratio (WHtR) with the inflammatory and adiposity profiles in adult women with abdominal obesity.*
Methods*: This study was a cross-sectional research with a total of 88 adult women with abdominal obesity aged 25-45 years who work in the Diponegoro University area of Semarang. Samples were taken by consecutive sampling technique. A serum inflammation profile was measured using the enzyme-linked immunosorbent assay (ELISA) method.*
Results*: The mean waist circumference of the research subjects was 93.82 ± 10.64. The mean WHtR, adiponectin, leptin and IL-6 were 0.61 ± 0.07; 14.15 ± 9.71; 4.64 ± 0.79; 6.49 ± 3.19. The results of the correlation test between WHtR with adiponectin, leptin and IL-6 were (r=-0.279; p=0.005), (r=0.233;*

p=0.029) and (r=0.271; p=0.011). Compared with anthropometric measurements using BMI, visceral fat, and WC, the WHtR was statistically higher (p<0.05).
***Conclusion**: WHtR was significantly negatively correlated with adiponectin and positively correlated with leptin and IL-6*

KEYWORDS: *Abdominal Obesity; WHtR; Adiponectin; Leptin; Interleukin 6*

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INTRODUCTION

The development of obesity is now labeled as "obesity pandemic", because every country is also focusing on the same problem.(1) According to WHO, the prevalence of obesity in women is higher than in men. Adults are expected to endure extreme obesity in the future if the obesity trend continues to rise.(2) Obese adults are at an increased risk of developing various chronic conditions.(3,4) The obesogenic environment includes a variety of highly processed foods with high sugar and fat content and automated technology that decreases or replaces physical activity. Obesity is also linked to a lower quality of life, a shorter lifespan, and higher healthcare costs due to its complex and multifactorial etiology.(1)

Obesity is divided into three groups: abdominal obesity, general obesity and a combination of both. Abdominal obesity is the main focus because it predicts future cardiometabolic events compared to other types.(5) The waist circumference is commonly used to assess abdominal obesity. In most populations, developmental studies show that the waist circumference to height ratio (WC/H) is superior and useful in predicting cardiovascular risk.(6) The distribution of adipose tissue/visceral fat mass can be described by WHtR, notably in persons with the same WC but varied H, who are more at risk for cardiovascular disease events at lower H.(7)

An energy imbalance in the body causes obesity. Metabolic problems, oxidative stress, immunological dysfunction, and low-grade chronic inflammation all occur in obese people.(8) Women are more likely to be overweight in general due to hormonal variables that drive weight growth and increase the incidence of abdominal obesity, which increases body fat tissue. Different adipocytokines are secreted by adipose tissue, and these hormonal alterations play a key role in metabolic diseases.(9) Leptin and adiponectin are adipocytokines, hormones mainly produced by adipose tissue and responsible for regulating lipid metabolism, insulin resistance and inflammation.(10) While interleukin 6 (IL-6) is a pro-inflammatory cytokine and an anti-inflammatory myokine. The accumulation of pro-inflammatory macrophages in adipose tissue becomes one of the hallmarks of obesity and chronic inflammatory disease. Under these conditions, the cytokine interleukin 6 (IL-6) is released which is pleiotropic associated with obesity and is considered a "metabolic hormone" because of its effect on glucose, protein and lipid metabolism.(11)

As a result of observational studies, more research is needed, particularly on the development of inflammation in people with a high adipose tissue density around the belly. Thus, the main point in this research is that high WHtR can worsen the inflammatory profile and adiposity in adult women with abdominal obesity.

MATERIALS AND METHODS

The subjects in this study were adult women aged 25-45 years who work as staff employees at Diponegoro University, Semarang. The researchers used a cross-sectional design with a sequential sampling strategy in their investigation. During the COVID-19 pandemic, the data were collected utilizing the appropriate health methodology. All data were taken at Diponegoro University, Semarang. Therefore, the collection of research subjects

was done by utilizing print media in the form of posters and distributed through social media. Anthropometric measurements were carried out at the Nutrition Building of the Faculty of Medicine, Diponegoro University. Meanwhile, blood samples were taken at the Diponegoro National Hospital Laboratory (RSND).

Subject inclusion criteria were women aged 25-45 years who work in the Diponegoro University area; filled out informed consent; have a BMI >25kg/m2; had a waist circumference >85 cm; wanted to fast 10 hours before blood sampling; not pregnant and breastfeeding; did not take diet drugs or replacement meals; did not take drugs that affect biochemical results; was not treated by a doctor. While the exclusion criteria were the subject resigned and died during the study. The number of subjects in this research was 88 people.

The subject's general features, anthropometric measurements of waist circumference, height, and body composition were determined using a Bio Impedance Analysis (BIA) tool to determine % body fat and visceral fat. Serum Leptin, Adiponectin, and Interleukin 6 were measured in blood samples (IL-6). The waist circumference was divided by the subject's height to get WHtR. The criteria for nutritional status based on Body Mass Index (BMI) use the reference for Indonesians.

