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Fillah Fithra Dieny

Department of Nutrition Science

Faculty of Medicine, Diponegoro University

JI Prof Soedharto SH, Tembalang. Semarang 50275, Central Java, Indonesia.

Phone/Fax (024) 845-37-08/ HP +62856-4020-4747

Website: www.gizi.undip.ac.id

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Corresponding Author	Dieny, F.F.				
(Only one)					
Email address of the	fillahdieny@gmail.com				
Corresponding Author					

SUGGESTED REVIEW	SUGGESTED REVIEWERS			
Name	Dr. Diana Nur Afifah, S.TP., M.Si.			
Salutation	Mrs.			
Area of Expertise	Food and Nutrition Science, Food Biotechnology			
(Please use comma for				
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Email	d.nurafifah.dna@gmail.com			

Name	Nurmasari Widyastuti, S.Gz., M.Si., Med.	
Salutation	Mrs.	
Area of Expertise	Clinical Nutrition	
(Please use comma for		
more than one)		
Email	widyastutianlene@gmail.com	

Name	Dr.Etika Ratna Noer, SGz, MSi
Salutation	Mrs
Area of Expertise	Obesity and syndrome metabolic
(Please use comma for	
more than one)	
Email	etika.ratna.noer@gmail.com

Name	Ahmad Syauqy, S.Gz., M.P.H., Ph.D.
Salutation	Mr
Area of Expertise	syndrome metabolic and dietary patterns
(Please use comma for	
more than one)	
Email	syauqy@fk.undip.ac.id

#### Anthropometric Profile and Its Correlation to Insulin Resistance in Female Students with Obesity

Dieny, F.F.<sup>1,2\*</sup>, Fitranti, D.Y.<sup>1,2</sup>, Jauharany, F.F.<sup>1</sup>, Tsani, A.F.A.<sup>1,2</sup>, Faradila, U.<sup>1</sup>, Rose, S.<sup>1</sup>

<sup>1</sup>Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia <sup>2</sup>CENURE (Center of Nutrition Research), Universitas Diponegoro, Semarang, Indonesia

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\*Corresponding author: fillahdieny@gmail.com

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- 9 Author No.1: 0000-0001-6071-8901
- 10 Author No. 2: 0000-0002-1656-9563
- 11 Author No. 3: 0000-0001-9471-9419
- 12 Author No. 4: 0000-0002-3407-5188
- 13 Author No. 5: 0000-0002-1244-6187
- 14 Author No. 6: 0000-0002-1898-1842

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#### Abstract

The prevalence of obesity in adolescent girls is increasing each year. Several anthropometric measurements can be used to detect the incidence of insulin resistance. This study aims to observe the correlation of anthropometric profiles with insulin resistance in adolescent girls with obesity. This was an observational study with a total of 120 female students of Universitas Diponegoro (Undip), aged between 18 and 21 years old, who have waist circumference >80 cm. They were chosen by simple random sampling technique. Anthropometric profile data taken was consisted of waist circumference, hip circumference, waist-hip circumference ratio (WHR), waist-to-height ratio (WHtR), neck circumference, wrist circumference, thigh circumference, and 2D:4D digit ratio. Insulin resistance data was determined using the Homeostasis Model Assessment-Insulin Resistance (HOMA-IR.). Bivariate analysis was completed with the Spearman Rank test. There was 83.3% of subjects experienced insulin resistance. High WHtR was found in 98.3% of total subjects as many as 90.8% of subjects were at risk based on WHR values. Based on 2D:4D ratio digits, neck circumference, wrist circumference <50% of subjects were found as at risk. There was no correlation between waist circumference, WHR, wrist circumference, 2D:4D digit ratio with HOMA-IR (p>0.05). However, there was a positive correlation between WHtR, neck circumference, and thigh circumference with HOMA-IR (p<0.05) Anthropometric profiles such as WHtR, neck circumference, and thigh circumference were correlation of insulin resistance in female adolescent with obesity.

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Keywords: Adolescent; Anthropometric Indicator; Insulin Resistance; Obesity.

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#### 1. Introduction

Nutritional status in adolescents is very important since adolescence is a transition period from children to adulthood. This transition causes biological, psychological and cognitive changes that influence their nutritional status (J. E. Brown et al., 2011). However, nutritional status problems in adolescents are still fairly high, including obesity. Prevalence of central obesity 15 years adolescents and older has increased from 26.6% in 2013 to 31% in 2018 (Badan Penelitian dan Pengembangan Kesehatan, 2018). Obesity incidence will later be associated with degenerative diseases. Women is at higher risk of suffering from degenerative disease, while Indonesian Basic Health Research 2018 results reports the prevalence of stroke, diabetes mellitus, heart disease, and hypertension is found higher in women than men (Badan Penelitian dan Pengembangan Kesehatan, 2018). Indonesian Basic Health Research 2018 results also states that women and people live in urban areas of all ages have high prevalence of diabetes mellitus (Badan Penelitian dan Pengembangan Kesehatan, 2018).

Type 2 diabetes mellitus is caused by insulin resistance, a condition in which patient's body is unable to absorb glucose (Srikanthan et al., 2016). Study in Semarang City showed that 96.1% of adolescents experienced insulin resistance which was measured by Homeostasis Insulin Resistance Assessment Model (HOMA-IR) (Nuraini et al., 2017). HOMA-IR is a formula for calculating insulin resistance based on fasting blood sugar and insulin levels. Its measurement is simple, inexpensive, often used and has been validated by the clamp method (Sumarni, 2017).

One factor causing insulin resistance is central or abdominal obesity as abdominal fat is more actively undergoing lipolysis (Sumarni, 2017). Recently, several measurements of the body's anthropometric profile that can describe the incidence of central obesity are reported, where the measurements are done easily. Central obesity in adolescents can be described generally using measurements of waist circumference and hip waist circumference ratio (WHR). Some studies also mention that waist circumference and WHR have a significant correlation with insulin resistance (Sumarni, 2017).

In addition to waist circumference and WHR, other anthropometric profile measurements are also progressively more used, namely Waist-to-Height Ratio (WHtR). WHtR describes central obesity in adolescents with more accurate results than Body Mass Index (BMI) (Ashwell & Gibson, 2016; Saraswati & Sulchan, 2016; Yang et al., 2017). Study in Mexico demonstrates WHtR as a better tool in identifying cardiometabolic obesity in adolescents used to predict hypertension and insulin resistance (Rodea-Montero et al., 2014). Other studies conducted in Semarang also showed correlation between WHtR and increasing insulin resistance (Asnelviana et al., 2017).

Wrist circumference can also be utilized as indicator. Studies conducted in late adolescents in Indonesia, show wrist circumference as one of the anthropometric measurements that can predict obesity and insulin resistance in late adolescents. Wrist circumference reflects bone in the wrist area as well as peripheral fat distribution and metabolism thus it can measure one's body frame and bone size easily (Fitriyanti, Tjahjono, et al., 2019).

Another measurement of anthropometric profiles that can be used to predict metabolic syndrome in adolescents is the measurement of neck circumference. Some study show correlation between neck circumference with insulin resistance (Liang et al., 2014; Saneei et al., 2019). Neck

circumference can represent upper-body subcutaneous adipose tissue that plays a role in predicting insulin resistance and type 2 diabetes (Saneei et al., 2019).

In addition, measurement of thigh circumference can also predict metabolic syndrome in adolescents since it reflects central adiposity (Bando et al., 2017). Results of a study conducted in Korea show that thigh circumference is positively related to insulin resistance (Park et al., 2012). Several studies also explain that thigh circumference is a good indicator in determining type 2 diabetes mellitus 2 (Jung et al., 2013; Ting et al., 2018).

Recently, it has been reported that there are other anthropometric measurements as indicators in predicting metabolic syndrome disease, namely The Ratio of Second to Fourth Digit Length (2D:4D) (Endang Purwaningsih, 2016). Ratio of the length of the index finger and ring finger (2D:4D) can describe the exposure to the hormone estrogen and prenatal testosterone. A study has shown that low digit ratio is associated with high testosterone levels in men, while high digit ratio is associated with low testosterone levels in women (Kumar et al., 2016). The size of digit ratio occurs since the end of the first trimester of fetal development (Oyeyemi et al., 2014). Inappropriate exposure of androgen hormone can cause Polycystic Ovary Syndrome (PCOS), causing infertility in premenopausal women. Women who experience PCOS often have metabolic diseases such as hypertension and insulin resistance (White et al., 2017). Study states that digit ratio is correlated with obesity, which is a risk factor for metabolic disease (Gölge et al., 2016). There aren't many studies showing the relationship between digit ratio with insulin resistance.

In this study, we want to find out the portrayal and correlation of anthropometric profiles (waist circumference, WHR, WHtR, wrist circumference, neck circumference, thigh circumference, and second to fourth digit ratio) and insulin resistance in female adolescents with obesity.

#### 2. Materials and methods

#### 2.1 Design, location, and time

This is an observational study and included within the scope of community nutrition science. This research conducted in Universitas Diponegoro Semarang, Indonesia at 10 Faculties in June until August 2019. There were 1,260 female students who participated in screening program. The entire study was approved by the Health Study Ethics Committee (KEPK) Faculty of Medicine, Universitas Diponegoro/Central General Hospital dr. Kariadi No. 373/EC/KEPK/FK UNDIP/VIII/2019.

#### 2.2 Samplings

Subjects of this study were 120 students from Universitas Diponegoro who were selected through simple random sampling, according to the following inclusion criteria: aged 18-21 years old, had 80 cm or more waist circumference, had intact fingers on both hands, were not currently consuming drugs that could affect the blood glucose and insulin levels, were willing to do fasting for at least 8 hours, did not smoke and/or consume alcohol, were not sick or in the care of a doctor, did not do heavy physical activity or exercise, were not pregnant and breastfeeding, were willing to be the subject of study by filling out informed consent. The exclusion criteria in this study were subject's withdrawal from the study, subject moved to another university, and subject passed away within study period.

#### 2.3 Data collected

Independent variables in this study were the anthropometric profile consisted of waist circumference, waist-hip circumference ratio (WHR), Waist-Height Ratio (WHtR), neck circumference, wrist circumference, thigh circumference, and ratio of index finger length and ring finger (2D:4D). The dependent variable in this study was insulin resistance.

Waist circumference data was obtained from waist circumference measurements measured at the midpoint between the iliac crest and costal margins (lower ribs) using a medical measuring tape with 0.1 cm precision/ Subjects used minimal clothing (Yang et al., 2017). Subjects were considered at risk when waist circumference was 80 cm or more (Saklayen, 2018).

WHR data was obtained from the waist circumference to hip circumference ratio. Measurement of pelvic circumference was done by medical measuring tape with 0.1 cm precision. Pelvic circumference is measured by determining the widest points on the buttock (Fitriyanti, Tjahjono, et al., 2019). Subjects are categorized as risky when WHR was more than 0.85 (Saklayen, 2018).

Data on the ratio of waist circumference and height (WHtR) was obtained from measurements of height and waist circumference of the subject. Height was measured using a microtoise with 0.01 cm precision. The subject stands without using footwear and accessories above the head. Subjects were considered at risk when WHtR was 0.5 or more (Zhang et al., 2016).

Neck circumference was measured by medical measuring tape with 0.1 cm precision. Its measurements in women was done by subject's upright head position and forward facing eyes, and then horizontally measured just below the protruding larynx.

Wrist circumference data was measured using medical measuring tape with 0.1 cm precision. Its measurement was done by placing the medical measuring tape horizontally on the distal side of ulna protrusion, around the wrist. Wrist circumference measurement results was divided into 3 categories: small if subjects whose height less than 155 cm had wrist circumference less than14 cm, subjects whose height 155-163 cm had wrist circumference 15.2 cm, subjects whose height more than 163 cm had wrist circumference less than 15.9 cm; moderate if subjects whose height less than 155 cm had wrist circumference 14-14.6 cm, subjects whose height 155-163 cm had wrist circumference 15.2-15.9 cm, subjects whose height more than 163 cm had wrist circumference 15.9-16.5 cm; large if subjects whose height less than 155 cm had wrist circumference more 14.6 cm, subjects whose height 155-163 cm had wrist circumference more 14.6 cm, subjects whose height 155-163 cm had wrist circumference more 14.6 cm, subjects had height more than 163 cm have wrist circumference more than 16.5 cm (Nabila et al., 2018).

Thigh circumference was measured by a medical measuring tape. Subjects were standing and wearing as little clothes as possible. Thigh circumference was measured 10 cm above the upper right patella. After that certain point was marked, tape is placed horizontally and encircles the thigh (Bando et al., 2017).

2D:4D ratio digit data is measured by a caliper with 0.001 mm precision. Measurements were made with the position of the palm of the hand open (Wu et al., 2013). The length of index finger or second finger is the length of finger measured from the midpoint of the second metacarpophalangeal joint and the most distal point of the second finger. The length of the ring finger or the fourth finger is the length of the finger measured from the midpoint of the fourth metacarpophalangeal joint and the most distal point of the fourth finger. 2D:4D ratio digit data was obtained from the length of the second finger divided by the length of the fourth finger. The

ratio digits were consideres high when the result show more than 0.9811 for the right hand and more than 0.9821 for the left hand (Balci et al., 2018).

Insulin resistance data was determined using HOMA-IR values. Measurement of Homeostasis Insulin Resistance Assessment Model (HOMA-IR) based on fasting blood glucose and fasting insulin level with the following formula (Nuraini et al., 2017):

Fasting Insulin 
$$\left(\frac{mU}{L}\right)x$$
 Fasting Blood Glucose  $\left(\frac{mmol}{L}\right)$ 

Threshold of HOMA-IR value for adolescents is less than 1,65 (Nuraini et al., 2017). This blood sampling was in collaboration with Sarana Medika laboratory.

#### 2.4 Data analysis

Data normality test was performed through Kolmogrov-Smirnov test. We used univariate analysis to describe each variable. Bivariate analysis was completed by Spearman Rank test. Bivariate analysis was performed to see whether there was a correlation between anthropometric profiles and insulin resistance.

#### 3. Results and discussion/Results

Table 1 described the anthropometric profile of the subjects. The median body weight was 66.6 kg. The median waist circumference and pelvic circumference were 85.75 cm and 103.5 cm, respectively, while the median WHR was 0.84 ± 0.23. Based on table 1, the median neck circumference, wrist circumference, WHtR was 32.5 cm, 15 cm, and 0.55 cm, respectively. The characteristic of the subjects could also be seen in table 2. Table 2 showed that all subjects (100%) had less than 80 cm waist circumference which meant they were at risk of developing metabolic syndrome. Another anthropometric profile showed that 98.3% subjects (n=118) had high WHtR values. Based on WHR, as many as 90.8% subjects (n=108) were at risk. A total of 83.3% subjects (n=100) also experienced insulin resistance as seen from the HOMA-IR value >1.65. However, anthropometric profiles, specifically neck circumference, wrist circumference, 2D:4D digit ratio of right hand; 2D:4D digit ratio of left hand, showed that less than 50% of subjects are at risk (10.8%; 21.7%; 39.2%; 44.2% respectively).

The correlation of anthropometric profile and insulin resistance incidence determined by HOMA-IR was shown in Table 3. Anthropometric profiles having a significant correlation with HOMA-IR were neck circumference (r=0.271; p=0.003), WHtR (r=0.33; p <0.001) and thigh circumference (r=0.224; p=0.014). Based on the analysis, higher the value of the neck circumference, thigh circumference, and WHtR, higher the HOMA-IR score. Table 3 also showed that waist circumference had no correlation with HOMA-IR (r=0.151; p=0.1). There was also no correlation between wrist circumference and HOMA-IR (r=0.12; p=0.19). In addition, there was no correlation between WHR and HOMA-IR in the study subjects (r=-0.019; p=0.836). Based on the analysis, other anthropometric profiles having no correlation with HOMA-IR were 2D:4D right hand digit ratios (r=0.139; p=0.129) and 2D:4D left hand digit ratios (r=0.169; p=0.065).

#### 4. Discussion

Late adolescents, especially women, have the risk of experiencing metabolic syndrome. Based on this study results, 83.3% of subjects experience insulin resistance determined by HOMA-IR. Since 2007, the Genome Wide Association Studies (GWAS) have identified around 88 loci associated with

the risk of developing type 2 diabetes mellitus where most of the loci are related to insulin secretion and pancreatic beta cell function, causing insulin resistance associated with obesity (A. E. Brown & Walker, 2016). Study conducted in Semarang City also showed that 96.1% of subjects experienced insulin resistance determined by HOMA-IR (Nuraini et al., 2017).

More than 50% of subjects of this study have high WHtR and WHR values. Study conducted in Jepara shows that 26.94% of adolescents experience abdominal obesity as seen from WHtR values of above 0.45 (Azizah & Sulchan, 2016). Other study conducted at the Faculty of Medicine Universitas Riau demonstrates that 44.1% students experience central obesity as seen in the ratio waist-hip circumference (Jannah et al., 2015). For women of reproductive age, fat storage is centralized in certain areas to protect important reproductive organs. This increases the risk of high WHR in women (Jannah et al., 2015).

Based on the analysis, neck circumference has a correlation with Homeostasis Model Assessment for Insulin Resistance (HOMA-IR), where the greater neck circumference of the subject, the higher HOMA-IR value. Study in China shows that neck circumference has a significant correlation with insulin resistance assessed by HOMA-IR (Liang et al., 2014). Previous case studies in Public Senior High School 2 Semarang and Public Junior High School 9 Semarang also stated that neck circumference has significant correlation with fasting blood sugar (Mayasari & Wirawanni, 2014).

Neck circumference is an easy anthropometric measurement. It can reflect central obesity index and is associated with several cardiovascular risk factors such as dyslipidemia, hypertension, hyperuricemia, and insulin resistance. It is also considered an estimation of upper-body subcutaneous adipose tissue which plays a role in predicting insulin resistance and type-2 diabetes (Nabila et al., 2018). Release of excess free fatty acids associated with upper body subcutaneous fat, explicitly the neck, can be one mechanism to explain the correlation between neck circumference and insulin resistance (Ebbert & Jensen, 2013).

Lipolytic function and releasing rate of free fatty acids in upper body subcutaneous fat is found higher than lower body subcutaneous fat. Excessive free fatty acids in muscles and other tissues induce the body to use more free fatty acids as energy. They will also inhibit glucose oxidation, causing insulin resistance (Ebbert & Jensen, 2013). Increased free fatty acids also play a role in increasing VLDL production and inhibition of insulin clearance which induces insulin resistance. In addition, neck circumference is also positively correlated with total fat body and visceral fat which are related to biological parameters of insulin resistance. Two perivascular ectopic fat depots are also found in the neck region. Adipokine secretion, such as leptin, adiponectin, and interleukin-6, from perivascular ectopic fat depots causes metabolic dysfunction including insulin resistance (Saneei et al., 2019).

Subjects with large neck circumferences have a greater risk for obesity (Saneei et al., 2019). Subcutaneous fat has a major role in the association of insulin resistance and obesity (Sri Yuliani et al., 2017). Insulin resistance is an important complication of obesity which causes hyperglycemia and impaired glycemic parameters (Saneei et al., 2019).

Waist to Height Ratio (WHtR) is a good predictor in determining insulin resistance in individual with obesity (Jamar et al., 2017). Based on the analysis, WHtR has a correlation with HOMA-IR, where the greater the WHtR score, the greater the value of HOMA-IR. A study conducted in Australia on the correlation of WHtR and metabolic syndrome in adolescents and children with obesity, result in a correlation between WHtR and HOMA-IR (Nambiar et al., 2013). Other studies conducted in Korea

also find that high WHtR values in obese adolescents would affect the incidence of insulin resistance measured by HOMA-IR (Lim et al., 2015).

WHtR plays a role in measuring central obesity which is often associated with metabolic disorders. Increase in fat tissue will promote increase in adipokine secretion. This can increase insulin resistance. The most important adipokin is TNF- $\alpha$  which plays a role in inducing insulin resistance through glucose transporter 4 (GLUT-4) and increasing the release of free fatty acids. Increased transfer of free fatty acids to muscles results in increased intracellular fatty acid metabolites such as diacylglycerol, ceramide, and acetyl-CoA. These metabolites will activate the serine pathway or threonine kinase that reduces the ability to activate insulin receptors. Hence, it can cause insulin resistance when occurs in the long termas it can damage visceral adipocyte  $\beta$  cells (Asnelviana et al., 2017).

Based on the statistical test results, we find a correlation between thigh circumference and insulin resistance as measured by HOMA-IR. This finding is in line with study conducted in Korea which shows the result that thigh circumference is positively related to HOMA-IR. The greater the thigh circumference, the greater the risk of insulin resistance (Park et al., 2012). Other study in Korea explains that the measurement of thigh circumference is an indicator of diabetes marker (Jung et al., 2013). Study conducted in Taiwan also shows the left thigh circumference is a significant predictor of determining type 2 diabetes mellitus 2 (Ting et al., 2018). Large thigh circumference not only indicates greater muscle mass, but also an increase in femoral subcutaneous fat mass. Lower muscle mass and subcutaneous fat in thigh are associated with insulin resistance which results in hyperglycemia and diabetes (Ting et al., 2018). Subcutaneous fat in the thighs is a metabolism of circulating fatty acids that are circulating because there is a difference in lipolysis activity between subcutaneous fat in the abdomen and thighs. Subcutaneous fat in the thigh is wasting metabolism of circulatory fatty acids as there is a difference between lypolisis activity of abdominal and thigh subcutaneous fat. Subcutaneous fat of the thigh tends to take fatty acids from the bloodstream, thus preventing the liver, pancreas, and ectopic fat such as the muscles from being exposed to high fatty acids (Nugraha et al., 2019).

Based on the study analysis, no correlation is found between neither waist circumference nor waist-hip circumference ratio with insulin resistance. This finding is contradictory to study conducted on adolescents in Korea which shows the results that waist circumference and waist-hip circumference ratio have significant correlation to HOMA-IR (Lim et al., 2015). Waist circumference and waist-hip circumference ratio can be used as a screening tool to detect the incidence of abdominal obesity which can cause metabolic disorders such as insulin resistance (Fitriyanti, Sulchan, et al., 2019).

However, a study conducted in Manado about correlation of waist circumference and blood sugar levels shows no correlation between waist circumference and blood sugar levels among teachers at the Middle School and High School Eben Haezar Christian Manado. Other study held in Ngawi also shows no correlation between waist circumference and blood sugar levels in early adulthood (Manungkalit et al., 2015). Several other studies, including a study conducted at the Pusti Pidie Health Center, show no correlation between waist circumference ratio pelvis and blood sugar among Community Health Center's employees (Mulyani & Rita, 2016). The study states that the ratio of waist-hip circumference is not an extremely decisive factor in increasing blood sugar levels as many other factors influence the increase in blood sugar levels. Therefor other anthropometric measurements need to be carried out (Mulyani & Rita, 2016).

