

Anthropometric Measurements and Inflammatory Marker in Obese Women

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ABSTRACT

Background: Obesity is one of global epidemic health problems and its prevalence is higher among women. Obesity can cause low grade chronic inflammation mechanism in adipose tissue, which is characterized by the increase of proinflammatory cytokines and adipokines. Neutrophil lymphocyte ratio (NLR) is a simple inflammatory marker which can be reliable in evaluating the inflammatory status occurring in obese women. Waist to height ratio (WHtR) and waist to hip ratio (WHR) are anthropometric measurements, have been reported to be associated with obesity and risk of metabolic syndrome.

Objective: This study aimed to determine the correlation of WHtR and WHR with NLR in population of obese women.

Materials and Methods: This was a cross sectional study enrolling 80 obese women with Body mass index (BMI) > 27 aged 30 - 50 years in National Diponegoro Hospital Semarang, Indonesia. WHtR was determined by dividing waist circumference by height and WHR was determined by dividing waist circumference by hip circumference. NLR was examined manually from automatic hematology analyzer by dividing absolute neutrophil count (ANC) and absolute lymphocyte count (ALC). Spearman correlation test was performed, $p < 0.05$ was considered as statistically significant.

Results: There was significant weak positive correlation between WHtR and NLR in obese women ($p = 0,046$; $r = 0,224$). There was no significant correlation between WHR and NLR in obese women ($p = 0,961$; $r = 0,006$).

Conclusion: The present study showed that WHtR is one of better anthropometric measurement because it is associate with NLR as a simple marker of inflammation in obese women.

Keywords: WHtR; WHR; NLR; Obesity

BACKGROUND

Obesity is one of the global health problem whose prevalence continues to increase every year. World Health Organization (WHO) in 2016 stated that 1.9 billion adults with 18 years of age or over are overweight and more than 650 million are obese. Based on WHO, approximately 13 % of world adult population were obese that more cases found in woman (15%) than man (11%)¹. Results of Basic Health Research (Riskesdas) 2007-2018 in Indonesia also shows an increasing trend of obesity, namely 10.5% (2007), 14.8% (2013) and 21.8% (2018)² and in Central Java, Indonesia prevalence obesity cases in woman (27,53 %) are higher than in man (13.09 %)³.

Obesity is defined as s abnormal or excessive fat accumulation that presents a risk to health. Obesity increase the risk of chronic diseases including type 2 diabetes mellitus (Type 2 DM) and cardiovascular disease⁴. There are two types of obesity based on where fat accumulate in body namely android obesity and gynoid obesity. Abdominal, central, or android obesity characterized by fat distributed around the waist or Gynoid obesity that fat accumulate in the lower part of the body⁵. Risk factor of obesity are multifactorial including genetic, lifestyle, and environmental factors⁶. Women are more at risk for obesity than men because they have more sedentary lifestyle like physical inactivity, consumption food that high simple sugar, high calories and fat that are risk factor of obesity⁷. Body Mass Index (BMI) is anthropometric measurements which is more often used as a parameter of obesity. WHO criteria for obesity are if BMI is ≥ 30 kg/m², while this study refers to the classification of obesity for Asia Pacific population which is having BMI ≥ 27 kg/m²⁸. Waist Circumference (WC), Waist to Hip Ratio (WHR), Waist to Height Ratio (WHtR) are another anthropometric measurements that also can be used to predict obesity. Kwang Pil Ko et al stated that WHR is a better method

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of predicting metabolic syndrome in obesity than WC, WHtR, and BMI⁹. A meta-analysis study by Labarrere et al in more than 300,000 multi-ethnic people, shown that measuring obesity with WHtR can better explain its association with cardiometabolic risk from inflammation than using BMI and WC¹⁰.

Obesity has a negative impact on tissues and body systems related to inflammatory mechanisms. Low grade inflammation due to obesity has been demonstrated in several studies using various markers of inflammation. Obesity measured using BMI parameters was shown to be positively associated with increased CRP levels, leukocyte count, IL-6, tumor necrosis factor alpha (TNF- α), and neutrophil lymphocyte ratio (NLR)¹¹. Neutrophil lymphocyte ratio is effective, simple, inexpensive parameter of inflammation and widely examined in various laboratory⁹. During the inflammatory process, neutrophil count can be increased up to five times the normal number, while the lymphocyte count tends to be constant due to continuous recycling by lymphoid tissue, lymph and blood. This difference in the distribution of cells during inflammation is the basis for the use of NLR. Neutrophil lymphocyte ratio is considered more stable as a marker of inflammation than the absolute leukocyte count which can change according to physiological and pathological conditions¹². No further study on the correlation between WHtR and WHR and the NLR value in Indonesian obese women. This encourages researchers to determine the correlation between WHtR and WHR and NLR values in obese women.