The independent variable was WHtR using the limit for Asian people, namely ≥0.50.(12) In the process of taking anthropometric data, the subject used clothes to a minimum so as not to give biased results. The dependent variables were the inflammatory and adiposity profiles, namely the levels of Leptin, Adiponectin, and Interleukin 6 (IL-6) which were measured using the enzyme-linked immunosorbent assay (ELISA) method. This research is in collaboration with the Diponegoro National Hospital Laboratory (RSND) and the Central Laboratory of the Faculty of Medicine (FK) Diponegoro University, Semarang.

Statistical data analysis was done using the IBM SPSS Statistics 25 application. The normality test of the data was done using Kolmogorov-Smirnov because the number of samples was >40 people. Univariate test was also conducted to describe the characteristics of the subject. While the bivariate analysis was done using the Spearman Correlation test because the data were not normally distributed. This research permit was registered with the Health Research Ethics Commission, Faculty of Medicine, Diponegoro University, with Number 154/EC/KEPK/FK-UNDIP/VII/2020.

RESULTS AND DISCUSSIONS

According to the data analysis on 88 obese women aged 25-45 years at Diponegoro University, Semarang, the results are shown in Table 1 and 2. Subject characteristic data includes anthropometric and biochemical data as shown in Table 1. While Table 2 shows the results of the bivariate test between independent and dependent variables.

The body weight mean of the subjects was 76.79 ± 14.77 with a mean BMI of 31.99 ± 5.62. This indicates that the subject is in obesity status. Meanwhile, the visceral fat and waist circumference mean were 9.64 ± 2.74 and 93.82 ± 10.64, respectively. This means that with the presence of abdominal obesity, fat distribution around the

Table 1. Subject Characteristics

Variable	Mean ± SD	Median (min – max)
BB	76.79 ± 14.77	72.95 (60 – 137.6)
BMI	31.99 ± 5.62	30.14 (25.95 – 53.08)
Visceral fat	9.64 ± 2.74	9 (6 – 19)
Waist Circumference	93.82 ± 10.64	89.95 (80.5 – 138)
WHtR	0.61 ± 0.07	0.59 (0.51 – 0.86)
Adiponektin	14.15 ± 9.71	11.78 (2.51 – 71.89)
Leptin	4.64 ± 0.79	4.65 (2.65 – 6.29)
IL-6	6.49 ± 3.19	6.09 (1.66 – 21.07)

Table 2. Results of Anthropometric Correlation Test on Inflammatory Biochemistry

Variable	Adiponectin		Leptin		IL-6	
	p	r	p	r	p	r
BMI	**0.002**[a]	-0.329	0.067[a]	0.196	0.376[a]	0.096
Visceral fat	**0.002**[a]	-0.323	**0.005**[a]	0.296	0.442[a]	0.083
WC	**0.026**[a]	-0.238	**0.037**[a]	0.223	**0.006**[a]	0.292
WHtR	**0.005**[a]	-0.279	**0.029**[a]	0.233	**0.011**[a]	0.271

[a]Spearman Correlation

abdomen shows a borderline. WHtR with a mean of 0.61 ± 0.07 indicates in the category of exceeding the limit. Furthermore, the mean inflammatory profile of leptin, adiponectin and IL-6 was 14.15 ± 9.71; 4.64 ± 0.79 and 6.49 ± 3.19.

Table 2 shows the statistical analysis results to correlate anthropometry with biochemical profiles. The bivariate analysis results using the Spearman correlation test stated that all anthropometric profiles were significantly negatively related to adiponectin levels. While anthropometric profiles of WC, WHtR, and visceral fat were significantly positively related to leptin levels, the BMI profile was borderline with leptin levels (r=0.196; p=0.067). Furthermore, WC and WHtR profiles were significantly positively related to IL-6 levels. A negative relationship means the higher the anthropometric profile, the lower the inflammatory profile. Conversely, if the correlation is positive, the higher the anthropometric profile, the higher the inflammatory profile.

This research aimed to identify and analyze the association of high WHtR with inflammatory and adiposity profiles in adult women with abdominal obesity. Obesity, particularly visceral adiposity, is linked to insulin resistance and dyslipidemia, leading to increased morbidity and mortality.(13) Obesity-related adiposity is linked to an increased risk of total mortality.(14) Obesity lowers the production of preventive factors like adiponectin and raises the risk of total mortality. C-Reactive Protein (CRP), IL-6, TNF-α, and resitin are all pro-inflammatory chemicals. Many anthropometric indices have been used to measure obesity to evaluate the risk of metabolic disease. WHtR is the most effective measurement method for describing obesity conditions since it correlates with the distribution of fat in the abdomen and is designed to quantify the risk between tall and short individuals with the same waist circumference, according to the study's findings.(13) Obesity in the abdomen contributes to pro-inflammatory conditions. In terms of metabolism, because abdominal obesity is an indication of adipose tissue malfunction. (7)