Wrist circumference is a strong predictor of diabetes (Jahangiri Noudeh et al., 2013). Wrist circumference is an easily measured anthropometric parameter that can determine body frame and bone size. Increased bone mass will also be associated with hyperinsulinemia (Fitriyanti, Tjahjono, et al., 2019). However, in this study, wrist circumference has no correlation with HOMA-IR. Inconsistent with study conducted by Kusmiyati et al. in 18 years old adolescents, which demonstrates a correlation between wrist circumference and fasting insulin and HOMA-IR in both male and female adolescents (Fitriyanti, Tjahjono, et al., 2019). However, the study conducted by Rumaisha et al. about the correlation of wrist circumference and the blood glucose level among obese women shows no correlation between wrist circumference with fasting blood glucose. Other study conducted at Public Senior High School 6 Semarang also results in no correlation between wrist circumference with fasting blood glucose levels (Arifin & Panunggal, 2014). Factors influencing HOMA-IR values were fasting blood glucose and fasting insulin levels, where higher glucose levels fasting blood means higher the HOMA-IR value in the subject (Mitrea et al., 2013).

The Second to Fourth Digit Ratio (2D:4D) can be used to evaluate prenatal androgen exposure in the postpartum period. The Homeobox genes, HoxA and HoxB, are responsible for urogenital differentiation, prenatal andogen synthesis and fingers development. In animals, prenatal and neonatal androgenic exposure can increase adiposity, insulin resistance, and changes in adipose tissue lipolysis later in adulthood (Yildiz et al., 2015). However, based on this study analysis, the Second to Fourth Digit Ratio (2D:4D) of the right and left hand is not related to HOMA-IR or insulin resistance incidence. This finding is supported by study conducted in Turkey, on the correlation between Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome. It shows that Second to Fourth Digit Ratio (2D:4D) is not related to insulin resistance or the incidence of diabetes mellitus in the subject. Researchers state that no available study that reports Second to Fourth Digit Ratio (2D:4D) as predictor of androgen exposure and explains its correlation with metabolic syndrome (Yildiz et al., 2015). Other studies conducted by Abdullahi Yusuf Asuku et al. regarding the correlation of Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome indicators in Nigeria shows the results that Second to Fourth Digit Ratio (2D:4D) of the right and left hand has no correlation with fasting blood sugar levels in the subjects (Asuku et al., 2017). Researchers explain the absence of correlation between Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome indicators is caused by small number of subjects, i.e. 465 subjects, meanwhile this study includes only 120 subjects. This might be there reason of no association found between Second to Fourth Digit Ratio (2D:4D) and the incidence of insulin resistance.

#### Conflict of interest - Disclose any potential conflict of interest appropriately.

The authors declare no conflict of interest.

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**Table 1. Characteristic of Subjects.** 

Variable	Median	Minimum	Maximum
Body weight (kg)	66.6	47.8	107.4
Body height (cm)	157.4	100.5	171.4
Waist circumference (cm)	85.75	80.5	114
Hip circumference (cm)	103.5	30	170
Neck circumference (cm)	32.5	14.5	39
Wrist circumference (cm)	15	13.5	17.5
Thigh circumference (cm)	57.4	31	78.4
Waist Height to Ratio (WHtR)	0.55	0.49	0.95
Waist-hip circumference ratio	0.84	0.6	3.33
(WHR)			
2D:4D digit ratio of the right hand	0.98	0.84	1.09
2D:4D digit ratio of the left hand	0.99	0.52	0.6
HOMA-IR	2.33	0.54	18.32

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**Table 2. Frequency Distribution.** 

Category	n	%
Waist circumference		
At risk >80 cm	120	100
Neck circumference		
At risk ≥35.5 cm	13	10.8
Under risk <35.5 cm	107	89.2
Wrist circumference		
At risk ≥16 cm	26	21.7
Under risk <16 cm	94	78.3
Waist Height to Ratio (WHtR)		
At risk ≥0.5	118	98.3
Under risk < 0.5	2	1.7
Waist-hip circumference ratio (WHR)		
At risk ≥0.8	109	90.8
Under risk < 0.8	11	9.2
2D:4D digit ratio of the right hand		
At risk	47	39.2
Under risk	73	60.8
2D:4D digit ratio of the left hand		
At risk	53	44.2
Under risk	67	55.8
HOMA-IR		
Normal	20	16.7
Resistance	100	83.3

Tabel 3. Correlation of Anthropometric Profile and HOMA-IR.

r	р
0.151	0.1
0.271	0.003*
0.12	0.19
0.224	0.014*
0.33	<0.001*
-0.019	0.836
0.139	0.129
0.169	0.065
	0.271 0.12 0.224 0.33 -0.019 0.139

Correlation test: Rank-Spearman

<sup>\*</sup>Significant (p<0.05)



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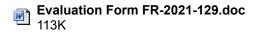
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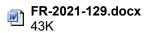
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#### Anthropometric Profile and Its Correlation to Insulin Resistance in Female Students with Obesity

Dieny, F.F.<sup>1,2\*</sup>, Fitranti, D.Y.<sup>1,2</sup>, Jauharany, F.F.<sup>1</sup>, Tsani, A.F.A.<sup>1,2</sup>, Faradila, U.<sup>1</sup>, Rose, S.<sup>1</sup>

<sup>1</sup>Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia <sup>2</sup>CENURE (Center of Nutrition Research), Universitas Diponegoro, Semarang, Indonesia

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7 \*Corresponding author: fillahdieny@gmail.com

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- 9 Author No.1: 0000-0001-6071-8901
- 10 Author No. 2: 0000-0002-1656-9563
- 11 Author No. 3: 0000-0001-9471-9419
- 12 Author No. 4: 0000-0002-3407-5188
- 13 Author No. 5: 0000-0002-1244-6187
- 14 Author No. 6: 0000-0002-1898-1842

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#### Abstract

The prevalence of obesity in adolescent girls is increasing each year. Several anthropometric measurements can be used to detect the incidence of insulin resistance. This study aims to observe the correlation of anthropometric profiles with insulin resistance in adolescent girls with obesity. This was an observational study with a total of 120 female students of Universitas Diponegoro (Undip), aged between 18 and 21 years old, who have waist circumference >80 cm. They were chosen by simple random sampling technique. Anthropometric profile data taken was consisted of waist circumference, hip circumference, waist-hip circumference ratio (WHR), waist-to-height ratio (WHtR), neck circumference, wrist circumference, thigh circumference, and 2D:4D digit ratio. Insulin resistance data was determined using the Homeostasis Model Assessment-Insulin Resistance (HOMA-IR.). Bivariate analysis was completed with the Spearman Rank test. There was 83.3% of subjects experienced insulin resistance. High WHtR was found in 98.3% of total subjects as many as 90.8% of subjects were at risk based on WHR values. Based on 2D:4D ratio digits, neck circumference, wrist circumference <50% of subjects were found as at risk. There was no correlation between waist circumference, WHR, wrist circumference, 2D:4D digit ratio with HOMA-IR (p>0.05). However, there was a positive correlation between WHtR, neck circumference, and thigh circumference with HOMA-IR (p<0.05) Anthropometric profiles such as WHtR, neck circumference, and thigh circumference were correlation of insulin resistance in female adolescent with obesity.

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**Keywords:** Adolescent; Anthropometric Indicator; Insulin Resistance; Obesity.

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#### 1. Introduction

Nutritional status in adolescents is very important since adolescence is a transition period from children to adulthood. This transition causes biological, psychological and cognitive changes that influence their nutritional status (Brown et al., 2011). However, nutritional status problems in adolescents are still fairly high, including obesity. Prevalence of central obesity 15 years adolescents and older has increased from 26.6% in 2013 to 31% in 2018 (Badan Penelitian dan Pengembangan Kesehatan, 2018). Obesity incidence will later be associated with degenerative diseases. Women is at higher risk of suffering from degenerative disease, while Indonesian Basic Health Research 2018 results reports the prevalence of stroke, diabetes mellitus, heart disease, and hypertension is found higher in women than men (Badan Penelitian dan Pengembangan Kesehatan, 2018). Indonesian Basic Health Research 2018 results also states that women and people live in urban areas of all ages have high prevalence of diabetes mellitus (Badan Penelitian dan Pengembangan Kesehatan, 2018).

Type 2 diabetes mellitus is caused by insulin resistance, a condition in which patient's body is unable to absorb glucose (Srikanthan et al., 2016). Study in Semarang City showed that 96.1% of adolescents experienced insulin resistance which was measured by Homeostasis Insulin Resistance Assessment Model (HOMA-IR) (Nuraini et al., 2017). HOMA-IR is a formula for calculating insulin resistance based on fasting blood sugar and insulin levels. Its measurement is simple, inexpensive, often used and has been validated by the clamp method (Sumarni, 2017).

One factor causing insulin resistance is central or abdominal obesity as abdominal fat is more actively undergoing lipolysis (Sumarni, 2017). Recently, several measurements of the body's anthropometric profile that can describe the incidence of central obesity are reported, where the measurements are done easily. Central obesity in adolescents can be described generally using measurements of waist circumference and hip waist circumference ratio (WHR). Some studies also mention that waist circumference and WHR have a significant correlation with insulin resistance (Sumarni, 2017).

In addition to waist circumference and WHR, other anthropometric profile measurements are also progressively more used, namely Waist-to-Height Ratio (WHtR). WHtR describes central obesity in adolescents with more accurate results than Body Mass Index (BMI) (Ashwell & Gibson, 2016; Saraswati & Sulchan, 2016; Yang et al., 2017). Study in Mexico demonstrates WHtR as a better tool in identifying cardiometabolic obesity in adolescents used to predict hypertension and insulin resistance (Rodea-Montero et al., 2014). Other studies conducted in Semarang also showed correlation between WHtR and increasing insulin resistance (Asnelviana et al., 2017).

Wrist circumference can also be utilized as indicator. Studies conducted in late adolescents in Indonesia, show wrist circumference as one of the anthropometric measurements that can predict obesity and insulin resistance in late adolescents. Wrist circumference reflects bone in the wrist area as well as peripheral fat distribution and metabolism thus it can measure one's body frame and bone size easily (Fitriyanti, Tjahjono, et al., 2019).

Another measurement of anthropometric profiles that can be used to predict metabolic syndrome in adolescents is the measurement of neck circumference. Some study show correlation between neck circumference with insulin resistance (Liang et al., 2014; Saneei et al., 2019). Neck

circumference can represent upper-body subcutaneous adipose tissue that plays a role in predicting insulin resistance and type 2 diabetes (Saneei et al., 2019).

In addition, measurement of thigh circumference can also predict metabolic syndrome in adolescents since it reflects central adiposity (Bando et al., 2017). Results of a study conducted in Korea show that thigh circumference is positively related to insulin resistance (Park et al., 2012). Several studies also explain that thigh circumference is a good indicator in determining type 2 diabetes mellitus 2 (Jung et al., 2013; Ting et al., 2018).

Recently, it has been reported that there are other anthropometric measurements as indicators in predicting metabolic syndrome disease, namely The Ratio of Second to Fourth Digit Length (2D:4D) (Endang Purwaningsih, 2016). Ratio of the length of the index finger and ring finger (2D:4D) can describe the exposure to the hormone estrogen and prenatal testosterone. A study has shown that low digit ratio is associated with high testosterone levels in men, while high digit ratio is associated with low testosterone levels in women (Kumar et al., 2016). The size of digit ratio occurs since the end of the first trimester of fetal development (Oyeyemi et al., 2014). Inappropriate exposure of androgen hormone can cause Polycystic Ovary Syndrome (PCOS), causing infertility in premenopausal women. Women who experience PCOS often have metabolic diseases such as hypertension and insulin resistance (White et al., 2017). Study states that digit ratio is correlated with obesity, which is a risk factor for metabolic disease (Gölge et al., 2016). There aren't many studies showing the relationship between digit ratio with insulin resistance.

In this study, we want to find out the portrayal and correlation of anthropometric profiles (waist circumference, WHR, WHtR, wrist circumference, neck circumference, thigh circumference, and second to fourth digit ratio) and insulin resistance in female adolescents with obesity.

#### 2. Materials and methods

#### 2.1 Design, location, and time

This is an observational study and included within the scope of community nutrition science. This research conducted in Universitas Diponegoro Semarang, Indonesia at 10 Faculties in June until August 2019. There were 1,260 female students who participated in screening program. The entire study was approved by the Health Study Ethics Committee (KEPK) Faculty of Medicine, Universitas Diponegoro/Central General Hospital dr. Kariadi No. 373/EC/KEPK/FK UNDIP/VIII/2019.

#### 2.2 Samplings

Subjects of this study were 120 students from Universitas Diponegoro who were selected through simple random sampling, according to the following inclusion criteria: aged 18-21 years old, had 80 cm or more waist circumference, had intact fingers on both hands, were not currently consuming drugs that could affect the blood glucose and insulin levels, were willing to do fasting for at least 8 hours, did not smoke and/or consume alcohol, were not sick or in the care of a doctor, did not do heavy physical activity or exercise, were not pregnant and breastfeeding, were willing to be the subject of study by filling out informed consent. The exclusion criteria in this study were subject's withdrawal from the study, subject moved to another university, and subject passed away within study period.

#### 2.3 Data collected

Independent variables in this study were the anthropometric profile consisted of waist circumference, waist-hip circumference ratio (WHR), Waist-Height Ratio (WHtR), neck circumference, wrist circumference, thigh circumference, and ratio of index finger length and ring finger (2D:4D). The dependent variable in this study was insulin resistance.

Waist circumference data was obtained from waist circumference measurements measured at the midpoint between the iliac crest and costal margins (lower ribs) using a medical measuring tape with 0.1 cm precision/ Subjects used minimal clothing (Yang et al., 2017). Subjects were considered at risk when waist circumference was 80 cm or more (Saklayen, 2018).

WHR data was obtained from the waist circumference to hip circumference ratio. Measurement of pelvic circumference was done by medical measuring tape with 0.1 cm precision. Pelvic circumference is measured by determining the widest points on the buttock (Fitriyanti, Tjahjono, et al., 2019). Subjects are categorized as risky when WHR was more than 0.85 (Saklayen, 2018).

Data on the ratio of waist circumference and height (WHtR) was obtained from measurements of height and waist circumference of the subject. Height was measured using a microtoise with 0.01 cm precision. The subject stands without using footwear and accessories above the head. Subjects were considered at risk when WHtR was 0.5 or more (Zhang et al., 2016).

Neck circumference was measured by medical measuring tape with 0.1 cm precision. Its measurements in women was done by subject's upright head position and forward facing eyes, and then horizontally measured just below the protruding larynx.

Wrist circumference data was measured using medical measuring tape with 0.1 cm precision. Its measurement was done by placing the medical measuring tape horizontally on the distal side of ulna protrusion, around the wrist. Wrist circumference measurement results was divided into 3 categories: small if subjects whose height less than 155 cm had wrist circumference less than14 cm, subjects whose height 155-163 cm had wrist circumference 15.2 cm, subjects whose height more than 163 cm had wrist circumference less than 15.9 cm; moderate if subjects whose height less than 155 cm had wrist circumference 14-14.6 cm, subjects whose height 155-163 cm had wrist circumference 15.2-15.9 cm, subjects whose height more than 163 cm had wrist circumference more 14.6 cm, subjects whose height 155-163 cm had wrist circumference more 14.6 cm, subjects whose height 155-163 cm had wrist circumference more 14.6 cm, subjects whose height 155-163 cm had wrist circumference more 15.9 cm, subjects had height more than 163 cm have wrist circumference more than 16.5 cm (Nabila et al., 2018).

Thigh circumference was measured by a medical measuring tape. Subjects were standing and wearing as little clothes as possible. Thigh circumference was measured 10 cm above the upper right patella. After that certain point was marked, tape is placed horizontally and encircles the thigh (Bando et al., 2017).

2D:4D ratio digit data is measured by a caliper with 0.001 mm precision. Measurements were made with the position of the palm of the hand open (Wu et al., 2013). The length of index finger or second finger is the length of finger measured from the midpoint of the second metacarpophalangeal joint and the most distal point of the second finger. The length of the ring finger or the fourth finger is the length of the finger measured from the midpoint of the fourth metacarpophalangeal joint and the most distal point of the fourth finger. 2D:4D ratio digit data was obtained from the length of the second finger divided by the length of the fourth finger. The

ratio digits were consideres high when the result show more than 0.9811 for the right hand and more than 0.9821 for the left hand (Balci et al., 2018).

Insulin resistance data was determined using HOMA-IR values. Measurement of Homeostasis Insulin Resistance Assessment Model (HOMA-IR) based on fasting blood glucose and fasting insulin level with the following formula (Nuraini et al., 2017):

Fasting Insulin 
$$\left(\frac{mU}{L}\right)x$$
 Fasting Blood Glucose  $\left(\frac{mmol}{L}\right)$ 

Threshold of HOMA-IR value for adolescents is less than 1,65 (Nuraini et al., 2017). This blood sampling was in collaboration with Sarana Medika laboratory.

#### 2.4 Data analysis

Data normality test was performed through Kolmogrov-Smirnov test. We used univariate analysis to describe each variable. Bivariate analysis was completed by Spearman Rank test. Bivariate analysis was performed to see whether there was a correlation between anthropometric profiles and insulin resistance.

#### 3. Results and discussion??

Table 1 described the anthropometric profile of the subjects. The median body weight was 66.6 kg. The median waist circumference and pelvic circumference were 85.75 cm and 103.5 cm, respectively, while the median WHR was 0.84 ± 0.23. Based on table 1, the median neck circumference, wrist circumference, WHtR was 32.5 cm, 15 cm, and 0.55 cm, respectively. The characteristic of the subjects could also be seen in table 2. Table 2 showed that all subjects (100%) had less than 80 cm waist circumference which meant they were at risk of developing metabolic syndrome. Another anthropometric profile showed that 98.3% subjects (n=118) had high WHtR values. Based on WHR, as many as 90.8% subjects (n=108) were at risk. A total of 83.3% subjects (n=100) also experienced insulin resistance as seen from the HOMA-IR value >1.65. However, anthropometric profiles, specifically neck circumference, wrist circumference, 2D:4D digit ratio of right hand; 2D:4D digit ratio of left hand, showed that less than 50% of subjects are at risk (10.8%; 21.7%; 39.2%; 44.2% respectively).

The correlation of anthropometric profile and insulin resistance incidence determined by HOMA-IR was shown in Table 3. Anthropometric profiles having a significant correlation with HOMA-IR were neck circumference (r=0.271; p=0.003), WHtR (r=0.33; p<0.001) and thigh circumference (r=0.224; p=0.014). Based on the analysis, higher the value of the neck circumference, thigh circumference, and WHtR, higher the HOMA-IR score. Table 3 also showed that waist circumference had no correlation with HOMA-IR (r=0.151; p=0.1). There was also no correlation between wrist circumference and HOMA-IR (r=0.12; p=0.19). In addition, there was no correlation between WHR and HOMA-IR in the study subjects (r=-0.019; p=0.836). Based on the analysis, other anthropometric profiles having no correlation with HOMA-IR were 2D:4D right hand digit ratios (r=0.139; p=0.129) and 2D:4D left hand digit ratios (r=0.169; p=0.065).

#### 4. Discussion

Late adolescents, especially women, have the risk of experiencing metabolic syndrome. Based on this study results, 83.3% of subjects experience insulin resistance determined by HOMA-IR. Since 2007, the Genome Wide Association Studies (GWAS) have identified around 88 loci associated with

the risk of developing type 2 diabetes mellitus where most of the loci are related to insulin secretion and pancreatic beta cell function, causing insulin resistance associated with obesity (A. E. Brown & Walker, 2016). Study conducted in Semarang City also showed that 96.1% of subjects experienced insulin resistance determined by HOMA-IR (Nuraini et al., 2017).

More than 50% of subjects of this study have high WHtR and WHR values. Study conducted in Jepara shows that 26.94% of adolescents experience abdominal obesity as seen from WHtR values of above 0.45 (Azizah & Sulchan, 2016). Other study conducted at the Faculty of Medicine Universitas Riau demonstrates that 44.1% students experience central obesity as seen in the ratio waist-hip circumference (Jannah et al., 2015). For women of reproductive age, fat storage is centralized in certain areas to protect important reproductive organs. This increases the risk of high WHR in women (Jannah et al., 2015).

Based on the analysis, neck circumference has a correlation with Homeostasis Model Assessment for Insulin Resistance (HOMA-IR), where the greater neck circumference of the subject, the higher HOMA-IR value. Study in China shows that neck circumference has a significant correlation with insulin resistance assessed by HOMA-IR (Liang et al., 2014). Previous case studies in Public Senior High School 2 Semarang and Public Junior High School 9 Semarang also stated that neck circumference has significant correlation with fasting blood sugar (Mayasari & Wirawanni, 2014).

Neck circumference is an easy anthropometric measurement. It can reflect central obesity index and is associated with several cardiovascular risk factors such as dyslipidemia, hypertension, hyperuricemia, and insulin resistance. It is also considered an estimation of upper-body subcutaneous adipose tissue which plays a role in predicting insulin resistance and type-2 diabetes (Nabila et al., 2018). Release of excess free fatty acids associated with upper body subcutaneous fat, explicitly the neck, can be one mechanism to explain the correlation between neck circumference and insulin resistance (Ebbert & Jensen, 2013).

Lipolytic function and releasing rate of free fatty acids in upper body subcutaneous fat is found higher than lower body subcutaneous fat. Excessive free fatty acids in muscles and other tissues induce the body to use more free fatty acids as energy. They will also inhibit glucose oxidation, causing insulin resistance (Ebbert & Jensen, 2013). Increased free fatty acids also play a role in increasing VLDL production and inhibition of insulin clearance which induces insulin resistance. In addition, neck circumference is also positively correlated with total fat body and visceral fat which are related to biological parameters of insulin resistance. Two perivascular ectopic fat depots are also found in the neck region. Adipokine secretion, such as leptin, adiponectin, and interleukin-6, from perivascular ectopic fat depots causes metabolic dysfunction including insulin resistance (Saneei et al., 2019).

Subjects with large neck circumferences have a greater risk for obesity (Saneei et al., 2019). Subcutaneous fat has a major role in the association of insulin resistance and obesity (Sri Yuliani et al., 2017). Insulin resistance is an important complication of obesity which causes hyperglycemia and impaired glycemic parameters (Saneei et al., 2019).

Waist to Height Ratio (WHtR) is a good predictor in determining insulin resistance in individual with obesity (Jamar et al., 2017). Based on the analysis, WHtR has a correlation with HOMA-IR, where the greater the WHtR score, the greater the value of HOMA-IR. A study conducted in Australia on the correlation of WHtR and metabolic syndrome in adolescents and children with obesity, result in a correlation between WHtR and HOMA-IR (Nambiar et al., 2013). Other studies conducted in Korea

also find that high WHtR values in obese adolescents would affect the incidence of insulin resistance measured by HOMA-IR (Lim et al., 2015).

WHtR plays a role in measuring central obesity which is often associated with metabolic disorders. Increase in fat tissue will promote increase in adipokine secretion. This can increase insulin resistance. The most important adipokin is TNF- $\alpha$  which plays a role in inducing insulin resistance through glucose transporter 4 (GLUT-4) and increasing the release of free fatty acids. Increased transfer of free fatty acids to muscles results in increased intracellular fatty acid metabolites such as diacylglycerol, ceramide, and acetyl-CoA. These metabolites will activate the serine pathway or threonine kinase that reduces the ability to activate insulin receptors. Hence, it can cause insulin resistance when occurs in the long termas it can damage visceral adipocyte  $\beta$  cells (Asnelviana et al., 2017).

