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ORIGINAL ARTICLE

Correlation of Waist Circumference with *Monocyte Lymphocyte Ratio*, Hemoglobin, and Hba1c in Obesity

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ABSTRACT

Background: Obesity is a condition of excessive BMI, accompanied by accumulation of abnormal fat, especially visceral fat. Visceral fat accumulation can be known by measuring waist circumference. Chronic inflammation in obesity, especially central obesity can cause insulin resistance. Monocyte lymphocyte ratio (MLR) is one of the inflammatory markers that is cheap and easy to examine. Anemia can be caused by chronic inflammatory in obesity and interfere by quality of life, activity, and nutrition. HbA1c as one of the glucose parameters can increase because of insulin resistance.

Method: Cross-sectional study of 46 obese young adults, based on WHO criteria during May-September 2018 was done. MLR was measured by manual calculation of differential counts hematology analyzer. Hemoglobin was measured by hematology analyzer and HbA1c was measured by high performance liquid chromatography (HPLC). Pearson test was performed for analyzing data with p <0.05 was significant.

Results: Waist circumference had significant weak positive correlation with MLR and HbA1c respectively (r = 0.376 p = 0.010 ; r = 0.378 p = 0.010) and waist circumference had significant moderate positive correlation with Hb (r = 0.452, p= 0.002).

Conclusions: There was significant weak positive correlation between waist circumference and MLR, and HbA1c. There was significant moderate positive correlation between waist circumference and Hb in obesity. Future examination of inflammatory parameters and anemia is needed for further study

Keywords: Waist circumference, MLR, Hb, and HbA1c.

INTRODUCTION

The Asian Development Bank in 2013 stated that overweight and obesity crisis was increased to 40.9% in the Asia Pacific region compared to previous finding in 1990 at 34.6%. Two of five adults in the Asian region are overweight or obese and it is a major risk factor for non-communicable disease. Moreover, various obesity complications cause 12% of total health care expenditures or 0.78% of gross domestic product in the Asia Pacific region.[1]

The World Health Organization (WHO) defines obesity as a condition of a person who has more weight than the height, accompanied by accumulation of abnormal fat that may impair health.[2] WHO in 2017 identifies four risk factors of obesity behavior: tobacco use, insufficient physical activity, unhealthy diet, and alcohol use. Overweight and obese parameters can be classified using body mass index (BMI). According to WHO (2016), overweight is a BMI greater than or equal to 25 and obesity is a BMI greater than 30. The disadvantage of BMI interpretation is that it does not describe fat accumulation, but instead it describe a person with excessive weight.[3] The waist circumference (WC), however, is an easy and inexpensive alternative parameter of obesity that can describes the visceral fat amount in a person body, hence, it is often used for central obesity measurement.[4,5] According WHO 2008 criteria, central obesity is defined as waist circumference >90 cm for men and > 80 cm for women.[6]

Obesity, especially central obesity is an inflammatory state. Inflammatory mechanism is started when the immune cell recognize adipocyte as an unknown protein and promote pro-inflammatory mediators e.g. cytokines and chemokines. This eliminate and neutralize foreign proteins by inducing apoptosis and phagocytosis mechanism and finally removed through lymphatic drainage. Disruption in this mechanism could cause long term inflammation state, called chronic inflammation.[7]

The monocyte lymphocytes ratio (MLR) is the distribution ratio between monocytes and lymphocytes count. They are relatively inexpensive, measurable inflammatory parameters that can be easily determined by a routine hematology test. Monocytes are one of the main sources of proinflammatory cytokines which promotes atherogenesis and insulin resistance in obese individuals.[8] Monocytes count and adipocyte accumulation is associated with chronic inflammation. Krinninger, et al (2014) found an increase in the percentage of monocytes as well as higher chemotactic activity in obese subjects.[9,10] Hence, monocyte lymphocytes ratio can be used as a sign of inflammation in obese patients.[8]

Chronic inflammation in obese patient could hamper iron absorption and cause anemia in obesity. Anemia parameter, hemoglobin (Hb), is calculated by measuring hemoglobin concentration in the red blood cells.[11] Fat accumulation in adipocyte tissue can reduce iron absorption and it is influenced by the quality of life, exercise and food nutrition.[7] Moreover obesity conditions with systemic chronic inflammation can be associated with anemia of chronic disease. This condition is due to fat accumulation which will triggers lipid peroxides formation, affects liver metabolic process and causes free radical formation, thus disrupt Hb synthesis and its survival. Red cells survival is also influenced by quality of life, exercise and nutrition [11]