MATERIALS AND METHODS

This cross-sectional study was conducted in July - September 2020 at the Diponegoro National Hospital Semarang, Central Java, Indonesia.

Subject of Study

Minimum subject for this study was 46 people that was calculate with formula below:

$$n = \left(\frac{Z_{\alpha} + Z_{\beta}}{0,5 \ln \frac{1+r}{1-r}} \right)^2 + 3$$

Although minimum subject for this study was 46 people, total subject in this study was eighty obese women with criteria aged 30-50 years, body mass index (BMI) ≥ 25 kg/m², healthy and having normal vital sign, and have regular menstrual cycles for 6 months before join the study. Subjects which have history of DM, subjects with cardiovascular disease, hematological abnormality, or pregnant at the time this study was conducted, were excluded from this study. Screening for subject in this study that meeting all criteria using short interview and simple screening form.

a. Antropometric Measurements

1. Body Mass Index (BMI)

Body mass index (BMI) in this study were calculated using weight data that obtained by using a digital scale and height data using microtoa with formula:

$$\text{Body Mass Index : } \frac{\text{Weight (kg)}}{\text{Height (meter)} \times \text{Height (meter)}}$$

2. Waist to Hip Ratio (WHR) and Waist to Height Ratio (WHtR)

Waist circumference was measured with inelastic band at the midpoint between the last rib and the anterior superior iliac crest at the end of respiratory movement of expiration in standing position. Hip circumference was measured over thin clothing at the point of the maximum circumference of the buttocks. Both circumferences were measured to the nearest 0.1 cm.

b. Blood Analysis

Blood was collected by venipuncture and tested using automatic hematology analyzer (Sysmex XN L Series XS 500, Sysmex Asia Pacific Pte Ltd.) for absolute neutrophil count (ANC) and absolute lymphocyte count (ALC). The NLR value was calculated manually from ANC divided by ALC.

Statistical analysis in this study was performed in this study by SPSS 16.0, Correlation Test using Pearson if data from this study normally distributed and Spearman correlation test if data not distributed normally with $p < 0.05$ was considered as statistically significant. This study was obtaining an ethical clearance from the Health Research Ethics Commission of the Faculty of Medicine, Diponegoro University / RSUP Dr. Kariadi Semarang No. 32/EC/KPEK/FK-UNDIP/III/2020. Study subjects were providing written informed

consent.

RESULTS

Subjects Characteristics Data

Total respondent in this study was 81 respondents, only 80 respondents that met the inclusion criteria. The mean age of respondent in this study was 36.61 ± 5.20 years with mean body mass index (BMI) were 31.97 ± 4.49 kg/m² and have regular menstrual cycles. Mean Waist Circumference respondent in this study were 93.86 ± 9.15 cm with WHtR and WHR score were 0.85 ± 0.06 and 0.61 ± 0.06 . Respondent mean leukocytes count, neutrophil, and lymphocyte in this study were 7.08 ± 1.48 (10³/μL), 61.15 ± 5.95 (%), 30.32 ± 5.58 (%). Average Neutrophil Leucocyte Ratio respondent in this study were 2.13 ± 0.63 . The baseline characteristics of the subjects is presented in table 1.

Table 1. Data on the Characteristic of Research Subjects

Parameter	Mean ± SD	Min – Max
Age (years)	36.61	3
Body weight (kg)	76.83 ±	60.4 –
Height (cm)	154.93	145.0 –
BMI (kg/m ²)	31.97	27.00 –
WC (cm)	93.86	80.00 – 1
WHR	0.85	0.71
WHtR	0.61	0.52
Leucocyte (10 ³ /μL)	7.08	4.50 –
Neutrophil (%)	61.15	47.00 –
Lymphocyte (%)	30.32	19.00 –
NLR	2.13	1.04

BMI : Body mass index, WC : Waist circumference, WHR: Waist to hip ratio, WHtR : Waist to height ratio

The Spearman correlation analysis test between WHtR and NLR showed $p = 0.046$; $r = 0.224$, this indicates that there is a significant correlation between WHtR and NLR in obese women. The Spearman correlation analysis test between WHR and NLR showed $p = 0.961$; $r = 0.006$, this indicates that there is no significant correlation between WHR and NLR in obese women. The results of the correlation test are shown in Table 2.