Based on the statistical test results, we find a correlation between thigh circumference and insulin resistance as measured by HOMA-IR. This finding is in line with study conducted in Korea which shows the result that thigh circumference is positively related to HOMA-IR. The greater the thigh circumference, the greater the risk of insulin resistance (Park et al., 2012). Other study in Korea explains that the measurement of thigh circumference is an indicator of diabetes marker (Jung et al., 2013). Study conducted in Taiwan also shows the left thigh circumference is a significant predictor of determining type 2 diabetes mellitus 2 (Ting et al., 2018). Large thigh circumference not only indicates greater muscle mass, but also an increase in femoral subcutaneous fat mass. Lower muscle mass and subcutaneous fat in thigh are associated with insulin resistance which results in hyperglycemia and diabetes (Ting et al., 2018). Subcutaneous fat in the thighs is a metabolism of circulating fatty acids that are circulating because there is a difference in lipolysis activity between subcutaneous fat in the abdomen and thighs. Subcutaneous fat in the thigh is wasting metabolism of circulatory fatty acids as there is a difference between lypolisis activity of abdominal and thigh subcutaneous fat. Subcutaneous fat of the thigh tends to take fatty acids from the bloodstream, thus preventing the liver, pancreas, and ectopic fat such as the muscles from being exposed to high fatty acids (Nugraha et al., 2019).

Based on the study analysis, no correlation is found between neither waist circumference nor waist-hip circumference ratio with insulin resistance. This finding is contradictory to study conducted on adolescents in Korea which shows the results that waist circumference and waist-hip circumference ratio have significant correlation to HOMA-IR (Lim et al., 2015). Waist circumference and waist-hip circumference ratio can be used as a screening tool to detect the incidence of abdominal obesity which can cause metabolic disorders such as insulin resistance (Fitriyanti, Sulchan, et al., 2019).

However, a study conducted in Manado about correlation of waist circumference and blood sugar levels shows no correlation between waist circumference and blood sugar levels among teachers at the Middle School and High School Eben Haezar Christian Manado. Other study held in Ngawi also shows no correlation between waist circumference and blood sugar levels in early adulthood (Manungkalit et al., 2015). Several other studies, including a study conducted at the Pusti Pidie Health Center, show no correlation between waist circumference ratio pelvis and blood sugar among Community Health Center's employees (Mulyani & Rita, 2016). The study states that the ratio of waist-hip circumference is not an extremely decisive factor in increasing blood sugar levels as many other factors influence the increase in blood sugar levels. Therefor other anthropometric measurements need to be carried out (Mulyani & Rita, 2016).

Wrist circumference is a strong predictor of diabetes (Jahangiri Noudeh et al., 2013). Wrist circumference is an easily measured anthropometric parameter that can determine body frame and bone size. Increased bone mass will also be associated with hyperinsulinemia (Fitriyanti, Tjahjono, et al., 2019). However, in this study, wrist circumference has no correlation with HOMA-IR. Inconsistent with study conducted by Kusmiyati et al. (XXXX) in 18 years old adolescents, which demonstrates a correlation between wrist circumference and fasting insulin and HOMA-IR in both male and female adolescents (Fitriyanti, Tjahjono, et al., 2019). However, the study conducted by Rumaisha et al. (XXXX) about the correlation of wrist circumference and the blood glucose level among obese women shows no correlation between wrist circumference with fasting blood glucose. Other study conducted at Public Senior High School 6 Semarang also results in no correlation between wrist circumference with fasting blood glucose levels (Arifin & Panunggal, 2014). Factors influencing HOMA-IR values were fasting blood glucose and fasting insulin levels, where higher glucose levels fasting blood means higher the HOMA-IR value in the subject (Mitrea et al., 2013).

The Second to Fourth Digit Ratio (2D:4D) can be used to evaluate prenatal androgen exposure in the postpartum period. The Homeobox genes, HoxA and HoxB, are responsible for urogenital differentiation, prenatal andogen synthesis and fingers development. In animals, prenatal and neonatal androgenic exposure can increase adiposity, insulin resistance, and changes in adipose tissue lipolysis later in adulthood (Yildiz et al., 2015). However, based on this study analysis, the Second to Fourth Digit Ratio (2D:4D) of the right and left hand is not related to HOMA-IR or insulin resistance incidence. This finding is supported by study conducted in Turkey, on the correlation between Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome. It shows that Second to Fourth Digit Ratio (2D:4D) is not related to insulin resistance or the incidence of diabetes mellitus in the subject. Researchers state that no available study that reports Second to Fourth Digit Ratio (2D:4D) as predictor of androgen exposure and explains its correlation with metabolic syndrome (Yildiz et al., 2015). Other studies conducted by Abdullahi Yusuf Asuku et al. regarding the correlation of Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome indicators in Nigeria shows the results that Second to Fourth Digit Ratio (2D:4D) of the right and left hand has no correlation with fasting blood sugar levels in the subjects (Asuku et al., 2017). Researchers explain the absence of correlation between Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome indicators is caused by small number of subjects, i.e. 465 subjects, meanwhile this study includes only 120 subjects. This might be there reason of no association found between Second to Fourth Digit Ratio (2D:4D) and the incidence of insulin resistance.

#### Conflict of interest - Disclose any potential conflict of interest appropriately.

The authors declare no conflict of interest.

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Table 1. Characteristic of **Subjects**.

Variable	Median	Minimum	Maximum
Body weight (kg)	66.6	47.8	107.4
Body height (cm)	157.4	100.5	171.4
Waist circumference (cm)	85.75	80.5	114
Hip circumference (cm)	103.5	30	170
Neck circumference (cm)	32.5	14.5	39
Wrist circumference (cm)	15	13.5	17.5
Thigh circumference (cm)	57.4	31	78.4
Waist Height to Ratio (WHtR)	0.55	0.49	0.95
Waist-hip circumference ratio	0.84	0.6	3.33
(WHR)			
2D:4D digit ratio of the right hand	0.98	0.84	1.09
2D:4D digit ratio of the left hand	0.99	0.52	0.6
HOMA-IR	2.33	0.54	18.32

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Table 2. Frequency Distribution.

Category	n	%
Waist circumference		
At risk >80 cm	120	100
Neck circumference		
At risk ≥35.5 cm	13	10.8
Under risk <35.5 cm	107	89.2
Wrist circumference		
At risk ≥16 cm	26	21.7
Under risk <16 cm	94	78.3
Waist Height to Ratio (WHtR)		
At risk ≥0.5	118	98.3
Under risk < 0.5	2	1.7
Waist-hip circumference ratio (WHR)		
At risk ≥0.8	109	90.8
Under risk < 0.8	11	9.2
2D:4D digit ratio of the right hand		
At risk	47	39.2
Under risk	73	60.8
2D:4D digit ratio of the left hand		
At risk	53	44.2
Under risk	67	55.8
HOMA-IR		
Normal	20	16.7
Resistance	100	83.3

Tabel 3. Correlation of Anthropometric Profile and HOMA-IR.

Variable	r	p
Waist circumference (cm)	0.151	0.1
Neck circumference (cm)	0.271	0.003*
Wrist circumference (cm)	0.12	0.19
Thigh circumference (cm)	0.224	0.014*
Waist Height to Ratio (WHtR)	0.33	<0.001*
Waist-hip circumference ratio (WHR)	-0.019	0.836
2D:4D digit ratio of the right hand	0.139	0.129
2D:4D digit ratio of the left hand	0.169	0.065

Correlation test: Rank-Spearman \*Significant (p<0.05)



# MANUSCRIPT EVALUATION FORM

Date : 23<sup>rd</sup> February 2021

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# Anthropometric Profile and Its Correlation to Insulin Resistance in Female Students with Obesity

# Abstract

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The prevalence of obesity in adolescent girls is increasing each year. Several anthropometric measurements can be used to detect the incidence of insulin resistance. This study aims to observe the correlation of anthropometric profiles with insulin resistance in adolescent girls with obesity. This was an observational study with a total of 120 female students of Universitas Diponegoro (Undip), aged between 18 and 21 years old, who have waist circumference >80 cm. They were chosen by simple random sampling technique. Anthropometric profile data taken was consisted of waist circumference, hip circumference, waist-hip circumference ratio (WHR), waist-to-height ratio (WHtR), neck circumference, wrist circumference, thigh circumference, and 2D:4D digit ratio. Insulin resistance data was determined using the Homeostasis Model Assessment-Insulin Resistance (HOMA-IR.). Bivariate analysis was completed with the Spearman Rank test. There was 83.3% of subjects experienced insulin resistance. High WHtR was found in 98.3% of total subjects as many as 90.8% of subjects were at risk based on WHR values. Based on 2D:4D ratio digits, neck circumference, wrist circumference <50% of subjects were found as at risk. There was no correlation between waist circumference, WHR, wrist circumference, 2D:4D digit ratio with HOMA-IR (p>0.05). However, there was a positive correlation between WHtR, neck circumference, and thigh circumference with HOMA-IR (p<0.05) Anthropometric profiles such as WHtR, neck circumference, and thigh circumference were correlation of insulin resistance in female adolescent with obesity.

Keywords: Adolescent; Anthropometric Indicator; Insulin Resistance; Obesity.

# 1. Introduction

Nutritional status in adolescents is very important since adolescence is a transition period from children to adulthood. This transition causes biological, psychological and cognitive changes that influence their nutritional status (Brown et al., 2011). However, nutritional status problems in adolescents are still fairly high, including obesity. Prevalence of central obesity 15 years adolescents and older has increased from 26.6% in 2013 to 31% in 2018 (Badan Penelitian dan Pengembangan Kesehatan, 2018). Obesity incidence will later be associated with degenerative diseases. Women is at higher risk of suffering from degenerative disease, while Indonesian Basic Health Research 2018 results reports the prevalence of stroke, diabetes mellitus, heart disease, and hypertension is found higher in women than men (Badan Penelitian dan Pengembangan Kesehatan, 2018). Indonesian Basic Health Research 2018 results also states that women and people live in urban areas of all ages have high prevalence of diabetes mellitus (Badan Penelitian dan Pengembangan Kesehatan, 2018).

Type 2 diabetes mellitus is caused by insulin resistance, a condition in which patient's body is unable to absorb glucose (Srikanthan et al., 2016). Study in Semarang City showed that 96.1% of adolescents experienced insulin resistance which was measured by Homeostasis Insulin Resistance Assessment Model (HOMA-IR) (Nuraini et al., 2017). HOMA-IR is a formula for calculating insulin resistance based on fasting blood sugar and insulin levels. Its measurement is simple, inexpensive, often used and has been validated by the clamp method (Sumarni, 2017).

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One factor causing insulin resistance is central or abdominal obesity as abdominal fat is more actively undergoing lipolysis (Sumarni, 2017). Recently, several measurements of the body's anthropometric profile that can describe the incidence of central obesity are reported, where the measurements are done easily. Central obesity in adolescents can be described generally using measurements of waist circumference and hip waist circumference ratio (WHR). Some studies also mention that waist circumference and WHR have a significant correlation with insulin resistance (Sumarni, 2017).

In addition to waist circumference and WHR, other anthropometric profile measurements are also progressively more used, namely Waist-to-Height Ratio (WHtR). WHtR describes central obesity in adolescents with more accurate results than Body Mass Index (BMI) (Ashwell & Gibson, 2016; Saraswati & Sulchan, 2016; Yang et al., 2017). Study in Mexico demonstrates WHtR as a better tool in identifying cardiometabolic obesity in adolescents used to predict hypertension and insulin resistance (Rodea-Montero et al., 2014). Other studies conducted in Semarang also showed correlation between WHtR and increasing insulin resistance (Asnelviana et al., 2017).

Wrist circumference can also be utilized as indicator. Studies conducted in late adolescents in Indonesia, show wrist circumference as one of the anthropometric measurements that can predict obesity and insulin resistance in late adolescents. Wrist circumference reflects bone in the wrist area as well as peripheral fat distribution and metabolism thus it can measure one's body frame and bone size easily (Fitriyanti, Tjahjono, et al., 2019).

Another measurement of anthropometric profiles that can be used to predict metabolic syndrome in adolescents is the measurement of neck circumference. Some study show correlation between neck circumference with insulin resistance (Liang et al., 2014; Saneei et al., 2019). Neck circumference can represent upper-body subcutaneous adipose tissue that plays a role in predicting insulin resistance and type 2 diabetes (Saneei et al., 2019).

In addition, measurement of thigh circumference can also predict metabolic syndrome in adolescents since it reflects central adiposity (Bando et al., 2017). Results of a study conducted in Korea show that thigh circumference is positively related to insulin resistance (Park et al., 2012). Several studies also explain that thigh circumference is a good indicator in determining type 2 diabetes mellitus 2 (Jung et al., 2013; Ting et al., 2018).

Recently, it has been reported that there are other anthropometric measurements as indicators in predicting metabolic syndrome disease, namely The Ratio of Second to Fourth Digit Length (2D:4D) (Endang Purwaningsih, 2016). Ratio of the length of the index finger and ring finger (2D:4D) can describe the exposure to the hormone estrogen and prenatal testosterone. A study has shown that low digit ratio is associated with high testosterone levels in men, while high digit ratio is associated with low testosterone levels in women (Kumar et al., 2016). The size of digit ratio occurs since the end of the first trimester of fetal development (Oyeyemi et al., 2014). Inappropriate exposure of androgen hormone can cause Polycystic Ovary Syndrome (PCOS), causing infertility in premenopausal women. Women who experience PCOS often have metabolic diseases such as hypertension and insulin resistance (White et al., 2017). Study states that digit ratio is correlated with obesity, which is a risk factor for metabolic disease (Gölge et al., 2016). There aren't many studies showing the relationship between digit ratio with insulin resistance.

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In this study, we want to find out the portrayal and correlation of anthropometric profiles (waist circumference, WHR, WHtR, wrist circumference, neck circumference, thigh circumference, and second to fourth digit ratio) and insulin resistance in female adolescents with obesity.

# 2. Materials and methods

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#### 2.1 Design, location, and time

This is an observational study and included within the scope of community nutrition science. This research conducted in Universitas Diponegoro Semarang, Indonesia at 10 Faculties in June until August 2019. There were 1,260 female students who participated in screening program. The entire study was approved by the Health Study Ethics Committee (KEPK) Faculty of Medicine, Universitas Diponegoro/Central General Hospital dr. Kariadi No. 373/EC/KEPK/FK UNDIP/VIII/2019.

# 2.2 Samplings

Subjects of this study were 120 students from Universitas Diponegoro who were selected through simple random sampling, according to the following inclusion criteria: aged 18-21 years old, had 80 cm or more waist circumference, had intact fingers on both hands, were not currently consuming drugs that could affect the blood glucose and insulin levels, were willing to do fasting for at least 8 hours, did not smoke and/or consume alcohol, were not sick or in the care of a doctor, did not do heavy physical activity or exercise, were not pregnant and breastfeeding, were willing to be the subject of study by filling out informed consent. The exclusion criteria in this study were subject's withdrawal from the study, subject moved to another university, and subject passed away within study period.

# 2.3 Data collected

Independent variables in this study were the anthropometric profile consisted of waist circumference, waist-hip circumference ratio (WHR), Waist-Height Ratio (WHtR), neck circumference, wrist circumference, thigh circumference, and ratio of index finger length and ring finger (2D:4D). The dependent variable in this study was insulin resistance.

Waist circumference data was obtained from waist circumference measurements measured at the midpoint between the iliac crest and costal margins (lower ribs) using a medical measuring tape with 0.1 cm precision/ Subjects used minimal clothing (Yang et al., 2017). Subjects were considered at risk when waist circumference was 80 cm or more (Saklayen, 2018).

WHR data was obtained from the waist circumference to hip circumference ratio. Measurement of pelvic circumference was done by medical measuring tape with 0.1 cm precision. Pelvic circumference is measured by determining the widest points on the buttock (Fitriyanti, Tjahjono, et al., 2019). Subjects are categorized as risky when WHR was more than 0.85 (Saklayen, 2018).

Data on the ratio of waist circumference and height (WHtR) was obtained from measurements of height and waist circumference of the subject. Height was measured using a microtoise with 0.01 cm precision. The subject stands without using footwear and accessories above the head. Subjects were considered at risk when WHtR was 0.5 or more (Zhang et al., 2016).

Neck circumference was measured by medical measuring tape with 0.1 cm precision. Its measurements in women was done by subject's upright head position and forward facing eyes, and then horizontally measured just below the protruding larynx.

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Wrist circumference da ta was measured using medical measuring tape with 0.1 cm precision. Its measurement was done by placing the medical measuring tape horizontally on the distal side of the ulna protrusion, around the wrist. Wrist circumference measurement results was divided into 3 categories: small if subjects whose height less than 155 cm had wrist circumference less than14 cm, subjects whose height 155-163 cm had wrist circumference 15.2 cm, subjects whose height more than 163 cm had wrist circumference less than 15.9 cm; moderate if subjects whose height less than 155 cm had wrist circumference 14-14.6 cm, subjects whose height 155-163 cm had wrist circumference 15.2-15.9 cm, subjects whose height more than 163 cm had wrist circumference 15.9-16.5 cm; large if subjects whose height less than 155 cm had wrist circumference more 14.6 cm, subjects whose height 155-163 cm had wrist circumference more 14.6 cm, subjects whose height 155-163 cm had wrist circumference more than 15.9 cm, subjects had height more than 163 cm have wrist circumference more than 16.5 cm (Nabila et al., 2018).

Thigh circumference was measured by a medical measuring tape. Subjects were standing and wearing as little clothes as possible. Thigh circumference was measured 10 cm above the upper right patella. After that certain point was marked, tape is placed horizontally and encircles the thigh (Bando et al., 2017).

2D:4D ratio digit data is measured by a caliper with 0.001 mm precision. Measurements were made with the position of the palm of the hand open (Wu et al., 2013). The length of index finger or second finger is the length of finger measured from the midpoint of the second metacarpophalangeal joint and the most distal point of the second finger. The length of the ring finger or the fourth finger is the length of the finger measured from the midpoint of the fourth metacarpophalangeal joint and the most distal point of the fourth finger. 2D:4D ratio digit data was obtained from the length of the second finger divided by the length of the fourth finger. The ratio digits were consideres high when the result show more than 0.9811 for the right hand and more than 0.9821 for the left hand (Balci et al., 2018).

Insulin resistance data was determined using HOMA-IR values. Measurement of Homeostasis Insulin Resistance Assessment Model (HOMA-IR) based on fasting blood glucose and fasting insulin level with the following formula (Nuraini et al., 2017):

Fasting Insulin 
$$\left(\frac{mU}{L}\right)$$
 x Fasting Blood Glucose  $\left(\frac{mmol}{L}\right)$  22,5

Threshold of HOMA-IR value for adolescents is less than 1,65 (Nuraini et al., 2017). This blood sampling was in collaboration with Sarana Medika laboratory.

# 2.4 Data analysis

Data normality test was performed through Kolmogrov-Smirnov test. We used univariate analysis to describe each variable. Bivariate analysis was completed by Spearman Rank test. Bivariate analysis was performed to see whether there was a correlation between anthropometric profiles and insulin resistance.

# 3. Results and discussion

Table 1 described the anthropometric profile of the subjects. The median body weight was 66.6 kg. The median waist circumference and pelvic circumference were 85.75 cm and 103.5 cm, respectively, while the median WHR was  $0.84 \pm 0.23$ . Based on table 1, the median neck circumference, wrist circumference, WHtR was 32.5 cm, 15 cm, and 0.55 cm, respectively. The

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characteristic of the subjects could also be seen in table 2. Table 2 showed that all subjects (100%) had less than 80 cm waist circumference which meant they were at risk of developing metabolic syndrome. Another anthropometric profile showed that 98.3% subjects (n=118) had high WHtR values. Based on WHR, as many as 90.8% subjects (n=108) were at risk. A total of 83.3% subjects (n=100) also experienced insulin resistance as seen from the HOMA-IR value >1.65. However, anthropometric profiles, specifically neck circumference, wrist circumference, 2D:4D digit ratio of right hand; 2D:4D digit ratio of left hand, showed that less than 50% of subjects are at risk (10.8%; 21.7%; 39.2%; 44.2% respectively).

The correlation of anthropometric profile and insulin resistance incidence determined by HOMA-IR was shown in Table 3. Anthropometric profiles having a significant correlation with HOMA-IR were neck circumference (r=0.271; p=0.003), WHtR (r=0.33; p <0.001) and thigh circumference (r=0.224; p=0.014). Based on the analysis, higher the value of the neck circumference, thigh circumference, and WHtR, higher the HOMA-IR score. Table 3 also showed that waist circumference had no correlation with HOMA-IR (r=0.151; p=0.1). There was also no correlation between wrist circumference and HOMA-IR (r=0.12; p=0.19). In addition, there was no correlation between WHR and HOMA-IR in the study subjects (r=-0.019; p=0.836). Based on the analysis, other anthropometric profiles having no correlation with HOMA-IR were 2D:4D right hand digit ratios (r=0.139; p=0.129) and 2D:4D left hand digit ratios (r=0.169; p=0.065).

# 4. Discussion

Late adolescents, especially women, have the risk of experiencing metabolic syndrome. Based on this study results, 83.3% of subjects experience insulin resistance determined by HOMA-IR. Since 2007, the Genome Wide Association Studies (GWAS) have identified around 88 loci associated with the risk of developing type 2 diabetes mellitus where most of the loci are related to insulin secretion and pancreatic beta cell function, causing insulin resistance associated with obesity (A. E. Brown & Walker, 2016). Study conducted in Semarang City also showed that 96.1% of subjects experienced insulin resistance determined by HOMA-IR (Nuraini et al., 2017).

More than 50% of subjects of this study have high WHtR and WHR values. Study conducted in Jepara shows that 26.94% of adolescents experience abdominal obesity as seen from WHtR values of above 0.45 (Azizah & Sulchan, 2016). Other study conducted at the Faculty of Medicine Universitas Riau demonstrates that 44.1% students experience central obesity as seen in the ratio waist-hip circumference (Jannah et al., 2015). For women of reproductive age, fat storage is centralized in certain areas to protect important reproductive organs. This increases the risk of high WHR in women (Jannah et al., 2015).

Based on the analysis, neck circumference has a correlation with Homeostasis Model Assessment for Insulin Resistance (HOMA-IR), where the greater neck circumference of the subject, the higher HOMA-IR value. Study in China shows that neck circumference has a significant correlation with insulin resistance assessed by HOMA-IR (Liang et al., 2014). Previous case studies in Public Senior High School 2 Semarang and Public Junior High School 9 Semarang also stated that neck circumference has significant correlation with fasting blood sugar (Mayasari & Wirawanni, 2014).

Neck circumference is an easy anthropometric measurement. It can reflect central obesity index and is associated with several cardiovascular risk factors such as dyslipidemia, hypertension, hyperuricemia, and insulin resistance. It is also considered an estimation of upper-body subcutaneous adipose tissue which plays a role in predicting insulin resistance and type-2 diabetes

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(Nabila et al., 2018). Release of excess free fatty acids associated with upper body subcutaneous fat, explicitly the neck, can be one mechanism to explain the correlation between neck circumference and insulin resistance (Ebbert & Jensen, 2013).