Central obesity can cause insulin resistance due to visceral fat accumulation in abdominal cavity and vital organs such as the liver, intestines and pancreas. Visceral fat also affects hormones and associated with various

health problems risk such as type 2 diabetes mellitus (T2DM).[12] Reduced pancreatic insulin sensitivity might impair pancreas insulin production thus lower insulin level and cause increased blood sugar and HbA1c levels.[13]

Hemoglobin A1c is a form of hemoglobin that is bound to glucose. It is used as one of the parameters for diagnosing and monitoring diabetes mellitus (DM). HbA1c often associated with higher prevalence of dyslipidemia and obesity. Jayesh sheth et al. (2015) found that overweight, obesity, and dyslipidemia had a significant linear correlation with HbA1c on T2DM subject.[14] Based on above description, increase waist circumference will affect MLR levels as one of the inflammation markers, increase HbA1c due to insulin resistance and decreased Hb concentration due to chronic inflammation. It prompted us to find out whether there was a relationship between waist circumference and MLR as well as HbA1c, and Hb levels in obese patient. This study was to prove the relationship of waist circumference with MLR, HbA1c and Hb in obese patient.

MATERIAL AND METHODS

Descriptive analytic with cross sectional study design was carried out on 46 adults with BMI >30 during May-September 2018 at academic community population in the Medical Faculty of Diponegoro University, Semarang.

Samples were taken using consecutive sampling method. Inclusion criteria were 18-45 years old, have a normal vital signs and willing to take part in the study. Exclusion criteria were history of anemia and hematological abnormalities. Ethical clearance was obtained from University Diponegoro Medical School committee on the ethics of human research, number 285/EC/FK-RSDK/V/2018.

Waist circumference measured by a measuring tape at the level of iliac crest at the end of normal expiration. Blood samples were collected using aseptic technique. Three ml of venous blood sample from each subject were collected on EDTA coated plastic tubes that served as an anticoagulant, and runs through hematology analyzer to obtain hemoglobin values and to calculate the monocyte lymphocyte ratio. HbA1c was measured using ion-exchange HPLC *ichroma* method.

The study results were statistically analyzed from 46 samples consisting of 20 men (43.5%) and 26 women (56.5%) with age range from 18-45 years. Data distribution was analyzed using Shapiro-Wilk test because the sample size was less than 50. Study correlation was analyzed using Pearson test, and considered significant if $p < 0.05$.

RESULTS

All study parameter (WC, MLR, Hb, and HbA1c) have normal data distribution. Study results were presented in Table 1.

Increase of waist circumference was found on all subject with average value of 96.23 ± 9.21 cm. Average waist circumference in men is 102.30 ± 6.77 cm and in women is 91.55 ± 8.10 cm (Figure 1).

There was a weak positive correlation between waist circumference and MLR ($r = 0.376$ $p = 0.010$), and HbA1c ($r = 0.378$ $p = 0.010$). There was a moderate positive correlation between waist circumference and Hb ($r = 0.002$, $p = 0.452$) with p value <0.05 (Table 2).

DISCUSSION

Waist circumference is an indicator of the visceral fat tissue content and influenced by several factors, including genetic, age, socioeconomic, and lifestyle.[15] Melanocortin 4 receptor (MC4R) is the main genetic factor that plays important role for increasing waist circumference. Experimental studies by Chambers et al.(2008) showed that MC4R is a key regulator of energy balance, food intake, and energy expenditure through central melanocrine neuronal pathways. Disruption in melanocortin 4 receptor (MC4R) can affect insulin sensitivity and glucose utilization.[16]

Waist circumference has a significant correlation with Hba1c because central obesity measured through waist circumference is correlated with visceral fat amount thus causing insulin resistance. Visceral fat also increased free fatty acids, which potentially harmful due to its effect on hormones and causes insulin resistance. Moreover, high amounts of visceral fat are associated with an increased risk of health problems such as type 2 diabetes mellitus.[12]