Table 2. Spearman Correlation Test Result of WHtR, WHR, and NLR in Obese Women

Variable	NLR	
	r	p
WHtR	0.224	0.046*
WHR	0.006	0.961

* = p value <0.05 is significant

DISCUSSION

Obesity

In this study we determined several anthropometric measurements include Body Mass Index (BMI), Waist to Hip Ratio (WHR) and Waist to Height Ratio (WHtR). Body mass index (BMI) is common anthropometric measurements as parameter of obesity. People with BMI score ≥ 25 kg/m² categorized as obese people. All respondents in this study have met the criteria of obesity from BMI score. Lowest BMI score in this study was 27 kg/m² and highest BMI score was 52 kg/m². Obesity is characterized by the accumulation of body fat and unfortunately, body mass index (BMI) cannot be used to determine body fat composition. Someone who has ≥ 25 kg/m² not necessarily having high body fat percentage because body weight also consist of muscle mass.

Waist Circumference (WC), Waist to Hip Ratio (WHR) and Waist to Height Ratio (WHtR) can be used as a better indicator to determine obesity. Waist circumference (WC) is better indicator that can predict fat deposit in abdominal area. Lowest waist circumference respondent in this study is 80 cm that has been

categorized as obese for adult Asian people (≥ 80 cm)¹³. The WHtR distribution in this study ranged from 0.52 to 0.77. The criteria for central obesity were enforced if the WHtR was ≥ 0.5 so that all study subjects met the criteria for central obesity¹⁴. The WHR distribution of study subjects ranged from 0.71 to 1.00. The cut off points of WHR according to WHO is ≥ 0.85 in women to categorized people having central obesity¹⁵. There are 42 (52.50%) study subjects who fall into the criteria for central obesity and 38 (47.50%) study subjects who do not meet the criteria for central obesity. According to the previous study by Hastuti et al, 2017 in Indonesia, it is stated that obesity is central if the WHR is ≥ 0.77 in women¹⁶. Based on these criteria, there are 74 (92.50%) research subjects who fall into the criteria for central obesity.

Inflammatory Parameters

This study using Neutrophil Leukocyte Ratio (NLR) to predict inflammatory state in obese respondents. Obese condition can lead to systemic inflammation in body that can increase Neutrophil Lymphocyte Ratio (NLR). An increase in NLR is determined by an increase of neutrophils and or reduction in lymphocytes. An increase in circulating neutrophils is thus suggestive of an acute or chronic inflammatory response. Chronic inflammation stimulating the release of immunoregulatory granulocytic myeloid-derived suppressor cells from the bone marrow, which can increase up to 10% of peripheral leucocyte and suppress lymphocyte counts and function¹⁷. The increase in NLR in the obese female population can be caused by increased neutrophils. An increase in the number of neutrophils in obesity is an acute inflammatory response to a chronic inflammatory state¹⁸. Neutrophils describe a nonspecific immune system condition that initiates the body's response to inflammation¹⁹. High levels of circulating neutrophils are associated with depressed activity of other immune cells such as T-lymphocytes and natural killer cells. Based on the results of several previous studies, obesity causes a chronic inflammatory condition associated with increased secretion of adipokines and cytokines proinflammatory of adipose tissue²⁰.

Currently there is no definite NLR intersection point value. Various studies use NLR intervals (ditile or quartile) or use a receiver operator curve (ROC) to classify NLR values. According to study by Patrice Forget et al., (2017) it was concluded that the threshold value of NLR in a non-geriatric adult population with good health was 0.78 - 3.5²¹. Based on these criteria, there were 4 (5.00%) research subjects who had a value NLR above normal. Possibility factor that cause not all respondents having high NLR value is subjects in this study were not grouped based on their degree of obesity. Dixon et al. revealed that a significant increase in the number of neutrophils occurred in severely obese patients (BMI >40 kg/m²) due to the mechanism of neutrophil activation by leptin through TNF- α ²². Atmaca et al. through his study reported that there was no significant increase in the number of leukocytes in mild obesity (BMI <35 kg/m²), besides that it was proved that inflammation which is characterized by an increase in the number of neutrophils and lymphocytes is parallel with the severity of obesity¹⁸.