Lipolytic function and releasing rate of free fatty acids in upper body subcutaneous fat is found higher than lower body subcutaneous fat. Excessive free fatty acids in muscles and other tissues induce the body to use more free fatty acids as energy. They will also inhibit glucose oxidation, causing insulin resistance (Ebbert & Jensen, 2013). Increased free fatty acids also play a role in increasing VLDL production and inhibition of insulin clearance which induces insulin resistance. In addition, neck circumference is also positively correlated with total fat body and visceral fat which are related to biological parameters of insulin resistance. Two perivascular ectopic fat depots are also found in the neck region. Adipokine secretion, such as leptin, adiponectin, and interleukin-6, from perivascular ectopic fat depots causes metabolic dysfunction including insulin resistance (Saneei et al., 2019).

Subjects with large neck circumferences have a greater risk for obesity (Saneei et al., 2019). Subcutaneous fat has a major role in the association of insulin resistance and obesity (Sri Yuliani et al., 2017). Insulin resistance is an important complication of obesity which causes hyperglycemia and impaired glycemic parameters (Saneei et al., 2019).

Waist to Height Ratio (WHtR) is a good predictor in determining insulin resistance in individual with obesity (Jamar et al., 2017). Based on the analysis, WHtR has a correlation with HOMA-IR, where the greater the WHtR score, the greater the value of HOMA-IR. A study conducted in Australia on the correlation of WHtR and metabolic syndrome in adolescents and children with obesity, result in a correlation between WHtR and HOMA-IR (Nambiar et al., 2013). Other studies conducted in Korea also find that high WHtR values in obese adolescents would affect the incidence of insulin resistance measured by HOMA-IR (Lim et al., 2015).

WHtR plays a role in measuring central obesity which is often associated with metabolic disorders. Increase in fat tissue will promote increase in adipokine secretion. This can increase insulin resistance. The most important adipokin is TNF- $\alpha$  which plays a role in inducing insulin resistance through glucose transporter 4 (GLUT-4) and increasing the release of free fatty acids. Increased transfer of free fatty acids to muscles results in increased intracellular fatty acid metabolites such as diacylglycerol, ceramide, and acetyl-CoA. These metabolites will activate the serine pathway or threonine kinase that reduces the ability to activate insulin receptors. Hence, it can cause insulin resistance when occurs in the long termas it can damage visceral adipocyte  $\beta$  cells (Asnelviana et al., 2017).

Based on the statistical test results, we find a correlation between thigh circumference and insulin resistance as measured by HOMA-IR. This finding is in line with study conducted in Korea which shows the result that thigh circumference is positively related to HOMA-IR. The greater the thigh circumference, the greater the risk of insulin resistance (Park et al., 2012). Other study in Korea explains that the measurement of thigh circumference is an indicator of diabetes marker (Jung et al., 2013). Study conducted in Taiwan also shows the left thigh circumference is a significant predictor of determining type 2 diabetes mellitus 2 (Ting et al., 2018). Large thigh circumference not only indicates greater muscle mass, but also an increase in femoral subcutaneous fat mass. Lower muscle mass and subcutaneous fat in thigh are associated with insulin resistance which results in hyperglycemia and diabetes (Ting et al., 2018). Subcutaneous fat in the thighs is a metabolism of circulating fatty acids that are circulating because there is a difference in lipolysis activity between

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subcutaneous fat in the abdomen and thighs. Subcutaneous fat in the thigh is wasting metabolism of circulatory fatty acids as there is a difference between lypolisis activity of abdominal and thigh subcutaneous fat. Subcutaneous fat of the thigh tends to take fatty acids from the bloodstream, thus preventing the liver, pancreas, and ectopic fat such as the muscles from being exposed to high fatty acids (Nugraha et al., 2019).

Based on the study analysis, no correlation is found between neither waist circumference nor waist-hip circumference ratio with insulin resistance. This finding is contradictory to study conducted on adolescents in Korea which shows the results that waist circumference and waist-hip circumference ratio have significant correlation to HOMA-IR (Lim et al., 2015). Waist circumference and waist-hip circumference ratio can be used as a screening tool to detect the incidence of abdominal obesity which can cause metabolic disorders such as insulin resistance (Fitriyanti, Sulchan, et al., 2019).b

However, a study conducted in Manado about correlation of waist circumference and blood sugar levels shows no correlation between waist circumference and blood sugar levels among teachers at the Middle School and High School Eben Haezar Christian Manado. Other study held in Ngawi also shows no correlation between waist circumference and blood sugar levels in early adulthood (Manungkalit et al., 2015). Several other studies, including a study conducted at the Pusti Pidie Health Center, show no correlation between waist circumference ratio pelvis and blood sugar among Community Health Center's employees (Mulyani & Rita, 2016). The study states that the ratio of waist-hip circumference is not an extremely decisive factor in increasing blood sugar levels as many other factors influence the increase in blood sugar levels. Therefor other anthropometric measurements need to be carried out (Mulyani & Rita, 2016).

Wrist circumference is a strong predictor of diabetes (Jahangiri Noudeh et al., 2013). Wrist circumference is an easily measured anthropometric parameter that can determine body frame and bone size. Increased bone mass will also be associated with hyperinsulinemia (Fitriyanti, Tjahjono, et al., 2019). However, in this study, wrist circumference has no correlation with HOMA-IR. Inconsistent with study conducted by Kusmiyati et al. in 18 years old adolescents, which demonstrates a correlation between wrist circumference and fasting insulin and HOMA-IR in both male and female adolescents (Fitriyanti, Tjahjono, et al., 2019). However, the study conducted by Rumaisha et al. about the correlation of wrist circumference and the blood glucose level among obese women shows no correlation between wrist circumference with fasting blood glucose. Other study conducted at Public Senior High School 6 Semarang also results in no correlation between wrist circumference with fasting blood glucose levels (Arifin & Panunggal, 2014). Factors influencing HOMA-IR values were fasting blood glucose and fasting insulin levels, where higher glucose levels fasting blood means higher the HOMA-IR value in the subject (Mitrea et al., 2013).

The Second to Fourth Digit Ratio (2D:4D) can be used to evaluate prenatal androgen exposure in the postpartum period. The Homeobox genes, HoxA and HoxB, are responsible for urogenital differentiation, prenatal andogen synthesis and fingers development. In animals, prenatal and neonatal androgenic exposure can increase adiposity, insulin resistance, and changes in adipose tissue lipolysis later in adulthood (Yildiz et al., 2015). However, based on this study analysis, the Second to Fourth Digit Ratio (2D:4D) of the right and left hand is not related to HOMA-IR or insulin resistance incidence. This finding is supported by study conducted in Turkey, on the correlation between Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome. It shows that Second to Fourth Digit Ratio (2D:4D) is not related to insulin resistance or the incidence of diabetes mellitus in

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the subject. Researchers state that no available study that reports Second to Fourth Digit Ratio (2D:4D) as predictor of androgen exposure and explains its correlation with metabolic syndrome (Yildiz et al., 2015). Other studies conducted by Abdullahi Yusuf Asuku et al. regarding the correlation of Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome indicators in Nigeria shows the results that Second to Fourth Digit Ratio (2D:4D) of the right and left hand has no correlation with fasting blood sugar levels in the subjects (Asuku et al., 2017). Researchers explain the absence of correlation between Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome indicators is caused by small number of subjects, i.e. 465 subjects, meanwhile this study includes only 120 subjects. This might be there reason of no association found between Second to Fourth Digit Ratio (2D:4D) and the incidence of insulin resistance.

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Conflict of interest - Disclose any potential conflict of interest appropriately.

The authors declare no conflict of interest.

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# Tables and Figures – 1 PAGE 1 TABLE/FIGURE. PLACE ALL TABLES AND FIGURES AT THE END OF THE MANUSCRIPT BODY AFTER THE REFERENCES

Table 1. Characteristic of Subjects.

Variable	Median	Minimum	Maximum
Body weight (kg)	66.6	47.8	107.4
Body height (cm)	157.4	100.5	171.4
Waist circumference (cm)	85.75	80.5	114
Hip circumference (cm)	103.5	30	170
Neck circumference (cm)	32.5	14.5	39
Wrist circumference (cm)	15	13.5	17.5
Thigh circumference (cm)	57.4	31	78.4
Waist Height to Ratio (WHtR)	0.55	0.49	0.95
Waist-hip circumference ratio	0.84	0.6	3.33
(WHR)			
2D:4D digit ratio of the right hand	0.98	0.84	1.09
2D:4D digit ratio of the left hand	0.99	0.52	0.6
HOMA-IR	2.33	0.54	18.32

Table 2. Frequency Distribution.

Category	n	%
Waist circumference		
At risk >80 cm	120	100
Neck circumference		
At risk ≥35.5 cm	13	10.8
Under risk <35.5 cm	107	89.2
Wrist circumference		
At risk ≥16 cm	26	21.7
Under risk <16 cm	94	78.3
Waist Height to Ratio (WHtR)		
At risk ≥0.5	118	98.3
Under risk < 0.5	2	1.7
Waist-hip circumference ratio (WHR)		
At risk ≥0.8	109	90.8
Under risk < 0.8	11	9.2
2D:4D digit ratio of the right hand		
At risk	47	39.2
Under risk	73	60.8
2D:4D digit ratio of the left hand		
At risk	53	44.2
Under risk	67	55.8
HOMA-IR		
Normal	20	16.7
Resistance	100	83.3

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Tabel 3. Correlation of Anthropometric Profile and HOMA-IR.

Variable	r	р
Waist circumference (cm)	0.151	0.1
Neck circumference (cm)	0.271	0.003*
Wrist circumference (cm)	0.12	0.19
Thigh circumference (cm)	0.224	0.014*
Waist Height to Ratio (WHtR)	0.33	<0.001*
Waist-hip circumference ratio (WHR)	-0.019	0.836
2D:4D digit ratio of the right hand	0.139	0.129
2D:4D digit ratio of the left hand	0.169	0.065

Correlation test: Rank-Spearman \*Significant (p<0.05)



Fillah Dieny <fillahdieny@gmail.com>

# Manuscript ID: FR-2021-129

Food Research <foodresearch.my@outlook.com>

2 April 2021 pukul 01.59

Kepada: Fillah Dieny <fillahdieny@gmail.com>, Deni Yudi <denyyudi@gmail.com>, fahmi tsani <fahmi.tsani@gmail.com>

Dear Dr. Fillah Dieny,

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Best regards, Son Radu, PhD Chief Editor

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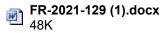
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## Abstract

The prevalence of obesity in adolescent girls is increasing each year. Several anthropometric measurements can be used to detect the incidence of insulin resistance. This study aims to observe the correlation of anthropometric profiles with insulin resistance in adolescent girls with obesity. This was an observational study with a total of 120 female students of Universitas Diponegoro (Undip), aged between 18 and 21 years old, who have waist circumference >80 cm. They were chosen by a simple random sampling technique. Anthropometric profile data taken has consisted of waist circumference, hip circumference, waist-hip circumference ratio (WHR), waist-to-height ratio (WHtR), neck circumference, waist circumference, thigh circumference, and 2D:4D digit ratio. Insulin resistance data was determined using the Homeostasis Model Assessment-Insulin Resistance (HOMA-IR.). Bivariate analysis was completed with the Spearman Rank test. There was 83.3% of subjects who experienced insulin resistance. High WHtR was found in 98.3% of total subjects as many as 90.8% of subjects were at risk based on WHR values. Based on 2D:4D ratio digits, neck circumference, wrist circumference <50% of subjects were found as at risk. There was no correlation between waist circumference, WHR, wrist circumference, 2D:4D digit ratio with HOMA-IR (p>0.05). However, there was a positive correlation between WHtR, neck circumference, and thigh circumference with HOMA-IR (p<0.05). Anthropometric profiles such as WHtR, neck circumference, and thigh circumference were correlated of insulin resistance in female adolescent with obesity.

Keywords: Adolescent; Anthropometric Indicator; Insulin Resistance; Obesity.

# 1. Introduction

Nutritional status in adolescents is very important since adolescence is a transition period from childhood to adulthood. This transition causes biological, psychological and cognitive changes that influence their nutritional status (Brown et al., 2011). However, nutritional status problems in adolescents are still fairly high, including obesity. The Prevalence of central obesity 15 years adolescents and older has increased from 26.6% in 2013 to 31% in 2018 (Badan Penelitian dan Pengembangan Kesehatan, 2018). Obesity incidence will later be associated with degenerative diseases. Women are at higher risk of suffering from degenerative disease, while Indonesian Basic Health Research 2018 results reports the prevalence of stroke, diabetes mellitus, heart disease, and hypertension is found higher in women than men (Badan Penelitian dan Pengembangan Kesehatan, 2018). Indonesian Basic Health Research 2018 results also state hat women and people live in urban areas of all ages have high prevalence of diabetes mellitus (Badan Penelitian dan Pengembangan Kesehatan, 2018).

Type 2 diabetes mellitus is caused by insulin resistance, a condition in which patient's body is unable to absorb glucose (Srikanthan et al., 2016). Study in Semarang City showed that 96.1% of adolescents experienced insulin resistance which was measured by Homeostasis Insulin Resistance Assessment Model (HOMA-IR) (Nuraini, Sulchan and Dieny, 2017). HOMA-IR is a formula for

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calculating insulin resistance based on fasting blood sugar and insulin levels. Its measurement is simple, inexpensive, often used and has been validated by the clamp method (Sumarni, 2017).

One factor causing insulin resistance is central or abdominal obesity as abdominal fat is more actively undergoing lipolysis (Sumarni, 2017). Recently, several measurements of the body's anthropometric profile that can describe the incidence of central obesity are reported, where the measurements are done easily. Central obesity in adolescents can be described generally using measurements of waist circumference and hip waist circumference ratio (WHR). Some studies also mention that waist circumference and WHR have a significant correlation with insulin resistance (Sumarni, 2017).

In addition to waist circumference and WHR, other anthropometric profile measurements are also progressively more used, namely Waist-to-Height Ratio (WHtR). WHtR describes central obesity in adolescents with more accurate results than Body Mass Index (BMI) (Ashwell and Gibson, 2016; Saraswati and Sulchan, 2016; Yang et al., 2017). Study in Mexico demonstrates WHtR as a better tool in identifying cardiometabolic obesity in adolescents used to predict hypertension and insulin resistance (Rodea-Montero, Evia-Viscarra and Apolinar-Jiménez, 2014). Other studies conducted in Semarang also showed the correlation between WHtR and increasing insulin resistance (Asnelviana, Sulchan and Panunggal, 2017).

Wrist circumference can also be utilized as the indicator. Studies conducted in late adolescents in Indonesia, show wrist circumference as one of the anthropometric measurements that can predict obesity and insulin resistance in late adolescents. Wrist circumference reflects bone in the wrist area as well as peripheral fat distribution and metabolism thus it can measure one's body frame and bone size easily (Fitriyanti, Tjahjono, et al., 2019).

Another measurement of anthropometric profiles that can be used to predict metabolic syndrome in adolescents is the measurement of neck circumference. Some studies show correlation between neck circumference with insulin resistance (Liang et al., 2014; Saneei et al., 2019). Neck circumference can represent upper-body subcutaneous adipose tissue that plays a role in predicting insulin resistance and type 2 diabetes (Saneei et al., 2019).

In addition, measurement of thigh circumference can also predict metabolic syndrome in adolescents since it reflects central adiposity (Bando et al., 2017). Results of a study conducted in Korea show that thigh circumference is positively related to insulin resistance (Park et al., 2012). Several studies also explain that thigh circumference is a good indicator in determining type 2 diabetes mellitus 2 (Jung et al., 2013; Ting et al., 2018).

Recently, it has been reported that there are other anthropometric measurements as indicators in predicting metabolic syndrome disease, namely The Ratio of Second to Fourth Digit Length (2D:4D) (Endang Purwaningsih, 2016). The Ratio of the length of the index finger and ring finger (2D:4D) can describe the exposure to the hormone estrogen and prenatal testosterone. A study has shown that a low digit ratio is associated with high testosterone levels in men, while a high digit ratio is associated with low testosterone levels in women (Kumar et al., 2016). The size of digit ratio occurs since the end of the first trimester of fetal development (Oyeyemi et al., 2014). Inappropriate exposure to androgen hormone can cause Polycystic Ovary Syndrome (PCOS), causing infertility in premenopausal women. Women who experience PCOS often have metabolic diseases such as

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hypertension and insulin resistance (White, Jarrett and Komar, 2017). The Study states that digit ratio is correlated with obesity, which is a risk factor for metabolic disease (Gölge et al., 2016). There aren't many studies showing the relationship between digit ratio with insulin resistance.

In this study, we want to find out the portrayal and correlation of anthropometric profiles (waist circumference, WHR, WHtR, wrist circumference, neck circumference, thigh circumference, and second to fourth digit ratio) and insulin resistance in female adolescents with obesity.

#### 2. Materials and methods

#### 2.1 Design, location, and time

This is an observational study and is included within the scope of community nutrition science. This research conducted in Universitas Diponegoro Semarang, Indonesia at 10 Faculties from June until August 2019. There were 1,260 female students who participated in a screening program. The entire study was approved by the Health Study Ethics Committee (KEPK) Faculty of Medicine, Universitas Diponegoro/Central General Hospital dr. Kariadi No. 373/EC/KEPK/FK UNDIP/VIII/2019.

# 2.2 Samplings

Subjects of this study were 120 students from Universitas Diponegoro who were selected through simple random sampling, according to the following inclusion criteria: aged 18-21 years old, had 80 cm or more waist circumference, had intact fingers on both hands, were not currently consuming drugs that could affect the blood glucose and insulin levels, were willing to do fasting for at least 8 hours, did not smoke and/or consume alcohol, were not sick or in the care of a doctor, did not do heavy physical activity or exercise, were not pregnant and breastfeeding, were willing to be the subject of study by filling out informed consent. The exclusion criteria in this study were the subject's withdrawal from the study, the subject's moved to another university, and the subjects passed away within study period.

## 2.3 Data collected

Independent variables in this study were the anthropometric profile consisted of waist circumference, waist-hip circumference ratio (WHR), Waist-Height Ratio (WHtR), neck circumference, wrist circumference, thigh circumference, and the ratio of index finger length and ring finger (2D:4D). The dependent variable in this study was insulin resistance.

Waist circumference data were obtained from waist circumference measurements measured at the midpoint between the iliac crest and costal margins (lower ribs) using a medical measuring tape with 0.1 cm precision/ Subjects used minimal clothing (Yang et al., 2017). Subjects were considered at risk when waist circumference was 80 cm or more (Saklayen, 2018).

WHR data was obtained from the waist circumference to hip circumference ratio. Measurement of pelvic circumference was done by medical measuring tape with 0.1 cm precision. The Pelvic circumference is measured by determining the widest points on the buttock (Fitriyanti, Sulchan, et al., 2019). Subjects are categorized as risky when WHR was more than 0.85 (Saklayen, 2018).

Data on the ratio of waist circumference and height (WHtR) was obtained from measurements of height and waist circumference of the subject. Height was measured using a

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microtoise with 0.01 cm precision. The subject stands without using footwear and accessories above the head. Subjects were considered at risk when WHtR was 0.5 or more (Zhang et al., 2016).

Neck circumference was measured by medical measuring tape with 0.1 cm precision. Its measurements in women were one by subject's upright head position and forward-facing eyes, and then horizontally measured just below the protruding larynx.

Wrist circumference data were measured using medical measuring tape with 0.1 cm precision. Its measurement was done by placing the medical measuring tape horizontally on the distal side of the ulna protrusion, around the wrist. Wrist circumference measurement results were divided into 3 categories: small if subjects whose height less than 155 cm had wrist circumference less than14 cm, subjects whose height 155-163 cm had wrist circumference 15.2 cm, subjects whose height more than 163 cm had wrist circumference less than 15.9 cm; moderate if subjects whose height less than 155 cm had wrist circumference 14-14.6 cm, subjects whose height 155-163 cm had wrist circumference 15.2-15.9 cm, subjects whose height more than 163 cm had wrist circumference 15.9-16.5 cm; large if subjects whose height less than 155 cm had wrist circumference more 14.6 cm, subjects whose height 155-163 cm had wrist circumference more than 15.9 cm, subjects had height more than 163 cm have wrist circumference more than 16.5 cm (Nabila, Widyastuti and Murbawani, 2018).

Thigh circumference was measured by a medical measuring tape. Subjects were standing and wearing as few clothes as possible. Thigh circumference was measured 10 cm above the upper right patella. After that certain point was marked, the tape is placed horizontally and encircles the thigh (Bando et al., 2017).

2D:4D ratio digit data is measured by a caliper with 0.001 mm precision. Measurements were made with the position of the palm of the hand open (Wu et al., 2013). The length of the index finger or second finger is the length of finger measured from the midpoint of the second metacarpophalangeal joint and the most distal point of the second finger. The length of the ring finger or the fourth finger is the length of the finger measured from the midpoint of the fourth metacarpophalangeal joint and the most distal point of the fourth finger. 2D:4D ratio digit data was obtained from the length of the second finger divided by the length of the fourth finger. The ratio digits were considered high when the result shows more than 0.9811 for the right hand and more than 0.9821 for the left hand (Balci et al., 2018). Anthtropometric data was collected by trained personnel.

Insulin resistance data was determined using HOMA-IR values. Measurement of Homeostasis Insulin Resistance Assessment Model (HOMA-IR) based on fasting blood glucose and fasting insulin level with the following formula (Matthews et al., 1985; Levy, Matthews and Hermans, 1998; Torrens et al., 2004):

Fasting Insulin 
$$\left(\frac{mU}{L}\right)$$
 x Fasting Blood Glucose  $\left(\frac{mmol}{L}\right)$ 

Threshold of HOMA-IR value for adolescents is less than 1,65 (Rocco et al., 2011). Blood sampling was collected by health workers. This blood sampling was in collaboration with Sarana Medika laboratory.

# 2.4 Data analysis

Data normality test was performed through Kolmogrov-Smirnov test. We used univariate analysis to describe each variable. Bivariate analysis was completed by Spearman Rank test.

Bivariate analysis was performed to see whether there was a correlation between anthropometric profiles and insulin resistance.