Metabolic problems and low-grade inflammation are caused by abdominal obesity, including adiposity production, monocyte recruitment, inflammatory monocyte differentiation into macrophage phenotype, and pro-inflammatory cytokine release.(13) According to a study conducted on obese female students, WHtR was substantially related to metabolic syndrome.(7) Meanwhile, WHtR was found to be the most powerful assessment method related to the history of hypertension, cardiovascular events, and cerebrovascular events in diabetes mellitus participants in a study conducted in patients at a Shanghai hospital. WHtR, rather than BMI, can be utilized to predict future cardiometabolic multimorbidity.(15)

Obesity is linked to inflammatory symptoms in the body. Although inflammation is a normal aspect of the immune system, obesity is associated with a low-grade chronic inflammatory state in which the immune system responds abnormally.(16) Inflammation is a series of actions that keep tissues and organs in a state of homeostasis. It is critical to release mediators and express receptors at the appropriate times to return the tissue to its former state. Inflammation also eliminates or dilutes the causative agents of tissue damage as a defensive tissue response to injury or tissue damage.(17) Obesity-related chronic inflammation is linked to adipose tissue and the immune system.(16)

The researchers discovered a strong association between the anthropometric profile and

the inflammatory profile based on the results of the correlation analysis in this study. Adiponectin has a negative connection with the anthropometric profile. Adiponectin is an anti-inflammatory protein generated by adipocytes that play a role in atherosclerosis prevention. It enhances adiposity in contrast to other proteins found in adipose tissue. Various animal and human research have shown a strong negative connection between adiponectin and anthropometric profiles. There is a contradiction that an increased adiponectin concentration in elderly subjects is considered to have a high visceral fat accumulation and a low pro-inflammatory state.(18) This is following the findings in this research, when viewed from the mean adiponectin concentration was higher than that of the pro-inflammatory state. Leptin and IL-6 concentrations are shown in Table 1. A study on obese adult female subjects in Korea reported a positive relationship between plasma adiponectin and visceral fat according to age.(18) In contrast to this research, which did not perform age grouping, thus unable to observe the differences between ages.

Adiponectin has anti-atherogenic and anti-inflammatory characteristics, and high levels in the blood are linked to a lower risk of coronary heart disease. On the other hand, low adiponectin levels were linked to high CRP and IL-6 levels.(19) Meanwhile, IL-6 levels were shown to be lower than adiponectin in this investigation. According to other studies, visceral fat has a negative link with adiponectin biomarkers, therefore it will act as a disease preventative.(19,20)

Leptin is also linked to anthropometric profiles like visceral fat, WC, and WHtR, as well as a sliver of BMI. Leptin is an adipose-derived cytokine that is mostly found in fat tissue. Leptin is a hormone that helps regulate hunger and energy expenditure. (21) Leptin is a hormone produced by adipocytes that affects the pathophysiology and physiology of a variety of organs and skeletal muscles. In skeletal muscle, leptin stimulates lipolysis and increases insulin sensitivity. Increased serum leptin will increase fat accumulation. Although leptin maintains its peripheral function, it will further stimulate the sympathetic nervous system and platelet aggregation, so this effect underlies the association of obesity with cardiovascular disease. Leptin receptors are regulated by leptin itself or through insulin resistance. Skeletal muscle is the main site of glucose consumption.(22) Leptin production from inflamed visceral fat through receptor-mediated oxidative stress and hormone activation, significantly worsens pancreatic cell function in obesity.(23)

In this research, IL-6 was associated with anthropometric WC and WHtR profiles. After an acute illness and exercise, IL-6, a cytokine implicated in regulating energy metabolism, will continue to rise in obese people. Increased levels of IL-6 in the blood affect glucose and fat metabolism homeostasis.(24) Obesity can lead to an increase in IL-6, a pro-inflammatory cytokine that causes acute and chronic inflammation. Il-6 receptors are in the prostate and are involved in cell growth regulation. (25) The results of another study suggest that severely obese individuals have much higher plasma concentrations of IL-6 in the portal vein than in the systemic arterial blood. This indicates that visceral fat is an important source of IL-6 production in obese individuals.(19) There is a case-control study using cell culture that compares the distribution of subcutaneous and visceral fat in the normal and obese groups, reporting that subcutaneous fat becomes a locus. Cytokine synthesis was stronger than visceral fat, because IL-6 and IL-15 were found to be significantly higher subcutaneously in both normal and obese groups. However, if viewed from the distribution of visceral fat, it was higher in the obese group than in the normal group. These findings are consistent with observations linking the fact that central adiposity increases inflammation with a higher risk of metabolic complications such as insulin resistance, hyperlipidemia, and hypertension. Another cell culture finding was that adipocytes derived from visceral fat in the obese group released more pro-inflammatory mediators than subcutaneous adipocytes.(26)

CONCLUSIONS AND RECOMMENDATIONS

WHtR was significantly correlated with the inflammatory profile in adult women with abdominal obesity. The WHtR assessment method is a simple

and effective way to describe the risk of basic level inflammation that obese abdominal people face. The higher the WHtR score, the greater the chance of inflammation. As a result, intervention is required for obese people.

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