Correlations of WHtR and NLR in Obese Women

Increased abdominal adiposity has been reported in previous study as major risk factor of metabolic syndrome. Main pathway to describe the correlation between metabolic syndrome and VAT is insulin resistance (IR). Excessive VAT decreasing insulin sensitivity that lead to systemic inflammation beside inflammation also occur in obesity condition²³. Increased secretion of inflammatory mediators from visceral fat in obese individuals reflects the ongoing chronic inflammation within the adipose tissue of the individual²⁴. NLR is one of the inflammation indicator that simple and easy to do with measuring ratio between neutrophil and leucocyte. Spearman test in this study show that there are no significant correlation between Waist to Hip Ratio (WHR) with NLR in obese woman ($p = 0.961$ and $r = 0.006$) meanwhile, there was a significant weak positive correlation between WHtR and NLR in obese women ($p = 0.046$ and $r = 0.224$). The results of this study are in accordance with several previous studies. Study conducted by Rodriguez et al. in 2020 stated that WHtR had a significant positive correlation with NLR in the abdominal obesity population ($p < 0.001$; $r^2 = 0.011$)²⁵. According to Rodriguez, both obese men and women with chronic inflammatory conditions characterized by increased NLR had higher WHtR values. Serbanescu et al. in 2015 through his study also stated that WHtR had a significant positive correlation with NLR in obesity ($p < 0.001$; $r = 0.203$)²⁶. WHtR is better indicator to identify central obesity that have higher risk to lead systemic inflammation. According to the Bener study in 2013, WC and WHtR are anthropometric parameters that have a better correlation with central obesity than WHR and BMI and can be used as predictors of cardiovascular and metabolic disease²⁷.

Correlations of WHR and NLR in Obese Women

There was no significant correlation between WHR and NLR in obese women ($p = 0.563$ and $r = -0.74$). The results of this study differ from several previous studies. Study conducted by Carranza et al. in 2020 states that there is a significant positive correlation between WHR and NLR in a population of obese women at premenopausal age ($p < 0.05$ and $r = 0.374$)²⁸. Differences in study conducted by Carranza et al. with this study is the subject inclusion criteria. The inclusion criteria in the Carranza study were obese premenopausal women (42 - 55 years) with vasomotor symptoms indicating decreased estrogen. Whereas in this study the subjects were obese women of productive age who still experienced regular menstruation.

The results of this study are consistent with the study of Dev et al. in 2012 which revealed that WHR was not significantly associated with several markers of inflammation, especially CRP in obese non-comorbid female subjects. According to Dev, WHR is not as good as WC in explaining the correlation between increased markers of inflammation²⁹.

No correlation between WHR and NLR can be caused by several factors. One of the factors that influence the results is the varied physical activity of the research subjects. According to study by Rias et al. in 2020 shows that moderate and excessive physical activity significantly reduces NLR in a population of women with type 2 diabetes mellitus with and without obesity³⁰.

Another factor that can cause an insignificant correlation is that the subjects in this study were not grouped based on the degree of obesity. Dixon et al. revealed that a significant increase in the number of neutrophils occurred in severely obese patients ($BMI > 40 \text{ kg/m}^2$) due to the mechanism of neutrophil activation by leptin through $TNF-\alpha$ ²². Atmaca et al. through his study reported that there was no significant increase in the number of leukocytes in mild obesity ($BMI < 35 \text{ kg/m}^2$), besides that it was proved that inflammation which is characterized by an increase in the number of neutrophils and lymphocytes is parallel with the severity of obesity¹⁸.

The age factor also influenced the subject's NLR. According to study by Jian Li et al. in 2015, NLR was positively correlated with age in the healthy adult female population ($p < 0.001$, $r = 0.119$)³¹. Jian Li's study showed that the NLR in the 40-49 years age group was higher than the 30-39 years age group. This is because the number of granulocytes shows an increasing trend with age and the number of lymphocytes shows a decreasing trend with age.

The limitation of this study is that only one type of inflammatory marker was used and the subjects were not classified based on the severity of obesity.

CONCLUSIONS

WHR is one of better anthropometric measurement because it is association with NLR as a simple marker of inflammation.

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