#### 3. Results

Table 1 described the anthropometric profile of the subjects. The median body weight was 66.6 kg. The median waist circumference and pelvic circumference were 85.75 cm and 103.5 cm, respectively, while the median WHR was  $0.84 \pm 0.23$ . Based on table 1, the median neck circumference, wrist circumference, WHtR was 32.5 cm, 15 cm, and 0.55 cm, respectively. The characteristic of the subjects could also be seen in table 2. Table 2 showed that all subjects (100%) had less than 80 cm waist circumference which meant they were at risk of developing metabolic syndrome. Another anthropometric profile showed that 98.3% of subjects (100%) had high WHtR values. Based on WHR, as many as 90.8% of the subjects (100%) were at risk. A total of 100%0 subjects (100%1 kg/s) also experienced insulin resistance as seen from the HOMA-IR value 100%1 cm 100%1 ratio of right hand; 100%2 digit ratio of left hand, showed that less than 100%3 of subjects are at risk (100%3; 100%4 and 100%3 cm 100%4 digit ratio of left hand, showed that less than 100%3 of subjects are at risk (100%3; 100%4 and 100%3 cm 100%4 and 100%4 digit ratio of left hand, showed that less than 100%3 of subjects are at risk (100%3; 100%4 digit ratio of left hand, showed that less than 100%4 digit ratio of left hand, showed that less than 100%4 digit ratio of left hand, showed that less than 100%4 digit ratio of left hand, showed that less than 100%4 digit ratio of left hand, showed that less than 100%4 digit ratio of left hand, showed that less than 100%4 digit ratio of left hand, showed that less than 100%4 digit ratio of left hand, showed that less than 100%6 subjects are at risk (100%6 digit ratio of left hand, showed that less than 100%6 subjects are at risk (100%6 digit ratio of left hand, showed that less than 100%6 subjects are at risk (100%6 digit ratio of left hand, showed that less than 100%6 subjects (100%6 digit ratio of left hand)

The correlation of anthropometric profile and insulin resistance incidence determined by HOMA-IR was shown in Table 3. Anthropometric profiles having a significant correlation with HOMA-IR were neck circumference (r=0.271; p=0.003), WHtR (r=0.33; p<0.001) and thigh circumference (r=0.224; p=0.014). Based on the analysis, higher the value of the neck circumference, thigh circumference, and WHtR, higher the HOMA-IR score. Table 3 also showed that waist circumference had no correlation with HOMA-IR (r=0.151; p=0.1). There was also no correlation between wrist circumference and HOMA-IR (r=0.12; p=0.19). In addition, there was no correlation between WHR and HOMA-IR in the study subjects (r=-0.019; p=0.836). Based on the analysis, other anthropometric profiles having no correlation with HOMA-IR were 2D:4D right hand digit ratios (r=0.139; p=0.129) and 2D:4D left hand digit ratios (r=0.169; p=0.065).

# 4. Discussion

Late adolescents, especially women, have the risk of experiencing metabolic syndrome. Based on this study results, 83.3% of subjects experience insulin resistance determined by HOMA-IR. Since 2007, the Genome Wide Association Studies (GWAS) have identified around 88 loci associated with the risk of developing type 2 diabetes mellitus where most of the loci are related to insulin secretion and pancreatic beta cell function, causing insulin resistance associated with obesity (Brown and Walker, 2016). Study conducted in Semarang City also showed that 96.1% of subjects experienced insulin resistance determined by HOMA-IR (Nuraini, Sulchan and Dieny, 2017).

More than 50% of subjects of this study have high WHtR and WHR values. The study conducted in Jepara shows that 26.94% of adolescents experience abdominal obesity as seen from WHtR values of above 0.45 (Azizah and Sulchan, 2016). Other study conducted at the Faculty of Medicine Universitas Riau demonstrates that 44.1% students experience central obesity as seen in the ratio waist-hip circumference (Jannah, Bebasari and Ernalia, 2015). For women of reproductive age, fat storage is centralized in certain areas to protect important reproductive organs. This increases the risk of high WHR in women (Jannah, Bebasari and Ernalia, 2015).

Based on the analysis, neck circumference has a significant correlation with Homeostasis Model Assessment for Insulin Resistance (HOMA-IR), where the greater the neck circumference of the

subject, the higher HOMA-IR value. A Study in China shows that neck circumference has a significant correlation with insulin resistance assessed by HOMA-IR (Liang et al., 2014). Previous case studies in Public Senior High School 2 Semarang and Public Junior High School 9 Semarang also stated that neck circumference has a significant correlation with fasting blood sugar (Mayasari and Wirawanni, 2014).

Neck circumference is an easy anthropometric measurement. It can reflect the central obesity index and is associated with several cardiovascular risk factors such as dyslipidemia, hypertension, hyperuricemia, and insulin resistance. It is also considered an estimation of upper-body subcutaneous adipose tissue which plays a role in predicting insulin resistance and type-2 diabetes (Nabila, Widyastuti and Murbawani, 2018). The release of excess free fatty acids associated with upper-body subcutaneous fat, explicitly the neck, can be one mechanism to explain the correlation between neck circumference and insulin resistance (Ebbert and Jensen, 2013).

Lipolytic function and releasing rate of free fatty acids in upper body subcutaneous fat is found higher than lower body subcutaneous fat. Excessive free fatty acids in muscles and other tissues induce the body to use more free fatty acids as energy. They will also inhibit glucose oxidation, causing insulin resistance (Ebbert and Jensen, 2013). Increased free fatty acids also play a role in increasing VLDL production and inhibition of insulin clearance which induces insulin resistance. In addition, neck circumference is also positively correlated with A total fat body and visceral fat which are related to biological parameters of insulin resistance. Two perivascular ectopic fat depots are also found in the neck region. Adipokine secretion, such as leptin, adiponectin, and interleukin-6, from perivascular ectopic fat depots causes metabolic dysfunction including insulin resistance (Saneei et al., 2019).

Subjects with large neck circumferences have a greater risk for obesity (Saneei et al., 2019). Subcutaneous fat has a major role in the association of insulin resistance and obesity (Sri Yuliani, Subagio and Murbawani, 2017). Insulin resistance is an important complication of obesity which causes hyperglycemia and impaired glycemic parameters (Saneei et al., 2019).

Waist to Height Ratio (WHtR) is a good predictor in determining insulin resistance in the individual with obesity (Jamar et al., 2017). Based on the analysis, WHtR has a correlation with HOMA-IR, where the greater the WHtR score, the greater the value of HOMA-IR. A study conducted in Australia on the correlation of WHtR and metabolic syndrome in adolescents and children with obesity, results in a correlation between WHtR and HOMA-IR (Nambiar et al., 2013). Other studies conducted in Korea also find that high WHtR values in obese adolescents would affect the incidence of insulin resistance measured by HOMA-IR (Lim et al., 2015).

WHtR plays a role in measuring central obesity which is often associated with metabolic disorders. An Increase in fat tissue will promote increase in adipokine secretion. This can increase insulin resistance. The most important adipokines is TNF- $\alpha$  which plays a role in inducing insulin resistance through glucose transporter 4 (GLUT-4) and increasing the release of free fatty acids. Increased transfer of free fatty acids to muscles results in increased intracellular fatty acid metabolites such as diacylglycerol, ceramide, and acetyl-CoA. These metabolites will activate the serine pathway or threonine kinase that reduces the ability to activate insulin receptors. Hence, it can cause insulin resistance when occurs in the long term it can damage visceral adipocyte  $\beta$  cells (Asnelviana, Sulchan and Panunggal, 2017).

Based on the statistical test results, we find a correlation between thigh circumference and insulin resistance as measured by HOMA-IR. This finding is in line with the study conducted in Korea which shows the result that thigh circumference is positively related to HOMA-IR. The greater the

thigh circumference, the greater the risk of insulin resistance (Park et al., 2012). Another study in Korea explains that the measurement of thigh circumference is an indicator of diabetes marker (Jung et al., 2013). The study conducted in Taiwan also shows the left thigh circumference is a significant predictor of determining type 2 diabetes mellitus 2 (Ting et al., 2018). Large thigh circumference not only indicates greater muscle mass, but also an increase in femoral subcutaneous fat mass. Lower muscle mass and subcutaneous fat in The thigh are associated with insulin resistance which results in hyperglycemia and diabetes (Ting et al., 2018). Subcutaneous fat in the thighs is a metabolism of circulating fatty acids that are circulating because there is a difference in lipolysis activity between subcutaneous fat in the abdomen and thighs. Subcutaneous fat in the thigh is wasting the metabolism of circulatory fatty acids as there is a difference between lipolysis activity of abdominal and thigh subcutaneous fat. Subcutaneous fat of the thigh tends to take fatty acids from the bloodstream, thus preventing the liver, pancreas, and ectopic fat such as the muscles from being exposed to high fatty acids (Nugraha et al., 2019).

Based on the study analysis, no correlation is found between neither waist circumference nor waist-hip circumference ratio with insulin resistance. This finding is contradictory to a study conducted on adolescents in Korea which shows the results that waist circumference and waist-hip circumference ratio have a significant correlation to HOMA-IR (Lim et al., 2015). Waist circumference and waist-hip circumference ratio can be used as a screening tool to detect the incidence of abdominal obesity which can cause metabolic disorders such as insulin resistance (Fitriyanti, Sulchan, et al., 2019).

However, a study conducted in Manado about the correlation of waist circumference and blood sugar levels shows no correlation between waist circumference and blood sugar levels among teachers at the Middle School and High School Eben Haezar Christian Manado. Other study held in Ngawi also shows no correlation between waist circumference and blood sugar levels in early adulthood (Manungkalit, Kusnanto and Purbosari, 2015). Several other studies, including a study conducted at the Pusti Pidie Health Center, show no correlation between waist circumference ratio pelvis and blood sugar among Community Health Center's employees (Mulyani and Rita, 2016). The study states that the ratio of waist-hip circumference is not an extremely decisive factor in increasing blood sugar levels as many other factors influence the increase in blood sugar levels. Therefore other anthropometric measurements need to be carried out (Mulyani and Rita, 2016).

Wrist circumference is a strong predictor of diabetes (Noudeh et al., 2013). Wrist circumference is an easily measured anthropometric parameter that can determine body frame and bone size. Increased bone mass will also be associated with hyperinsulinemia (Fitriyanti, Tjahjono, et al., 2019). However, in this study, wrist circumference does not correlate with HOMA-IR. Inconsistent with the study conducted by Kusmiyati et al. in 18 years old adolescents, which demonstrates a correlation between wrist circumference and fasting insulin and HOMA-IR in both male and female adolescents (Fitriyanti, Tjahjono, et al., 2019). However, the study conducted by Nabila et al. about the correlation of wrist circumference and the blood glucose level among obese women shows no correlation between wrist circumference with fasting blood glucose (Nabila, Widyastuti and Murbawani, 2018). Another study conducted at Public Senior High School 6 Semarang also results in no correlation between wrist circumference with fasting blood glucose levels (Arifin and Panunggal, 2014). Factors influencing HOMA-IR values were fasting blood glucose and fasting insulin levels, where higher glucose levels fasting blood means higher the HOMA-IR value in the subject (Mitrea et al., 2013).

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The Second to Fourth Digit Ratio (2D:4D) can be used to evaluate prenatal androgen exposure in the postpartum period. The Homeobox genes, HoxA and HoxB, are responsible for urogenital differentiation, prenatal androgen synthesis and fingers development. In animals, prenatal and neonatal androgenic exposure can increase adiposity, insulin resistance, and changes in adipose tissue lipolysis later in adulthood (Yildiz et al., 2015). However, based on this study analysis, the Second to Fourth Digit Ratio (2D:4D) of the right and left hand is not related to HOMA-IR or insulin resistance incidence. This finding is supported by study conducted in Turkey, on the correlation between Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome. It shows that the Second to Fourth Digit Ratio (2D:4D) is not related to insulin resistance or the incidence of diabetes mellitus in the subject. Researchers state that no available study that reports Second to Fourth Digit Ratio (2D:4D) as a predictor of androgen exposure and explains its correlation with metabolic syndrome (Yildiz et al., 2015). Other studies conducted by Abdullahi Yusuf Asuku et al. regarding the correlation of Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome indicators in Nigeria shows the results that Second to Fourth Digit Ratio (2D:4D) of the right and left hand has no correlation with fasting blood sugar levels in the subjects (Asuku et al., 2017). Researchers explain the absence of correlation between Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome indicators is caused by the small number of subjects, i.e. 465 subjects, meanwhile this study includes only 120 subjects. This might be there reason for no association found between the Second to Fourth Digit Ratio (2D:4D) and the incidence of insulin resistance.

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# Conflict of interest - Disclose any potential conflict of interest appropriately.

The authors declare no conflict of interest.

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Variable	Median	Minimum	Maximum
Body weight (kg)	66.6	47.8	107.4
Body height (cm)	157.4	100.5	171.4
Waist circumference (cm)	85.75	80.5	114
Hip circumference (cm)	103.5	30	170
Neck circumference (cm)	32.5	14.5	39
Wrist circumference (cm)	15	13.5	17.5
Thigh circumference (cm)	57.4	31	78.4
Waist Height to Ratio (WHtR)	0.55	0.49	0.95
Waist-hip circumference ratio	0.84	0.6	3.33
(WHR)			
2D:4D digit ratio of the right hand	0.98	0.84	1.09
2D:4D digit ratio of the left hand	0.99	0.52	0.6
HOMA-IR	2.33	0.54	18.32

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Table 2. Frequency Distribution.

Category	n	%
Waist circumference		
At risk >80 cm	120	100
Neck circumference		
At risk ≥35.5 cm	13	10.8
Under risk <35.5 cm	107	89.2
Wrist circumference		
At risk ≥16 cm	26	21.7
Under risk <16 cm	94	78.3
Waist Height to Ratio (WHtR)		
At risk ≥0.5	118	98.3
Under risk < 0.5	2	1.7
Waist-hip circumference ratio (WHR)		
At risk ≥0.8	109	90.8
Under risk < 0.8	11	9.2
2D:4D digit ratio of the right hand		
At risk	47	39.2
Under risk	73	60.8
2D:4D digit ratio of the left hand		
At risk	53	44.2
Under risk	67	55.8
HOMA-IR		
Normal	20	16.7
Resistance	100	83.3

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Tabel 3. Correlation of Anthropometric Profile and HOMA-IR.

Variable	r	р
Waist circumference (cm)	0.151	0.100
Neck circumference (cm)	0.271	0.003*
Wrist circumference (cm)	0.12	0.190
Thigh circumference (cm)	0.224	0.014*
Waist Height to Ratio (WHtR)	0.33	<0.001*
Waist-hip circumference ratio (WHR)	-0.019	0.836
2D:4D digit ratio of the right hand	0.139	0.129
2D:4D digit ratio of the left hand	0.169	0.065

Correlation test: Rank-Spearman \*Significant (p<0.05)

## Abstract

 The prevalence of obesity in adolescent girls is increasing each year. Several anthropometric measurements can be used to detect the incidence of insulin resistance. This study aims to observe the correlation of anthropometric profiles with insulin resistance in adolescent girls with obesity. This was an observational study with a total of 120 female students of Universitas Diponegoro (Undip), aged between 18 and 21 years old, who have waist circumference >80 cm. They were chosen by a simple random sampling technique. Anthropometric profile data taken has consisted of waist circumference, hip circumference, waist-hip circumference ratio (WHR), waist-to-height ratio (WHtR), neck circumference, waist circumference, thigh circumference, and 2D:4D digit ratio. Insulin resistance data was determined using the Homeostasis Model Assessment-Insulin Resistance (HOMA-IR.). Bivariate analysis was completed with the Spearman Rank test. There was 83.3% of subjects who experienced insulin resistance. High WHtR was found in 98.3% of total subjects as many as 90.8% of subjects were at risk based on WHR values. Based on 2D:4D ratio digits, neck circumference, wrist circumference <50% of subjects were found as at risk. There was no correlation between waist circumference, WHR, wrist circumference, 2D:4D digit ratio with HOMA-IR (p>0.05). However, there was a positive correlation between WHtR, neck circumference, and thigh circumference with HOMA-IR (p<0.05). Anthropometric profiles such as WHtR, neck circumference, and thigh circumference were correlated of insulin resistance in female adolescent with obesity.

Keywords: Adolescent; Anthropometric Indicator; Insulin Resistance; Obesity.

# 1. Introduction

Nutritional status in adolescents is very important since adolescence is a transition period from childhood to adulthood. This transition causes biological, psychological and cognitive changes that influence their nutritional status (Brown, 2011). However, nutritional status problems in adolescents are still fairly high, including obesity. The Prevalence of central obesity 15 years adolescents and older has increased from 26.6% in 2013 to 31% in 2018 (Badan Penelitian dan Pengembangan Kesehatan, 2018). Obesity incidence will later be associated with degenerative diseases. Women are at higher risk of suffering from degenerative disease, while Indonesian Basic Health Research 2018 results reports the prevalence of stroke, diabetes mellitus, heart disease, and hypertension is found higher in women than men (Badan Penelitian dan Pengembangan Kesehatan, 2018). Indonesian Basic Health Research 2018 results also state hat women and people live in urban areas of all ages have high prevalence of diabetes mellitus (Badan Penelitian dan Pengembangan Kesehatan, 2018).

Type 2 diabetes mellitus is caused by insulin resistance, a condition in which patient's body is unable to absorb glucose (Srikanthan *et al.*, 2016). Study in Semarang City showed that 96.1% of adolescents experienced insulin resistance which was measured by Homeostasis Insulin Resistance Assessment Model (HOMA-IR) (Nuraini, *et al.*, 2017). HOMA-IR is a formula for calculating insulin resistance based on fasting blood sugar and insulin levels. Its measurement is simple, inexpensive, often used and has been validated by the clamp method (Sumarni, 2017).

One factor causing insulin resistance is central or abdominal obesity as abdominal fat is more actively undergoing lipolysis (Sumarni, 2017). Recently, several measurements of the body's anthropometric profile that can describe the incidence of central obesity are reported, where the measurements are done easily. Central obesity in adolescents can be described generally using measurements of waist circumference and hip waist circumference ratio (WHR). Some studies also mention that waist circumference and WHR have a significant correlation with insulin resistance (Sumarni, 2017).

In addition to waist circumference and WHR, other anthropometric profile measurements are also progressively more used, namely Waist-to-Height Ratio (WHtR). WHtR describes central obesity in adolescents with more accurate results than Body Mass Index (BMI) (Ashwell and Gibson, 2016; Saraswati and Sulchan, 2016; Yang et al., 2017). Study in Mexico demonstrates WHtR as a better tool in identifying cardiometabolic obesity in adolescents used to predict hypertension and insulin resistance (Rodea-Montero, et al., 2014). Other studies conducted in Semarang also showed the correlation between WHtR and increasing insulin resistance (Asnelviana, et al., 2017).

Wrist circumference can also be utilized as the indicator. Studies conducted in late adolescents in Indonesia, show wrist circumference as one of the anthropometric measurements that can predict obesity and insulin resistance in late adolescents. Wrist circumference reflects bone in the wrist area as well as peripheral fat distribution and metabolism thus it can measure one's body frame and bone size easily (Fitriyanti, et al., 2019).

Another measurement of anthropometric profiles that can be used to predict metabolic syndrome in adolescents is the measurement of neck circumference. Some studies show correlation between neck circumference with insulin resistance (Liang *et al.*, 2014). Neck circumference can represent upper-body subcutaneous adipose tissue that plays a role in predicting insulin resistance and type 2 diabetes (Saneei *et al.*, 2019).

In addition, measurement of thigh circumference can also predict metabolic syndrome in adolescents since it reflects central adiposity (Bando *et al.*, 2017). Results of a study conducted in Korea show that thigh circumference is positively related to insulin resistance (Park *et al.*, 2012). Several studies also explain that thigh circumference is a good indicator in determining type 2 diabetes mellitus 2 (Jung *et al.*, 2013; Ting *et al.*, 2018).

Recently, it has been reported that there are other anthropometric measurements as indicators in predicting metabolic syndrome disease, namely The Ratio of Second to Fourth Digit Length (2D:4D) (Purwaningsih, 2016). The Ratio of the length of the index finger and ring finger (2D:4D) can describe the exposure to the hormone estrogen and prenatal testosterone. A study has shown that a low digit ratio is associated with high testosterone levels in men, while a high digit ratio is associated with low testosterone levels in women (Kumar *et al.*, 2016). The size of digit ratio occurs since the end of the first trimester of fetal development (Oyeyemi *et al.*, 2014). Inappropriate exposure to androgen hormone can cause Polycystic Ovary Syndrome (PCOS), causing infertility in premenopausal women. Women who experience PCOS often have metabolic diseases such as hypertension and insulin resistance (White, *et al.*, 2017). The Study states that digit ratio is correlated with obesity, which is a risk factor for metabolic disease (Gölge *et al.*, 2016). There aren't many studies showing the relationship between digit ratio with insulin resistance.

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In this study, we want to find out the portrayal and correlation of anthropometric profiles (waist circumference, WHR, WHtR, wrist circumference, neck circumference, thigh circumference, and second to fourth digit ratio) and insulin resistance in female adolescents with obesity.

# 2. Materials and methods

## 2.1 Design, location, and time

This is an observational study and is included within the scope of community nutrition science. This research conducted in Universitas Diponegoro Semarang, Indonesia at 10 Faculties from June until August 2019. There were 1,260 female students who participated in a screening program. The entire study was approved by the Health Study Ethics Committee (KEPK) Faculty of Medicine, Universitas Diponegoro/Central General Hospital dr. Kariadi No. 373/EC/KEPK/FK UNDIP/VIII/2019.

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## 2.2 Samplings

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Subjects of this study were 120 students from Universitas Diponegoro who were selected through simple random sampling, according to the following inclusion criteria: aged 18-21 years old, had 80 cm or more waist circumference, had intact fingers on both hands, were not currently consuming drugs that could affect the blood glucose and insulin levels, were willing to do fasting for at least 8 hours, did not smoke and/or consume alcohol, were not sick or in the care of a doctor, did not do heavy physical activity or exercise, were not pregnant and breastfeeding, were willing to be the subject of study by filling out informed consent. The exclusion criteria in this study were the subject's withdrawal from the study, the subject's moved to another university, and the subjects passed away within study period.

# 2.3 Data collected

Independent variables in this study were the anthropometric profile consisted of waist circumference, waist-hip circumference ratio (WHR), Waist-Height Ratio (WHtR), neck circumference, wrist circumference, thigh circumference, and the ratio of index finger length and ring finger (2D:4D). The dependent variable in this study was insulin resistance.

Waist circumference data were obtained from waist circumference measurements measured at the midpoint between the iliac crest and costal margins (lower ribs) using a medical measuring tape with 0.1 cm precision. Subjects used minimal clothing (Yang et al., 2017). Subjects were considered at risk when waist circumference was 80 cm or more (Saklayen, 2018).

WHR data was obtained from the waist circumference to hip circumference ratio. Measurement of pelvic circumference was done by medical measuring tape with 0.1 cm precision. The Pelvic circumference is measured by determining the widest points on the buttock (Fitriyanti, et al., 2019). Subjects are categorized as risky when WHR was more than 0.85 (Saklayen, 2018).

Data on the ratio of waist circumference and height (WHtR) was obtained from measurements of height and waist circumference of the subject. Height was measured using a microtoise with 0.01 cm precision. The subject stands without using footwear and accessories above the head. Subjects were considered at risk when WHtR was 0.5 or more (Zhang et al., 2016).

Neck circumference was measured by medical measuring tape with 0.1 cm precision. Its measurements in women were one by subject's upright head position and forward-facing eyes, and then horizontally measured just below the protruding larynx.

Wrist circumference data were measured using medical measuring tape with 0.1 cm precision. Its measurement was done by placing the medical measuring tape horizontally on the distal side of the ulna protrusion, around the wrist. Wrist circumference measurement results were divided into 3 categories: small if subjects whose height less than 155 cm had wrist circumference less than14 cm, subjects whose height 155-163 cm had wrist circumference 15.2 cm, subjects whose height more than 163 cm had wrist circumference less than 15.9 cm; moderate if subjects whose height less than 155 cm had wrist circumference 14-14.6 cm, subjects whose height 155-163 cm had wrist circumference 15.9-16.5 cm; large if subjects whose height less than 155 cm had wrist circumference more 14.6 cm, subjects whose height 155-163 cm had wrist circumference more than 15.9 cm, subjects had height more than 163 cm have wrist circumference more than 16.5 cm (Nabila, et al., 2018).