Hemoglobin A1c as one of the glucose parameters can increase because of insulin resistance. The increasing insulin is produced by pancreas until it is unable to compensate, and insulin secretion will gradually decrease, resulting in fasting hyperglycemia.[17] Central obesity can decrease pancreatic function by promote pancreatic insensitivity to blood insulin level, causing insulin reduction and increase blood sugar and HbA1c levels. Our results were in accordance with previous finding by Hasanudin et al.(2011) which linked Hba1c with waist circumference of obese adolescent and found higher average Hba1c level in obese compared to non-obese adolescent.[13]

Significant correlation was found between waist circumference and MLR. This result was similar with previous findings by Dalvand et al. (2015) that reported correlation between MLR and diabetic retinopathy diagnosis, hence it could be viewed as diabetic risk factors.[14] Other study by Kullo et al. (2002) shows that increased fat tissue was associated with a higher number of circulated monocytes in middle-aged men and have linear correlation with BMI values.[8]

Fat tissue accumulation in obese patient mediate atherogenic effect, however, its exact mechanism as pro-atherogenic mediator is poorly understood. Adipose tissue has been known as a major source of proinflammatory cytokines. Subcutaneous fat tissue secreted interleukin-6 (IL-6) *in vivo*. Moreover, systemic IL-6 level has a linear association with adipose tissue and up to 30% of circulated IL-6 originates from healthy fat tissue. *In vitro* tumor necrotizing factor (TNF) secretion also observed in healthy fat tissue. These cytokines may have direct or indirect atherogenesis role that triggers inflammation, thrombosis, or fibrinolysis. Monocytes were simple indicators of chronic inflammation associated with increased fat tissue. This because monocytes were source of proinflammatory cytokines and its circulation level has linier association with atherogenesis and insulin resistance in obese patient.[8]

We observe a significant correlation between waist circumference and increased Hb levels. Maria et al. (2017)

reported a significant difference between elevated Hb levels in normal and obese groups based on hip waist circumference ratio, where central obese patients have higher risk of anemia.[19] Gozkaman et al (2015) also found a positive correlation between hemoglobin and body mass index in overweight and obese patients, influenced by quality of life, exercise, and nutrition.[20] However, Bagni et al.(2013) stated that there was no correlation between low hemoglobin levels and obesity in adolescent women. [21]

Low hemoglobin, serum iron, and transferrin levels with high ferritin level due to systemic chronic inflammation in obese patient is associated with anemia of chronic diseases, but it was confounded by patient's quality of life, exercise, nutrition and age. Adolescence and productive age patient have a compensated risk for anemia. Hemoglobin level decrement in obese patient is influenced by the quality of lifestyle, daily activities, and nutrition. Waist circumference is often associated with cardiovascular risk.

Table 1. Characteristic of study subject

Variable	F	%	Mean ± SD	Median (min – max)
Sex				
Male	20	43,5		
Female	26	56,5		
Age (years)			24,00 ± 7,45	20 (18 – 46)
Waist circumference (cm)			96,23 ± 9,21	
HbA1c (%)			5,13 ± 0,40	
Hb (g/dl)			13,89 ± 1,71	
MLR			0,26 ± 0,08	

WC: Waist circumference, MLR: Monocyte Lymphocyte Ratio, Hb: Hemoglobin.

Table 2. Relationship of waist circumference with MLR, Hb, and HbA1c

Parameters	Waist Circumference		Notes
	p	R	
MLR	0,010	0,376	Weak positive correlation
Hb	0,002	0,452	Moderate positive correlation
HbA1c	0,010	0,378	Weak positive correlation

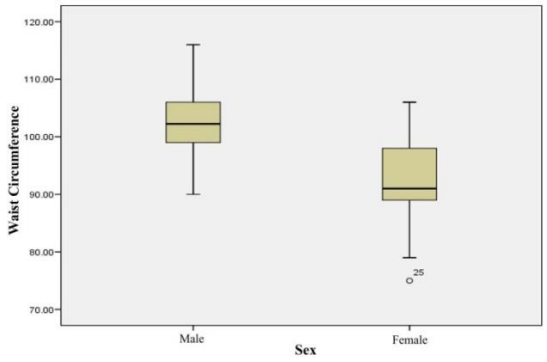

Figure 1. Increased waist circumference based on se

CONCLUSION

There was a weak positive correlation between waist circumference, MLR parameters, and HbA1c, as well as a moderate positive correlation between waist circumference and Hb in obesity. Further studies with additional inflamatory and metabolic characteristic are needed.

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