Thigh circumference was measured by a medical measuring tape. Subjects were standing and wearing as few clothes as possible. Thigh circumference was measured 10 cm above the upper right patella. After that certain point was marked, the tape is placed horizontally and encircles the thigh (Bando *et al.*, 2017).

2D:4D ratio digit data is measured by a caliper with 0.001 mm precision. Measurements were made with the position of the palm of the hand open (Wu et al., 2013). The length of the index finger or second finger is the length of finger measured from the midpoint of the second metacarpophalangeal joint and the most distal point of the second finger. The length of the ring finger or the fourth finger is the length of the finger measured from the midpoint of the fourth metacarpophalangeal joint and the most distal point of the fourth finger. 2D:4D ratio digit data was obtained from the length of the second finger divided by the length of the fourth finger. The ratio digits were considered high when the result shows more than 0.9811 for the right hand and more than 0.9821 for the left hand (Balci et al., 2018). Anthtropometric data was collected by trained personnel.

Insulin resistance data was determined using HOMA-IR values. Measurement of Homeostasis Insulin Resistance Assessment Model (HOMA-IR) based on fasting blood glucose and fasting insulin level with the following formula (Matthews *et al.*, 1985; Levy, *et al.*, 1998; Torréns *et al.*, 2004):

$$\frac{Fasting\; Insulin\; \left(\frac{mU}{L}\right)x\; Fasting\; Blood\; Glucose\; (\frac{mmol}{L})}{22.5}$$

Threshold of HOMA-IR value for adolescents is less than 1,65 (Rocco *et al.*, 2011). Blood sampling was collected by health workers. This blood sampling was in collaboration with Sarana Medika laboratory.

# 2.4 Data analysis

Data normality test was performed through Kolmogrov-Smirnov test. We used univariate analysis to describe each variable. Bivariate analysis was completed by Spearman Rank test. Bivariate analysis was performed to see whether there was a correlation between anthropometric profiles and insulin resistance.

# 3. Results

Table 1 described the anthropometric profile of the subjects. The median body weight was 66.6 kg. The median waist circumference and pelvic circumference were 85.75 cm and 103.5 cm, respectively, while the median WHR was  $0.84 \pm 0.23$ . Based on table 1, the median neck circumference, wrist circumference, WHtR was 32.5 cm, 15 cm, and 0.55 cm, respectively. The characteristic of the subjects could also be seen in table 2. Table 2 showed that all subjects (100%) had less than 80 cm waist circumference which meant they were at risk of developing metabolic syndrome. Another anthropometric profile showed that 98.3% of subjects (100%) had high WHtR values. Based on WHR, as many as 100%0 of the subjects (100%1) were at risk. A total of 100%1 subjects (100%2) also experienced insulin resistance as seen from the HOMA-IR value 100%2. However, anthropometric profiles, specifically neck circumference, wrist circumference, 100%2 digit ratio of left hand, showed that less than 100%3 of subjects are at risk (100%3; 100%3 and 100%3 and 100%3 are respectively).

The correlation of anthropometric profile and insulin resistance incidence determined by HOMA-IR was shown in Table 3. Anthropometric profiles having a significant correlation with HOMA-IR were neck circumference (r=0.271; p=0.003), WHtR (r=0.33; p <0.001) and thigh circumference (r=0.224; p=0.014). Based on the analysis, higher the value of the neck circumference, thigh circumference, and WHtR, higher the HOMA-IR score. Table 3 also showed that waist circumference had no correlation with HOMA-IR (r=0.151; p=0.1). There was also no correlation between wrist circumference and HOMA-IR (r=0.12; p=0.19). In addition, there was no correlation between WHR and HOMA-IR in the study subjects (r=-0.019; p=0.836). Based on the analysis, other anthropometric profiles having no correlation with HOMA-IR were 2D:4D right hand digit ratios (r=0.139; p=0.129) and 2D:4D left hand digit ratios (r=0.169; p=0.065).

## 4. Discussion

Late adolescents, especially women, have the risk of experiencing metabolic syndrome. Based on this study results, 83.3% of subjects experience insulin resistance determined by HOMA-IR. Since 2007, the Genome Wide Association Studies (GWAS) have identified around 88 loci associated with the risk of developing type 2 diabetes mellitus where most of the loci are related to insulin secretion and pancreatic beta cell function, causing insulin resistance associated with obesity (Brown and Walker, 2016). Study conducted in Semarang City also showed that 96.1% of subjects experienced insulin resistance determined by HOMA-IR (Nuraini, et al., 2017).

More than 50% of subjects of this study have high WHtR and WHR values. The study conducted in Jepara shows that 26.94% of adolescents experience abdominal obesity as seen from WHtR values of above 0.45 (Azizah and Sulchan, 2016). Other study conducted at the Faculty of Medicine Universitas Riau demonstrates that 44.1% students experience central obesity as seen in the ratio waist-hip circumference (Jannah, et al., 2015). For women of reproductive age, fat storage is centralized in certain areas to protect important reproductive organs. This increases the risk of high WHR in women (Jannah, et al., 2015).

Based on the analysis, neck circumference has a significant correlation with Homeostasis Model Assessment for Insulin Resistance (HOMA-IR), where the greater the neck circumference of the subject, the higher HOMA-IR value. A Study in China shows that neck circumference has a significant correlation with insulin resistance assessed by HOMA-IR (Liang et al., 2014). Previous case studies in Public Senior High School 2 Semarang and Public Junior High School 9 Semarang also stated that neck circumference has a significant correlation with fasting blood sugar (Mayasari and Wirawanni, 2014).

Neck circumference is an easy anthropometric measurement. It can reflect the central obesity index and is associated with several cardiovascular risk factors such as dyslipidemia, hypertension, hyperuricemia, and insulin resistance. It is also considered an estimation of upper-body subcutaneous adipose tissue which plays a role in predicting insulin resistance and type-2 diabetes (Nabila, et al., 2018). The release of excess free fatty acids associated with upper-body subcutaneous fat, explicitly the neck, can be one mechanism to explain the correlation between neck circumference and insulin resistance (Ebbert and Jensen, 2013).

Lipolytic function and releasing rate of free fatty acids in upper body subcutaneous fat is found higher than lower body subcutaneous fat. Excessive free fatty acids in muscles and other tissues induce the body to use more free fatty acids as energy. They will also inhibit glucose oxidation, causing insulin resistance (Ebbert and Jensen, 2013). Increased free fatty acids also play a role in increasing VLDL production and inhibition of insulin clearance which induces insulin resistance. In addition, neck circumference is also positively correlated with A total fat body and visceral fat which are related to biological parameters of insulin resistance. Two perivascular ectopic fat depots are also found in the neck region. Adipokine secretion, such as leptin, adiponectin, and interleukin-6, from perivascular ectopic fat depots causes metabolic dysfunction including insulin resistance (Saneei *et al.*, 2019).

Subjects with large neck circumferences have a greater risk for obesity (Saneei *et al.*, 2019). Subcutaneous fat has a major role in the association of insulin resistance and obesity (Yuliani, *et al.* Insulin resistance is an important complication of obesity which causes hyperglycemia and impaired glycemic parameters (Saneei *et al.*, 2019).

Waist to Height Ratio (WHtR) is a good predictor in determining insulin resistance in the individual with obesity (Jamar *et al.*, 2017). Based on the analysis, WHtR has a correlation with HOMA-IR, where the greater the WHtR score, the greater the value of HOMA-IR. A study conducted in Australia on the correlation of WHtR and metabolic syndrome in adolescents and children with obesity, results in a correlation between WHtR and HOMA-IR (Nambiar *et al.*, 2013). Other studies conducted in Korea also find that high WHtR values in obese adolescents would affect the incidence of insulin resistance measured by HOMA-IR (Lim *et al.*, 2015).

WHtR plays a role in measuring central obesity which is often associated with metabolic disorders. An Increase in fat tissue will promote increase in adipokine secretion. This can increase insulin resistance. The most important adipokines is TNF- $\alpha$  which plays a role in inducing insulin resistance through glucose transporter 4 (GLUT-4) and increasing the release of free fatty acids. Increased transfer of free fatty acids to muscles results in increased intracellular fatty acid metabolites such as diacylglycerol, ceramide, and acetyl-CoA. These metabolites will activate the serine pathway or threonine kinase that reduces the ability to activate insulin receptors. Hence, it can cause insulin resistance when occurs in the long term it can damage visceral adipocyte  $\beta$  cells (Asnelviana, et al., 2017).

Based on the statistical test results, we find a correlation between thigh circumference and insulin resistance as measured by HOMA-IR. This finding is in line with the study conducted in Korea which shows the result that thigh circumference is positively related to HOMA-IR. The greater the thigh circumference, the greater the risk of insulin resistance (Park et al., 2012). Another study in Korea explains that the measurement of thigh circumference is an indicator of diabetes marker (Jung et al., 2013). The study conducted in Taiwan also shows the left thigh circumference is a significant predictor of determining type 2 diabetes mellitus 2 (Ting et al., 2018). Large thigh circumference not

only indicates greater muscle mass, but also an increase in femoral subcutaneous fat mass. Lower muscle mass and subcutaneous fat in The thigh are associated with insulin resistance which results in hyperglycemia and diabetes (Ting *et al.*, 2018). Subcutaneous fat in the thighs is a metabolism of circulating fatty acids that are circulating because there is a difference in lipolysis activity between subcutaneous fat in the abdomen and thighs. Subcutaneous fat in the thigh is wasting the metabolism of circulatory fatty acids as there is a difference between lipolysis activity of abdominal and thigh subcutaneous fat. Subcutaneous fat of the thigh tends to take fatty acids from the bloodstream, thus preventing the liver, pancreas, and ectopic fat such as the muscles from being exposed to high fatty acids (Nugraha *et al.*, 2019).

Based on the study analysis, no correlation is found between neither waist circumference nor waist-hip circumference ratio with insulin resistance. This finding is contradictory to a study conducted on adolescents in Korea which shows the results that waist circumference and waist-hip circumference ratio have a significant correlation to HOMA-IR (Lim *et al.*, 2015). Waist circumference and waist-hip circumference ratio can be used as a screening tool to detect the incidence of abdominal obesity which can cause metabolic disorders such as insulin resistance (Fitriyanti, *et al.*, 2019).

However, a study conducted in Manado about the correlation of waist circumference and blood sugar levels shows no correlation between waist circumference and blood sugar levels among teachers at the Middle School and High School Eben Haezar Christian Manado. Other study held in Ngawi also shows no correlation between waist circumference and blood sugar levels in early adulthood (Manungkalit, et al., 2015). Several other studies, including a study conducted at the Pusti Pidie Health Center, show no correlation between waist circumference ratio pelvis and blood sugar among Community Health Center's employees (Mulyani and Rita, 2016). The study states that the ratio of waist-hip circumference is not an extremely decisive factor in increasing blood sugar levels as many other factors influence the increase in blood sugar levels. Therefore other anthropometric measurements need to be carried out (Mulyani and Rita, 2016).

Wrist circumference is a strong predictor of diabetes (Noudeh *et al.*, 2013). Wrist circumference is an easily measured anthropometric parameter that can determine body frame and bone size. Increased bone mass will also be associated with hyperinsulinemia (Fitriyanti, *et al.*, 2019) However, in this study, wrist circumference does not correlate with HOMA-IR. Inconsistent with the study conducted by Kusmiyati et al. in 18 years old adolescents, which demonstrates a correlation between wrist circumference and fasting insulin and HOMA-IR in both male and female adolescents (Fitriyanti, *et al.*, 2019). However, the study conducted by Nabila et al. about the correlation of wrist circumference and the blood glucose level among obese women shows no correlation between wrist circumference with fasting blood glucose (Nabila, *et al.*, 2018). Another study conducted at Public Senior High School 6 Semarang also results in no correlation between wrist circumference with fasting blood glucose levels (Arifin and Panunggal, 2014). Factors influencing HOMA-IR values were fasting blood glucose and fasting insulin levels, where higher glucose levels fasting blood means higher the HOMA-IR value in the subject (Mitrea *et al.*, 2013).

The Second to Fourth Digit Ratio (2D:4D) can be used to evaluate prenatal androgen exposure in the postpartum period. The Homeobox genes, HoxA and HoxB, are responsible for urogenital differentiation, prenatal androgen synthesis and fingers development. In animals, prenatal and neonatal androgenic exposure can increase adiposity, insulin resistance, and changes in adipose tissue lipolysis later in adulthood (Yıldız et al., 2015). However, based on this study analysis, the

Second to Fourth Digit Ratio (2D:4D) of the right and left hand is not related to HOMA-IR or insulin resistance incidence. This finding is supported by study conducted in Turkey, on the correlation between Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome. It shows that the Second to Fourth Digit Ratio (2D:4D) is not related to insulin resistance or the incidence of diabetes mellitus in the subject. Researchers state that no available study that reports Second to Fourth Digit Ratio (2D:4D) as a predictor of androgen exposure and explains its correlation with metabolic syndrome (Yıldız et al., 2015). Other studies conducted by Abdullahi Yusuf Asuku et al. regarding the correlation of Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome indicators in Nigeria shows the results that Second to Fourth Digit Ratio (2D:4D) of the right and left hand has no correlation with fasting blood sugar levels in the subjects (Asuku et al., 2017). Researchers explain the absence of correlation between Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome indicators is caused by the small number of subjects, i.e. 465 subjects, meanwhile this study includes only 120 subjects. This might be there reason for no association found between the Second to Fourth Digit Ratio (2D:4D) and the incidence of insulin resistance.

#### Conflict of interest - Disclose any potential conflict of interest appropriately.

The authors declare no conflict of interest.

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## Tables and Figures – 1 PAGE 1 TABLE/FIGURE. PLACE ALL TABLES AND FIGURES AT THE END OF THE MANUSCRIPT BODY AFTER THE REFERENCES

Table 1. Characteristic of Subjects.

Variable	Median	Minimum	Maximum
Body weight (kg)	66.6	47.8	107.4
Body height (cm)	157.4	100.5	171.4
Waist circumference (cm)	85.75	80.5	114
Hip circumference (cm)	103.5	30	170
Neck circumference (cm)	32.5	14.5	39
Wrist circumference (cm)	15	13.5	17.5
Thigh circumference (cm)	57.4	31	78.4
Waist Height to Ratio (WHtR)	0.55	0.49	0.95
Waist-hip circumference ratio	0.84	0.6	3.33
(WHR)			
2D:4D digit ratio of the right hand	0.98	0.84	1.09
2D:4D digit ratio of the left hand	0.99	0.52	0.6
HOMA-IR	2.33	0.54	18.32

Table 2. Frequency Distribution.

Category	n	%
Waist circumference		
At risk >80 cm	120	100
Neck circumference		
At risk ≥35.5 cm	13	10.8
Under risk <35.5 cm	107	89.2
Wrist circumference		
At risk ≥16 cm	26	21.7
Under risk <16 cm	94	78.3
Waist Height to Ratio (WHtR)		
At risk ≥0.5	118	98.3
Under risk <0.5	2	1.7
Waist-hip circumference ratio (WHR)		
At risk ≥0.8	109	90.8
Under risk <0.8	11	9.2
2D:4D digit ratio of the right hand		
At risk	47	39.2
Under risk	73	60.8
2D:4D digit ratio of the left hand		
At risk	53	44.2
Under risk	67	55.8
HOMA-IR		
Normal	20	16.7
Resistance	100	83.3

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Tabel 3. Correlation of Anthropometric Profile and HOMA-IR.

Variable	r	р
Waist circumference (cm)	0.151	0.100
Neck circumference (cm)	0.271	0.003*
Wrist circumference (cm)	0.12	0.190
Thigh circumference (cm)	0.224	0.014*
Waist Height to Ratio (WHtR)	0.33	<0.001*
Waist-hip circumference ratio (WHR)	-0.019	0.836
2D:4D digit ratio of the right hand	0.139	0.129
2D:4D digit ratio of the left hand	0.169	0.065

Correlation test: Rank-Spearman \*Significant (p<0.05)

#### Anthropometric Profile and Its Correlation to Insulin Resistance in Female Students with Obesity

#### Abstract

The prevalence of obesity in adolescent girls is increasing each year. Several anthropometric measurements can be used to detect the incidence of insulin resistance. This study aims to observe the correlation of anthropometric profiles with insulin resistance in adolescent girls with obesity. This was an observational study with a total of 120 female students of Universitas Diponegoro (Undip), aged between 18 and 21 years old, who have waist circumference >80 cm. They were chosen by a simple random sampling technique. Anthropometric profile data taken has consisted of waist circumference, hip circumference, waist-hip circumference ratio (WHR), waist-to-height ratio (WHtR), neck circumference, waist circumference, thigh circumference, and 2D:4D digit ratio. Insulin resistance data was determined using the Homeostasis Model Assessment-Insulin Resistance (HOMA-IR.). Bivariate analysis was completed with the Spearman Rank test. There was 83.3% of subjects who experienced insulin resistance. High WHtR was found in 98.3% of total subjects as many as 90.8% of subjects were at risk based on WHR values. Based on 2D:4D ratio digits, neck circumference, wrist circumference <50% of subjects were found as at risk. There was no correlation between waist circumference, WHR, wrist circumference, 2D:4D digit ratio with HOMA-IR (p>0.05). However, there was a positive correlation between WHtR, neck circumference, and thigh circumference with HOMA-IR (p<0.05). Anthropometric profiles such as WHtR, neck circumference, and thigh circumference were correlated of insulin resistance in female adolescent with obesity.

**Keywords:** Adolescent; Anthropometric Indicator; Insulin Resistance; Obesity.

## 1. Introduction

Nutritional status in adolescents is very important since adolescence is a transition period from childhood to adulthood. This transition causes biological, psychological and cognitive changes that influence their nutritional status (Brown et al., 2011). However, nutritional status problems in adolescents are still fairly high, including obesity. The Prevalence of central obesity 15 years adolescents and older has increased from 26.6% in 2013 to 31% in 2018 (Badan Penelitian dan Pengembangan Kesehatan, 2018). Obesity incidence will later be associated with degenerative diseases. Women are at higher risk of suffering from degenerative disease, while Indonesian Basic Health Research 2018 results reports the prevalence of stroke, diabetes mellitus, heart disease, and hypertension is found higher in women than men (Badan Penelitian dan Pengembangan Kesehatan, 2018). Indonesian Basic Health Research 2018 results also state hat women and people live in urban areas of all ages have high prevalence of diabetes mellitus (Badan Penelitian dan Pengembangan Kesehatan, 2018).

Type 2 diabetes mellitus is caused by insulin resistance, a condition in which patient's body is unable to absorb glucose (Srikanthan et al., 2016). Study in Semarang City showed that 96.1% of adolescents experienced insulin resistance which was measured by Homeostasis Insulin Resistance Assessment Model (HOMA-IR) (Nuraini, Sulchan and Dieny, 2017). HOMA-IR is a formula for

calculating insulin resistance based on fasting blood sugar and insulin levels. Its measurement is simple, inexpensive, often used and has been validated by the clamp method (Sumarni, 2017).

One factor causing insulin resistance is central or abdominal obesity as abdominal fat is more actively undergoing lipolysis (Sumarni, 2017). Recently, several measurements of the body's anthropometric profile that can describe the incidence of central obesity are reported, where the measurements are done easily. Central obesity in adolescents can be described generally using measurements of waist circumference and hip waist circumference ratio (WHR). Some studies also mention that waist circumference and WHR have a significant correlation with insulin resistance (Sumarni, 2017).

In addition to waist circumference and WHR, other anthropometric profile measurements are also progressively more used, namely Waist-to-Height Ratio (WHtR). WHtR describes central obesity in adolescents with more accurate results than Body Mass Index (BMI) (Ashwell and Gibson, 2016; Saraswati and Sulchan, 2016; Yang et al., 2017). Study in Mexico demonstrates WHtR as a better tool in identifying cardiometabolic obesity in adolescents used to predict hypertension and insulin resistance (Rodea-Montero, Evia-Viscarra and Apolinar-Jiménez, 2014). Other studies conducted in Semarang also showed the correlation between WHtR and increasing insulin resistance (Asnelviana, Sulchan and Panunggal, 2017).

Wrist circumference can also be utilized as the indicator. Studies conducted in late adolescents in Indonesia, show wrist circumference as one of the anthropometric measurements that can predict obesity and insulin resistance in late adolescents. Wrist circumference reflects bone in the wrist area as well as peripheral fat distribution and metabolism thus it can measure one's body frame and bone size easily (Fitriyanti, Tjahjono, et al., 2019).

Another measurement of anthropometric profiles that can be used to predict metabolic syndrome in adolescents is the measurement of neck circumference. Some studies show correlation between neck circumference with insulin resistance (Liang et al., 2014; Saneei et al., 2019). Neck circumference can represent upper-body subcutaneous adipose tissue that plays a role in predicting insulin resistance and type 2 diabetes (Saneei et al., 2019).

In addition, measurement of thigh circumference can also predict metabolic syndrome in adolescents since it reflects central adiposity (Bando et al., 2017). Results of a study conducted in Korea show that thigh circumference is positively related to insulin resistance (Park et al., 2012). Several studies also explain that thigh circumference is a good indicator in determining type 2 diabetes mellitus 2 (Jung et al., 2013; Ting et al., 2018).

Recently, it has been reported that there are other anthropometric measurements as indicators in predicting metabolic syndrome disease, namely The Ratio of Second to Fourth Digit Length (2D:4D) (Endang Purwaningsih, 2016). The Ratio of the length of the index finger and ring finger (2D:4D) can describe the exposure to the hormone estrogen and prenatal testosterone. A study has shown that a low digit ratio is associated with high testosterone levels in men, while a high digit ratio is associated with low testosterone levels in women (Kumar et al., 2016). The size of digit ratio occurs since the end of the first trimester of fetal development (Oyeyemi et al., 2014). Inappropriate exposure to androgen hormone can cause Polycystic Ovary Syndrome (PCOS), causing infertility in premenopausal women. Women who experience PCOS often have metabolic diseases such as

hypertension and insulin resistance (White, Jarrett and Komar, 2017). The Study states that digit ratio is correlated with obesity, which is a risk factor for metabolic disease (Gölge et al., 2016). There aren't many studies showing the relationship between digit ratio with insulin resistance.

In this study, we want to find out the portrayal and correlation of anthropometric profiles (waist circumference, WHR, WHtR, wrist circumference, neck circumference, thigh circumference, and second to fourth digit ratio) and insulin resistance in female adolescents with obesity.

## 2. Materials and methods

## 2.1 Design, location, and time

This is an observational study and is included within the scope of community nutrition science. This research conducted in Universitas Diponegoro Semarang, Indonesia at 10 Faculties from June until August 2019. There were 1,260 female students who participated in a screening program. The entire study was approved by the Health Study Ethics Committee (KEPK) Faculty of Medicine, Universitas Diponegoro/Central General Hospital dr. Kariadi No. 373/EC/KEPK/FK UNDIP/VIII/2019.

## 2.2 Samplings

Subjects of this study were 120 students from Universitas Diponegoro who were selected through simple random sampling, according to the following inclusion criteria: aged 18-21 years old, had 80 cm or more waist circumference, had intact fingers on both hands, were not currently consuming drugs that could affect the blood glucose and insulin levels, were willing to do fasting for at least 8 hours, did not smoke and/or consume alcohol, were not sick or in the care of a doctor, did not do heavy physical activity or exercise, were not pregnant and breastfeeding, were willing to be the subject of study by filling out informed consent. The exclusion criteria in this study were the subject's withdrawal from the study, the subject's moved to another university, and the subjects passed away within study period.

## 2.3 Data collected

Independent variables in this study were the anthropometric profile consisted of waist circumference, waist-hip circumference ratio (WHR), Waist-Height Ratio (WHtR), neck circumference, wrist circumference, thigh circumference, and the ratio of index finger length and ring finger (2D:4D). The dependent variable in this study was insulin resistance.

Waist circumference data were obtained from waist circumference measurements measured at the midpoint between the iliac crest and costal margins (lower ribs) using a medical measuring tape with 0.1 cm precision/ Subjects used minimal clothing (Yang et al., 2017). Subjects were considered at risk when waist circumference was 80 cm or more (Saklayen, 2018).

WHR data was obtained from the waist circumference to hip circumference ratio. Measurement of pelvic circumference was done by medical measuring tape with 0.1 cm precision. The Pelvic circumference is measured by determining the widest points on the buttock (Fitriyanti, Sulchan, et al., 2019). Subjects are categorized as risky when WHR was more than 0.85 (Saklayen, 2018).

Data on the ratio of waist circumference and height (WHtR) was obtained from measurements of height and waist circumference of the subject. Height was measured using a

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microtoise with 0.01 cm precision. The subject stands without using footwear and accessories above the head. Subjects were considered at risk when WHtR was 0.5 or more (Zhang et al., 2016).

Neck circumference was measured by medical measuring tape with 0.1 cm precision. Its measurements in women were one by subject's upright head position and forward-facing eyes, and then horizontally measured just below the protruding larynx.

Wrist circumference data were measured using medical measuring tape with 0.1 cm precision. Its measurement was done by placing the medical measuring tape horizontally on the distal side of the ulna protrusion, around the wrist. Wrist circumference measurement results were divided into 3 categories: small if subjects whose height less than 155 cm had wrist circumference less than14 cm, subjects whose height 155-163 cm had wrist circumference 15.2 cm, subjects whose height more than 163 cm had wrist circumference less than 15.9 cm; moderate if subjects whose height less than 155 cm had wrist circumference 14-14.6 cm, subjects whose height 155-163 cm had wrist circumference 15.2-15.9 cm, subjects whose height more than 163 cm had wrist circumference 15.9-16.5 cm; large if subjects whose height less than 155 cm had wrist circumference more 14.6 cm, subjects whose height 155-163 cm had wrist circumference more than 15.9 cm, subjects had height more than 163 cm have wrist circumference more than 16.5 cm (Nabila, Widyastuti and Murbawani, 2018).

Thigh circumference was measured by a medical measuring tape. Subjects were standing and wearing as few clothes as possible. Thigh circumference was measured 10 cm above the upper right patella. After that certain point was marked, the tape is placed horizontally and encircles the thigh (Bando et al., 2017).

2D:4D ratio digit data is measured by a caliper with 0.001 mm precision. Measurements were made with the position of the palm of the hand open (Wu et al., 2013). The length of the index finger or second finger is the length of finger measured from the midpoint of the second metacarpophalangeal joint and the most distal point of the second finger. The length of the ring finger or the fourth finger is the length of the finger measured from the midpoint of the fourth metacarpophalangeal joint and the most distal point of the fourth finger. 2D:4D ratio digit data was obtained from the length of the second finger divided by the length of the fourth finger. The ratio digits were considered high when the result shows more than 0.9811 for the right hand and more than 0.9821 for the left hand (Balci et al., 2018). Anthtropometric data was collected by trained personnel.

Insulin resistance data was determined using HOMA-IR values. Measurement of Homeostasis Insulin Resistance Assessment Model (HOMA-IR) based on fasting blood glucose and fasting insulin level with the following formula (Matthews et al., 1985; Levy, Matthews and Hermans, 1998; Torrens et al., 2004):

Fasting Insulin 
$$\left(\frac{mU}{L}\right)x$$
 Fasting Blood Glucose  $\left(\frac{mmol}{L}\right)$ 

Threshold of HOMA-IR value for adolescents is less than 1,65 (Rocco et al., 2011). Blood sampling was collected by health workers. This blood sampling was in collaboration with Sarana Medika laboratory.

## 2.4 Data analysis

Data normality test was performed through Kolmogrov-Smirnov test. We used univariate analysis to describe each variable. Bivariate analysis was completed by Spearman Rank test.

Bivariate analysis was performed to see whether there was a correlation between anthropometric profiles and insulin resistance.

## 3. Results

Table 1 described the anthropometric profile of the subjects. The median body weight was 66.6 kg. The median waist circumference and pelvic circumference were 85.75 cm and 103.5 cm, respectively, while the median WHR was 0.84 ± 0.23. Based on table 1, the median neck circumference, wrist circumference, WHtR was 32.5 cm, 15 cm, and 0.55 cm, respectively. The characteristic of the subjects could also be seen in table 2. Table 2 showed that all subjects (100%) had less than 80 cm waist circumference which meant they were at risk of developing metabolic syndrome. Another anthropometric profile showed that 98.3% of subjects (n=118) had high WHtR values. Based on WHR, as many as 90.8% of the subjects (n=108) were at risk. A total of 83.3% subjects (n=100) also experienced insulin resistance as seen from the HOMA-IR value >1.65. However, anthropometric profiles, specifically neck circumference, wrist circumference, 2D:4D digit ratio of right hand; 2D:4D digit ratio of left hand, showed that less than 50% of subjects are at risk (10.8%; 21.7%; 39.2%; 44.2% respectively).

The correlation of anthropometric profile and insulin resistance incidence determined by HOMA-IR was shown in Table 3. Anthropometric profiles having a significant correlation with HOMA-IR were neck circumference (r=0.271; p=0.003), WHtR (r=0.33; p<0.001) and thigh circumference (r=0.224; p=0.014). Based on the analysis, higher the value of the neck circumference, thigh circumference, and WHtR, higher the HOMA-IR score. Table 3 also showed that waist circumference had no correlation with HOMA-IR (r=0.151; p=0.1). There was also no correlation between wrist circumference and HOMA-IR (r=0.12; p=0.19). In addition, there was no correlation between WHR and HOMA-IR in the study subjects (r=-0.019; p=0.836). Based on the analysis, other anthropometric profiles having no correlation with HOMA-IR were 2D:4D right hand digit ratios (r=0.139; p=0.129) and 2D:4D left hand digit ratios (r=0.169; p=0.065).

## 4. Discussion

Late adolescents, especially women, have the risk of experiencing metabolic syndrome. Based on this study results, 83.3% of subjects experience insulin resistance determined by HOMA-IR. Since 2007, the Genome Wide Association Studies (GWAS) have identified around 88 loci associated with the risk of developing type 2 diabetes mellitus where most of the loci are related to insulin secretion and pancreatic beta cell function, causing insulin resistance associated with obesity (Brown and Walker, 2016). Study conducted in Semarang City also showed that 96.1% of subjects experienced insulin resistance determined by HOMA-IR (Nuraini, Sulchan and Dieny, 2017).

More than 50% of subjects of this study have high WHtR and WHR values. The study conducted in Jepara shows that 26.94% of adolescents experience abdominal obesity as seen from WHtR values of above 0.45 (Azizah and Sulchan, 2016). Other study conducted at the Faculty of Medicine Universitas Riau demonstrates that 44.1% students experience central obesity as seen in the ratio waist-hip circumference (Jannah, Bebasari and Ernalia, 2015). For women of reproductive age, fat storage is centralized in certain areas to protect important reproductive organs. This increases the risk of high WHR in women (Jannah, Bebasari and Ernalia, 2015).

Based on the analysis, neck circumference has a significant correlation with Homeostasis Model Assessment for Insulin Resistance (HOMA-IR), where the greater the neck circumference of the

subject, the higher HOMA-IR value. A Study in China shows that neck circumference has a significant correlation with insulin resistance assessed by HOMA-IR (Liang et al., 2014). Previous case studies in Public Senior High School 2 Semarang and Public Junior High School 9 Semarang also stated that neck circumference has a significant correlation with fasting blood sugar (Mayasari and Wirawanni, 2014).

Neck circumference is an easy anthropometric measurement. It can reflect the central obesity index and is associated with several cardiovascular risk factors such as dyslipidemia, hypertension, hyperuricemia, and insulin resistance. It is also considered an estimation of upper-body subcutaneous adipose tissue which plays a role in predicting insulin resistance and type-2 diabetes (Nabila, Widyastuti and Murbawani, 2018). The release of excess free fatty acids associated with upper-body subcutaneous fat, explicitly the neck, can be one mechanism to explain the correlation between neck circumference and insulin resistance (Ebbert and Jensen, 2013).

Lipolytic function and releasing rate of free fatty acids in upper body subcutaneous fat is found higher than lower body subcutaneous fat. Excessive free fatty acids in muscles and other tissues induce the body to use more free fatty acids as energy. They will also inhibit glucose oxidation, causing insulin resistance (Ebbert and Jensen, 2013). Increased free fatty acids also play a role in increasing VLDL production and inhibition of insulin clearance which induces insulin resistance. In addition, neck circumference is also positively correlated with A total fat body and visceral fat which are related to biological parameters of insulin resistance. Two perivascular ectopic fat depots are also found in the neck region. Adipokine secretion, such as leptin, adiponectin, and interleukin-6, from perivascular ectopic fat depots causes metabolic dysfunction including insulin resistance (Saneei et al., 2019).

Subjects with large neck circumferences have a greater risk for obesity (Saneei et al., 2019). Subcutaneous fat has a major role in the association of insulin resistance and obesity (Sri Yuliani, Subagio and Murbawani, 2017). Insulin resistance is an important complication of obesity which causes hyperglycemia and impaired glycemic parameters (Saneei et al., 2019).

Waist to Height Ratio (WHtR) is a good predictor in determining insulin resistance in the individual with obesity (Jamar et al., 2017). Based on the analysis, WHtR has a correlation with HOMA-IR, where the greater the WHtR score, the greater the value of HOMA-IR. A study conducted in Australia on the correlation of WHtR and metabolic syndrome in adolescents and children with obesity, results in a correlation between WHtR and HOMA-IR (Nambiar et al., 2013). Other studies conducted in Korea also find that high WHtR values in obese adolescents would affect the incidence of insulin resistance measured by HOMA-IR (Lim et al., 2015).

WHtR plays a role in measuring central obesity which is often associated with metabolic disorders. An Increase in fat tissue will promote increase in adipokine secretion. This can increase insulin resistance. The most important adipokines is TNF- $\alpha$  which plays a role in inducing insulin resistance through glucose transporter 4 (GLUT-4) and increasing the release of free fatty acids. Increased transfer of free fatty acids to muscles results in increased intracellular fatty acid metabolites such as diacylglycerol, ceramide, and acetyl-CoA. These metabolites will activate the serine pathway or threonine kinase that reduces the ability to activate insulin receptors. Hence, it can cause insulin resistance when occurs in the long term it can damage visceral adipocyte  $\beta$  cells (Asnelviana, Sulchan and Panunggal, 2017).

Based on the statistical test results, we find a correlation between thigh circumference and insulin resistance as measured by HOMA-IR. This finding is in line with the study conducted in Korea which shows the result that thigh circumference is positively related to HOMA-IR. The greater the

thigh circumference, the greater the risk of insulin resistance (Park et al., 2012). Another study in Korea explains that the measurement of thigh circumference is an indicator of diabetes marker (Jung et al., 2013). The study conducted in Taiwan also shows the left thigh circumference is a significant predictor of determining type 2 diabetes mellitus 2 (Ting et al., 2018). Large thigh circumference not only indicates greater muscle mass, but also an increase in femoral subcutaneous fat mass. Lower muscle mass and subcutaneous fat in The thigh are associated with insulin resistance which results in hyperglycemia and diabetes (Ting et al., 2018). Subcutaneous fat in the thighs is a metabolism of circulating fatty acids that are circulating because there is a difference in lipolysis activity between subcutaneous fat in the abdomen and thighs. Subcutaneous fat in the thigh is wasting the metabolism of circulatory fatty acids as there is a difference between lipolysis activity of abdominal and thigh subcutaneous fat. Subcutaneous fat of the thigh tends to take fatty acids from the bloodstream, thus preventing the liver, pancreas, and ectopic fat such as the muscles from being exposed to high fatty acids (Nugraha et al., 2019).

Based on the study analysis, no correlation is found between neither waist circumference nor waist-hip circumference ratio with insulin resistance. This finding is contradictory to a study conducted on adolescents in Korea which shows the results that waist circumference and waist-hip circumference ratio have a significant correlation to HOMA-IR (Lim et al., 2015). Waist circumference and waist-hip circumference ratio can be used as a screening tool to detect the incidence of abdominal obesity which can cause metabolic disorders such as insulin resistance (Fitriyanti, Sulchan, et al., 2019).

However, a study conducted in Manado about the correlation of waist circumference and blood sugar levels shows no correlation between waist circumference and blood sugar levels among teachers at the Middle School and High School Eben Haezar Christian Manado. Other study held in Ngawi also shows no correlation between waist circumference and blood sugar levels in early adulthood (Manungkalit, Kusnanto and Purbosari, 2015). Several other studies, including a study conducted at the Pusti Pidie Health Center, show no correlation between waist circumference ratio pelvis and blood sugar among Community Health Center's employees (Mulyani and Rita, 2016). The study states that the ratio of waist-hip circumference is not an extremely decisive factor in increasing blood sugar levels as many other factors influence the increase in blood sugar levels. Therefore other anthropometric measurements need to be carried out (Mulyani and Rita, 2016).

Wrist circumference is a strong predictor of diabetes (Noudeh et al., 2013). Wrist circumference is an easily measured anthropometric parameter that can determine body frame and bone size. Increased bone mass will also be associated with hyperinsulinemia (Fitriyanti, Tjahjono, et al., 2019). However, in this study, wrist circumference does not correlate with HOMA-IR. Inconsistent with the study conducted by Kusmiyati et al. in 18 years old adolescents, which demonstrates a correlation between wrist circumference and fasting insulin and HOMA-IR in both male and female adolescents (Fitriyanti, Tjahjono, et al., 2019). However, the study conducted by Nabila et al. about the correlation of wrist circumference and the blood glucose level among obese women shows no correlation between wrist circumference with fasting blood glucose (Nabila, Widyastuti and Murbawani, 2018). Another study conducted at Public Senior High School 6 Semarang also results in no correlation between wrist circumference with fasting blood glucose levels (Arifin and Panunggal, 2014). Factors influencing HOMA-IR values were fasting blood glucose and fasting insulin levels, where higher glucose levels fasting blood means higher the HOMA-IR value in the subject (Mitrea et al., 2013).

The Second to Fourth Digit Ratio (2D:4D) can be used to evaluate prenatal androgen exposure in the postpartum period. The Homeobox genes, HoxA and HoxB, are responsible for urogenital differentiation, prenatal androgen synthesis and fingers development. In animals, prenatal and neonatal androgenic exposure can increase adiposity, insulin resistance, and changes in adipose tissue lipolysis later in adulthood (Yildiz et al., 2015). However, based on this study analysis, the Second to Fourth Digit Ratio (2D:4D) of the right and left hand is not related to HOMA-IR or insulin resistance incidence. This finding is supported by study conducted in Turkey, on the correlation between Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome. It shows that the Second to Fourth Digit Ratio (2D:4D) is not related to insulin resistance or the incidence of diabetes mellitus in the subject. Researchers state that no available study that reports Second to Fourth Digit Ratio (2D:4D) as a predictor of androgen exposure and explains its correlation with metabolic syndrome (Yildiz et al., 2015). Other studies conducted by Abdullahi Yusuf Asuku et al. regarding the correlation of Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome indicators in Nigeria shows the results that Second to Fourth Digit Ratio (2D:4D) of the right and left hand has no correlation with fasting blood sugar levels in the subjects (Asuku et al., 2017). Researchers explain the absence of correlation between Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome indicators is caused by the small number of subjects, i.e. 465 subjects, meanwhile this study includes only 120 subjects. This might be there reason for no association found between the Second to Fourth Digit Ratio (2D:4D) and the incidence of insulin resistance.

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## Conflict of interest - Disclose any potential conflict of interest appropriately.

The authors declare no conflict of interest.

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# Tables and Figures – 1 PAGE 1 TABLE/FIGURE. PLACE ALL TABLES AND FIGURES AT THE END OF THE MANUSCRIPT BODY AFTER THE REFERENCES

Table 1. Characteristic of Subjects.

Variable	Median	Minimum	Maximum
Body weight (kg)	66.6	47.8	107.4
Body height (cm)	157.4	100.5	171.4
Waist circumference (cm)	85.75	80.5	114

Hip circumference (cm)	103.5	30	170
Neck circumference (cm)	32.5	14.5	39
Wrist circumference (cm)	15	13.5	17.5
Thigh circumference (cm)	57.4	31	78.4
Waist Height to Ratio (WHtR)	0.55	0.49	0.95
Waist-hip circumference ratio	0.84	0.6	3.33
(WHR)			
2D:4D digit ratio of the right hand	0.98	0.84	1.09
2D:4D digit ratio of the left hand	0.99	0.52	0.6
HOMA-IR	2.33	0.54	18.32

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**Table 2. Frequency Distribution.** 

Category	n	%
Waist circumference		
At risk >80 cm	120	100
Neck circumference		
At risk ≥35.5 cm	13	10.8
Under risk <35.5 cm	107	89.2
Wrist circumference		
At risk ≥16 cm	26	21.7
Under risk <16 cm	94	78.3
Waist Height to Ratio (WHtR)		
At risk ≥0.5	118	98.3
Under risk < 0.5	2	1.7
Waist-hip circumference ratio (WHR)		
At risk ≥0.8	109	90.8
Under risk < 0.8	11	9.2
2D:4D digit ratio of the right hand		
At risk	47	39.2
Under risk	73	60.8
2D:4D digit ratio of the left hand		
At risk	53	44.2
Under risk	67	55.8
HOMA-IR		
Normal	20	16.7
Resistance	100	83.3

Tabel 3. Correlation of Anthropometric Profile and HOMA-IR.

Variable	r	р
Waist circumference (cm)	0.151	0.100
Neck circumference (cm)	0.271	0.003*
Wrist circumference (cm)	0.12	0.190
Thigh circumference (cm)	0.224	0.014*
Waist Height to Ratio (WHtR)	0.33	<0.001*
Waist-hip circumference ratio (WHR)	-0.019	0.836

2D:4D digit ratio of the right hand	0.139	0.129
2D:4D digit ratio of the left hand	0.169	0.065

Correlation test: Rank-Spearman

<sup>\*</sup>Significant (p<0.05)



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Fillah Dieny <fillahdieny@gmail.com>
Kepada: Food Research <foodresearch.my@outlook.com>

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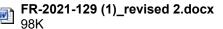
## Dear Editorial Board FR

Here We send attached revised manuscript with the title **Anthropometric Profile and Its Correlation to Insulin Resistance in Female Students with Obesity.** We hope this article can be processed further. Thank you

## Fillah Fithra Dieny

Department of Nutrition Science
Faculty of Medicine, Diponegoro University
JI Prof Soedharto SH, Tembalang. Semarang 50275, Central Java, Indonesia.
Phone/Fax (024) 845-37-08/ HP +62856-4020-4747
Website: www.gizi.undip.ac.id

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## Manuscript ID: FR-2021-129

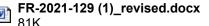
Fillah Dieny <fillahdieny@gmail.com> Kepada: Food Research <foodresearch.my@outlook.com> 5 April 2021 pukul 13.04

Dear Editorial Board Food Research Team

Here We send attached revised manuscript with the title Anthropometric Profile and Its Correlation to Insulin **Resistance in Female Students with Obesity.** We hope this article can be processed further. Thank you Fillah Fithra Dieny

Department of Nutrition Science Faculty of Medicine, Diponegoro University JI Prof Soedharto SH, Tembalang. Semarang 50275, Central Java, Indonesia. Phone/Fax (024) 845-37-08/ HP +62856-4020-4747 Website: www.gizi.undip.ac.id

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## Manuscript ID: FR-2021-129

Food Research <foodresearch.my@outlook.com> Kepada: Fillah Dieny <fillahdieny@gmail.com>

9 April 2021 pukul 15.12

Dear Dr. Fillah Dieny,

Thank you for the revised copy of your manuscript. We will contact you again for further processing.

Best regards, Son Radu, PhD **Chief Editor** 

From: Fillah Dieny <fillahdieny@gmail.com>

Sent: Thursday, 8 April, 2021 9:06 PM

To: Food Research < foodresearch.my@outlook.com>

Subject: Re: Manuscript ID: FR-2021-129

## Dear Editorial Board FR

Here We send attached revised manuscript with the title Anthropometric Profile and Its Correlation to Insulin **Resistance in Female Students with Obesity.** We hope this article can be processed further. Thank you

## Fillah Fithra Dieny

Department of Nutrition Science Faculty of Medicine, Diponegoro University JI Prof Soedharto SH, Tembalang. Semarang 50275, Central Java, Indonesia. Phone/Fax (024) 845-37-08/ HP +62856-4020-4747

Website: www.gizi.undip.ac.id

Pada tanggal Sen, 5 Apr 2021 pukul 23.55 Food Research <foodresearch.my@outlook.com> menulis:

Dear Dr. Fillah Dieny,

Please revise the manuscript according to the comments raised in the file attached.

Adhering strictly to Food Research format is greatly appreciated.

Kindly revert to us at your earliest convenience.

Best regards, Son Radu, PhD Chief Editor

From: Fillah Dieny <fillahdieny@gmail.com>

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To: Food Research <foodresearch.my@outlook.com>

Subject: Re: Manuscript ID: FR-2021-129



28th June 2021

Dear Dr Dieny, F.F.

#### **ACCEPTANCE LETTER**

Food Research, is pleased to inform you that the following manuscript has been accepted for publication in Food Research journal.

Manuscript Title : Anthropometric profile and its correlation to insulin resistance in

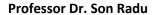
female students with obesity

Authors : Dieny, F.F., Fitranti, D.Y., Jauharany, F.F., Tsani, A.F.A., Faradila, U. and

Rose, S.

We thank you for your fine contribution to the Food Research journal and encourage you to submit other articles to the Journal.

Yours sincerely,



**Chief Editor** 

Food Research







## FR-2021-129 - Decision on your manuscript

Food Research <foodresearch.my@outlook.com> Kepada: Fillah Dieny <fillahdieny@gmail.com>

28 Juni 2021 pukul 19.28

Dear Dr Dieny,

It is a pleasure to accept your manuscript for publication in Food Research journal. Please refer to the attachment for your acceptance letter. I will contact you again once the galley proof is ready for viewing and approval.

Thank you for your fine contribution. We look forward to your continued contributions to the Journal.

Sincerely, Dr Vivian New Editor Food Research

From: Food Research < foodresearch.my@outlook.com >

Sent: Friday, 9 April, 2021 4:12 PM

To: Fillah Dieny <fillahdieny@gmail.com> Subject: Re: Manuscript ID: FR-2021-129

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Department of Nutrition Science Faculty of Medicine, Diponegoro University JI Prof Soedharto SH, Tembalang. Semarang 50275, Central Java, Indonesia. Phone/Fax (024) 845-37-08/ HP +62856-4020-4747

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## Re: FR-2021-129 - Article Production

Food Research <foodresearch.my@outlook.com> Kepada: Fillah Dieny <fillahdieny@gmail.com>

29 Januari 2022 pukul 10.14

Dear Dr Dieny,

Please refer to the attachment for the galley proof of your manuscript FR-2021-129 entitled 'Anthropometric profile and its correlation to insulin resistance in female students with obesity'. Please check the content of the galley proof. If there are any mistakes, please comment and highlight in the PDF itself and revert to us within two (2) days of receipt. Once we have finalized the PDF version, your manuscript will be published online for early viewing.

Please see the attachment for the invoice INV22028. We hope that you can make the payment as soon as possible before 19 February 2022 for us to complete the publication of your manuscript. The manuscript information e.g. volume, issue, page numbers and DOI, will be provided once we have received the payment.

Thanks & Regards, Vivian New Editor Food Research

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Sent: Monday, 28 June, 2021 8:28 PM To: Fillah Dieny <fillahdieny@gmail.com>

Subject: FR-2021-129 - Decision on your manuscript

Dear Dr Dieny,

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Sent: Friday, 9 April, 2021 4:12 PM

To: Fillah Dieny <fillahdieny@gmail.com> Subject: Re: Manuscript ID: FR-2021-129

Dear Dr. Fillah Dieny,

## Food Research (2022): pp - pp

Journal homepage: https://www.myfoodresearch.com



# Anthropometric profile and its correlation to insulin resistance in female students with obesity

<sup>1,2,\*</sup>Dieny, F.F., <sup>1,2</sup>Fitranti, D.Y., <sup>1</sup>Jauharany, F.F., <sup>1,2</sup>Tsani, A.F.A., <sup>1</sup>Faradila, U. and <sup>1</sup>Rose, S.

<sup>1</sup>Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia <sup>2</sup>CENURE (Center of Nutrition Research), Universitas Diponegoro, Semarang, Indonesia

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Adolescent, Anthropometric Indicator, Insulin Resistance, Obesity.

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## Abstract

The prevalence of obesity in adolescent girls is increasing each year. Several anthropometric measurements can be used to detect the incidence of insulin resistance. This study was aimed to observe the correlation of anthropometric profiles with insulin resistance in adolescent girls with obesity. This was an observational study with a total of 120 female students of Universitas Diponegoro (Undip), aged between 18 and 21 years old, who have waist circumference >80 cm. They were chosen by a simple random sampling technique. Anthropometric profile data taken has consisted of waist circumference, hip circumference, waist-hip circumference ratio (WHR), waist-to-height ratio (WHtR), neck circumference, waist circumference, thigh circumference, and 2D:4D digit ratio. Insulin resistance data was determined using the Homeostasis Model Assessment-Insulin Resistance (HOMA-IR.). Bivariate analysis was completed with the Spearman rank test. There was 83.3% of subjects who experienced insulin resistance. High WHtR was found in 98.3% of total subjects as many as 90.8% of subjects were at risk based on WHR values. Based on 2D:4D ratio digits, neck circumference, wrist circumference <50% of subjects were found as at risk. There was no correlation between waist circumference, WHR, wrist circumference, 2D:4D digit ratio with HOMA-IR (p>0.05). However, there was a positive correlation between WHtR, neck circumference, and thigh circumference with HOMA-IR (p<0.05). Anthropometric profiles such as WHtR, neck circumference, and thigh circumference were correlated with insulin resistance in female adolescent with obesity.

## 1. Introduction

Nutritional status in adolescents is very important since adolescence is a transition period from childhood adulthood. This transition causes biological, psychological and cognitive changes that influence their nutritional status (15, 7n, 2011). However, nutritional status problems in adolescents are still fairly high, including obesity. The prevalence of central obesity 15 years adolescents and older has increased from 26.6% in 2013 to 31% in 2018 (Badan Penelitian dan Pengembangan Kesehatan, 2018). Obesity incidence will later be associated with degenerative diseases. Women are at higher risk of suffering from degenerative disease, while Indonesian Basic Health Research 2018 results report the prevalence of stroke, diabetes mellitus, heart disease, and hypertension is found higher in women than men (Badan Penelitian dan Pengembangan Kesehatan, 2018). Indonesian Basic Health Research 2018 results

also state that women and people who live in urban areas of all ages have a high prevalence of diabetes mellitus (Badan Penelitian dan Pengembangan Kesehatan, 2018).

Type 2 diabetes mellitus is caused by insulin resistance, a condition in which the patient's body is unable to absorb glucose (Srikanthan *et al.*, 2016). A study in Semarang City showed that 96.1% of adolescents experienced insulin resistance which was measured by Homeostasis Insulin Resistance Assessment Model (HOMA-IR) (Nuraini, *et al.*, 2017). HOMA-IR is a formula for calculating insulin resistance based on fasting blood sugar and insulin levels. Its measurement is simple, inexpensive, often used and has been validated by the clamp method (Sumarni, 2017).

One factor causing insulin resistance is central or abdominal obesity as abdominal fat is more actively undergoing lipolysis (Sumarni, 2017). Recently, several measurements of the body's anthropometric profile that can describe the incidence of central obesity are reported, where the measurements are done easily. Central obesity in adolescents can be described generally using measurements of waist circumference and hip waist circumference ratio (WHR). Some studies also mention that waist circumference and WHR have a significant correlation with insulin resistance (Sumarni, 2017).

In addition to waist circumference and WHR, other anthropometric profile measurements are also progressively more used, namely Waist-to-Height Ratio (WHtR). WHtR describes central obesity in adolescents with more accurate results than Body Mass Index (BMI) (Ashwell and Gibson, 2016; Saraswati and Sulchan, 2016; Yang *et al.*, 2017). A study in Mexico demonstrates WHtR as a better tool in identifying cardiometabolic obesity in adolescents used to predict hypertension and insulin resistance (Rodea-Montero, *et al.*, 2014). Other studies conducted in Semarang also showed the correlation between WHtR and increasing insulin resistance (Asnelviana, *et al.*, 2017).

Wrist circumference can also be utilized as an indicator. Studies conducted in late adolescents in Indonesia show wrist circumference as one of the anthropometric measurements that can predict obesity and insulin resistance in late adolescents. Wrist circumference reflects bone in the wrist area as well as peripheral fat distribution and metabolism thus it can measure one's body frame and bone size easily (Fitriyanti *et al.*, 2019).

Another measurement of anthropometric profiles that can be used to predict metabolic syndrome in adolescents is the measurement of neck circumference. Some studies show a correlation between neck circumference with insulin resistance (Liang *et al.*, 2014). Neck circumference can represent upper-body subcutaneous adipose tissue that plays a role in predicting insulin resistance and type 2 diabetes (Saneei *et al.*, 2019).

In addition, measurement of thigh circumference can also predict metabolic syndrome in adolescents since it reflects central adiposity (Bando *et al.*, 2017). Results of a study conducted in Korea show that thigh circumference is positively related to insulin resistance (Park *et al.*, 2012). Several studies also explain that thigh circumference is a good indicator in determining type 2 diabetes mellitus 2 (Jung *et al.*, 2013; Ting *et al.*, 2018).

Recently, it has been reported that there are other anthropometric measurements as indicators in predicting metabolic syndrome disease, namely The Ratio of Second to Fourth Digit Length (2D:4D) (Purwaningsih, 2016). The Ratio of the length of the index finger and

ring finger (2D:4D) can describe the exposure to the hormone oestrogen and prenatal testosterone. A study has shown that a lo ratio is associated with high testosterone levels in men, while a high digit ratio is associated with low testosterone levels in women (Kumar et al., 2016). The size of digit ratio occurs since the end of the first trimester of foetal - elopment (Oyeyemi et al., 2014). Inappropriate posure to androgen hormone can cause Polycystic Ovary Syndrome (PCOS), causing infertility in premenopausal women. Women who experience PCOS often have metabolic diseases such as hypertension and insulin resistance (White et al., 2017). The Study states that digit ratio is correlated with obesity, which is a risk factor for metabolic disease (Gölge et al., 2016). There aren't many studies showing the relationship between digit ratio with insulin resistance.

In this study, the portrayal and correlation of anthropometric profiles (waist circumference, WHR, WHtR, wrist circumference, neck circumference, thigh circumference, and second to fourth digit ratio) and insulin resistance in female adolescents with obesity were studied.

## 2. Materials and methods

## 2.1 Experimental design, location, and time

This is an observational study and is included within the scope of community nutrition science. This research was conducted in Universitas Diponegoro Semarang, Indonesia at 10 Faculties from June until August 2019. There were 1,260 female students who participated in screening program. The entire study was approved by Health Study Ethics Committee (KEPK) Faculty of Medicine, Universitas Diponegoro/Central General Hospital dr. Kariadi No. 373/EC/KEPK/FK UNDIP/VIII/2019.

## 2.2 Samplings

Subjects of this study were 120 students from Universitas Diponegoro who were selected through simple random sampling, according to the following inclusion criteria: aged 18-21 years old, had 80 cm or more waist circumference, had intact fingers on both hands, were not currently consuming drugs that could affect the blood glucose and insulin levels, were willing to do fasting for at least 8 hours, did not smoke and/or consume alcohol, were not sick or in the care of a doctor, did not do heavy physical activity or exercise, were not pregnant and breastfeeding were willing to be the subject of study by filling out informed sent. The exclusion criteria in this study were the subject's withdrawal from the study, the subject's moved to another university, and the subjects passed away within the study period.

## 2.3 Data collected

Independent variables in this study were the anthropometric profile consisting of waist circumference, waist-hip circumference ratio (WHR), Waist-Height Ratio (WHtR), neck circumference, wrist circumference, thigh circumference, and the ratio of index finger length and ring finger (2D:4D). The dependent variable in this study was insulin resistance.

Waist circumference data were obtained from waist circumference measurements measured at the midpoint between the iliac crest and costal margins (lower ribs) using a medical measuring tape with 0.1 cm precision. Subjects used minimal clothing (Yang *et al.*, 2017). Subjects were considered at risk when waist circumference was 80 cm or more (Saklayen, 2018).

WHR data was obtained from the waist circumference to hip circumference ratio. Measurement of pelvic circumference was done by medical measuring tape with 0.1 cm precision. The Pelvic circumference is measured by determining the widest points on the buttock (Fitriyanti, *et al.*, 2019). Subjects are categorized as risky when WHR was more than 0.85 (Saklayen, 2018).

Data on the ratio of waist circumference and height (WHtR) was obtained from measurements of the height and waist circumference of the subject. Height was measured using a microtoise with 0.01 cm precision. The subject stands without using footwear and accessories above the head. Subjects were considered at risk when WHtR was 0.5 or more (Zhang et al., 2016).

Neck circumference was measured by medical measuring tape with 0.1 cm precision. Its measurements in women were one by subject's upright head position and forward-facing eyes, and then horizontally measured just below the protruding larynx.

Wrist circumference data were measured using medical measuring tape with 0.1 cm precision. Its measurement was done by placing the medical measuring tape horizontally on the distal side of the ulna protrusion, around the wrist. Wrist circumference measurement results were divided into 3 categories: small if subjects whose height less than 155 cm had wrist circumference less than 14 cm, subjects whose height 155-163 cm had wrist circumference 15.2 cm, subjects whose height more than 163 cm had wrist circumference less than 15.9 cm; moderate if subjects whose height less than 155 cm had wrist circumference 14-14.6 cm, subjects whose height 155-163 cm had wrist circumference 15.2-15.9 cm, subjects whose height more than 163 cm had wrist circumference 15.9-16.5 cm; large if subjects whose height less than 155 cm had wrist circumference more 14.6 cm, subjects whose height 155-163 cm had wrist circumference more than 15.9 cm, subjects had height more 163 cm have wrist circumference more than 16.5 cm (Nabila, et al., 2018).

Thigh circumference was measured by a medical measuring tape. Subjects were standing and wearing as few clothes as possible. Thigh circumference was measured 10 cm above the upper right patella. After that certain point was marked, the tape is placed horizontally and encircles the thigh (Bando *et al.*, 2017).

2D:4D ratio digit data is measured by a calliper with 0.001 mm precision. Measurements were made witl position of the palm open (Wu et al., 2013). The length of the index finger or second finger is the length of the finger measured from the midpoint of the second metacarpophalangeal joint and the most distal point of the second finger. The length of the ring finger or the fourth finger is the length of the finger measured from the midpoint of the fourth metacarpophalangeal joint and the most distal point of the fourth finger. 2D:4D ratio digit data was obtained from the length of the second finger divided by the length of the fourth finger. The ratio digits were considered high when the result shows more than 0.9811 for the right hand and more than 0.9821 for the left hand (Balci et al., 2018). Anthropometric data collected by trained were personnel.

Insulin resistance data was determined using HOMA -IR values. Measurement of Homeostasis Insulin Resistance Assessment Model (HOMA-IR) based on fasting blood glucose and fasting insulin level with the following formula (Matthews *et al.*, 1985; Levy, *et al.*, 1998; Torréns *et al.*, 2004):

$$\frac{Fasting\;Insulin\;\left(\frac{mU}{L}\right)x\;Fasting\;Blood\;Glucose\;\left(\frac{mmol}{L}\right)}{22.5}$$

The threshold of HOMA-IR value for adolescents is less than 1.65 (Rocco *et al.*, 2011). Blood sampling was collected by health workers. This blood sampling was in collaboration with Sarana Modika laboratory.

2.4 Data analysis

Data normality test was performed through Kolmogrov-irnov test. We used univariate analysis to describe each variable. Bivariate analysis was completed by the Spearman Rank test. Bivariate analysis was performed to see whether there was a correlation between anthropometric profiles and insulin resistance.

## 3. Results

Table 1 described the anthropometric profile of the subjects. The median body weight was 66.6 kg. The

Table 1. Characteristics of subjects.

Variable	Median	Minimum	Maximum
Body weight (kg)	66.6	47.8	107.4
Body height (cm)	157.4	100.5	171.4
Waist circumference (cm)	85.75	80.5	114
Hip circumference (cm)	103.5	30	170
Neck circumference (cm)	32.5	14.5	39
Wrist circumference (cm)	15	13.5	17.5
Thigh circumference (cm)	57.4	31	78.4
Waist Height to Ratio (WHtR)	0.55	0.49	0.95
Waist-hip circumference ratio (WHR)	0.84	0.6	3.33
2D:4D digit ratio of the right hand	0.98	0.84	1.09
2D:4D digit ratio of the left hand	0.99	0.52	0.6
HOMA-IR	2.33	0.54	18.32

median waist circumference and pelvic circumferences were 85.75 cm and 103.5 cm, respectively, while the median WHR was 0.84±0.23. Based on Table 1, the median neck circumference, wrist circumference, WHtR was 32.5 cm, 15 cm, and 0.55 cm, respectively. The characteristic of the subjects could also be seen in Table 2. Table 2 showed that all subjects (100%) had less than 80 cm waist circumference which meant they were at risk of developing metabolic syndrome. Another anthropometric profile showed that 98.3% of subjects (n = 118) had high WHtR values. Based on WHR, as many as 90.8% of the subjects (n = 108) were at risk. A total of 83.3% of subjects (n = 100) also experienced insulin resistance as seen from the HOMA-IR value >1.65. However, anthropometric profiles, specifically neck circumference, wrist circumference, 2D:4D digit ratio of less than 5000 of subjects are at risk (10.000, 21.7%; 39.2%; 44.2% respectively).

Table 2. Frequency distribution of the subjects

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Table 2. Frequency distribution of the subje	Cis	
Category	n	%
Waist circumference		
At risk >8	120	100
Neck circumfere		
At risk ≥35.5 cm	13	10.8
Under risk <35.5 cm	107	89.2
Wrist circumference		
At risk ≥16 cm	26	21.7
Under risk <16 cm	94	78.3
Waist Height to Ratio (WHtR)		
At risk $\geq 0.5$	118	98.3
Under risk < 0.5	2	1.7
Waist-hip circumference ratio (WHR)		
At risk $\geq 0.8$	109	90.8
Under risk < 0.8	11	9.2
2D:4D digit ratio of the right hand		
At risk	47	39.2
Under risk	73	60.8
2D:4D digit ratio of the left hand		
At risk	53	44.2
Under risk	67	55.8
HOMA-IR		
Normal	20	16.7
Resistance	100	83.3

The correlation of anthropometric profile and insulin resistance incidence determined by HOMA-IR was shown in Table 3. Anthropometric profiles having a significant correlation with HOMA-IR were neck circumference (r = 0.271; p = 0.003), WHtR (r = 0.33; p < 0.001) and thigh circumference (r = 0.224; p = 0.014). Based on the analysis, the higher the value of the neck circumference, thigh circumference, and WHtR, the higher the HOMA-IR score. Table 3 also show that waist circumference had no correlation with HOMA-IR (r = 0.151; p = 0.1). There was also no correlation between wrist circumference and HOMA-IR (r = 0.12; p = 0.19). In addition, there was no correlation between WHR and HOMA-IR in the study subjects (r = -0.019; p = 0.836). Based on the analysis, other anthropometric profiles having no correlation with HOMA-IR were 2D:4D righthand digit ratios (r = 0.139; p = 0.129) and 2D:4D left hand digit ratios (r = 0.169; p = 0.065).

Table 3. Correlation of Anthropometric Profile and HOMA-IR.

r	p
0.151	0.100
0.271	$0.003^{*}$
0.120	0.190
0.224	0.014*
0.330	<0.001*
-0.019	0.836
0.139	0.129
0.169	0.065
	0.151 0.271 0.120 0.224 0.330 -0.019 0.139

Correlation test: Rank-Spearman, \*Significant (p<0.05)

#### 4. Discussion

Late adolescents, especially women, have the risk of experiencing the metabolic syndrome. Based on this study results, 83.3% of subjects experience insulin resistance determined by HOMA-IR. Since 2007, the Genome Wide Association Studies (GWAS) have identified around 88 loci associated with the risk of developing type 2 diabetes mellitus where most of the loci are related to insulin secretion and pancreatic betacell function, causing insulin resistance associated with

obesity (Brown and Walker, 2016). A study conducted in Semarang City also showed that 96.1% of subjects experienced insulin resistance determined by HOMA-IR (Nuraini *et al.*, 2017).

More than 50% of subjects of this study have high WHtR and WHR values. The study conducted in Jepara shows that 26.94% of adolescents experience abdominal obesity as seen from WHtR values of above 0.45 (Azizah and Sulchan, 2016). Another study conducted at the Faculty of Medicine Universitas Riau demonstrates that 44.1% of students experience central obesity as seen in the ratio waist-hip circumference (Jannah *et al.*, 2015). For women of reproductive age, fat storage is centralized in certain areas to protect important reproductive organs. This increases the risk of high WHR in women (Jannah *et al.*, 2015).

Based on the analysis, neck circumference has a significant correlation with Homeostasis Model Assessment for Insulin Resistance (HOMA-IR), where the greater the neck circumference of the subject, the higher HOMA-IR value. A Study in China shows that neck circumference has a significant correlation with insulin resistance assessed by HOMA-IR (Liang et al., 2014). Previous case studies in Public Senior High School 2 Semarang and Public Junior High School 9 Semarang also stated that neck circumference has a significant correlation with fasting blood sugar (Mayasari and Wirawanni, 2014).

Neck circumference is an easy anthropometric measurement. It can reflect the central obesity index and is associated with several cardiovascular risk factors such as dyslipidemia, hypertension, hyperuricemia, and insulin resistance. It is also considered an estimation of upper-body subcutaneous adipose tissue which plays a role in predicting insulin resistance and type-2 diabetes (Nabila *et al.*, 2018). The release of excess free fatty acids associated with upper-body subcutaneous fat, explicitly the neck, can be one mechanism to explain the correlation between neck circumference and insulin resistance (Ebbert and Jensen, 2013).

Lipolytic function and releasing rate of free fatty acids in upper body subcutaneous fat is found higher than lower body subcutaneous fat. Excessive free fatty acids in muscles and other tissues induce the body to use more free fatty acids as energy. They will also inhibit glucose oxidation, causing insulin resistance (Ebbert and Jensen, 2013). Increased free fatty acids also play a role in increasing VLDL production and inhibition of insulin clearance which induces insulin resistance. In addition, neck circumference is also positively correlated with A total fat body and visceral fat which are related to biological parameters of insulin resistance. Two

perivascular ectopic fat depots are also found in the neck region. Adipokine secretion, such as leptin, adiponectin, and interleukin-6, from perivascular ectopic fat depots, causes metabolic dysfunction including insulin resistance (Saneei *et al.*, 2019).

Subjects with large neck circumferences have a greater risk for obesity (Saneei *et al.*, 2019). Subcutaneous fat has a major role in the association of insulin resistance and obesity (Yuliani *et al.*, 2017). Insulin resistance is an important complication of obesity that causes hyperglycaemia impaired glycemic parameters (Saneei *et al.*, 2019

Waist to Height Ratio (WHtR) is a good predictor in determining insulin resistance in individual control obesity (Jamar et al., 2017). Based on the analysis, and the correlation with HOMA-IR, where the greater the WHtR score, the greater the value of HOMA-IR. A study conducted in Australia on the correlation of WHtR and metabolic syndrome in adolescents and children with obesity, results in a correlation between WHtR and HOMA-IR (Nambiar et al., 2013). Other studies conducted in Korea also find that high WHtR values in obese adolescents would affect the incidence of insulin resistance measured by HOMA-IR (Lim et al., 2015).

WHtR plays a role in measuring central obesity which is often associated with metabolic disorders. An increase in fat tissue will promote an increase in adipokine secretion. This can increase insulin resistance. The most important adipokines is TNF- $\alpha$  which plays a role in inducing insulin resistanthrough glucose transporter 4 (GLUT-4) and increasing the release of free fatty acids. Increased transfer of free fatty acids to muscles results in increased intracellular fatty acid metabolites such as diacylglycerol, ceramide, and acetyl-CoA. These metabolites will activate the serine pathway or threonine kinase that reduces the ability to activate insulin receptors. Hence, it can cause insulin resistance when occurs in the long term it can damage visceral adipocyte  $\beta$  cells (Asnelviana *et al.*, 2017).

Based on the statistical test results, we find a correlation between thigh circumference and insulin resistance as measured by HOMA-IR. This finding is in line with the study conducted in Korea which shows the result that thigh circumference is positively related to HOMA-IR. The greater the thigh circumference, the greater the risk of insulin resistance (Park *et al.*, 2012). Another study in Korea explains that the measurement of thigh circumference is an indicator of diabetes marker (Jung *et al.*, 2013). The study conducted in Taiwan also shows the left thigh circumference is a significant predictor of determining type 2 diabetes mellitus 2 (Ting *et al.*, 2018). Large thigh circumference not only

indicates greater muscle mass but also an increase in femoral subcutaneous fat mass. Lower muscle mass and subcutaneous fat in the thigh are associated with insulin resistance which results in hyperglycaemia and diabetes (Ting et al., 2018). Subcutaneous fat in tempishs is metabolism of circulating fatty acids that are circulating because there is = fference in lipolysis activity between fat in the abdomen and subcutaneous Subcutaneous fat in the thigh is wasting the metabolism of circulatory fatty acids as there is a difference between lipolysis activity of abdominal and thigh subcutaneous fat. Subcutaneous fat of the thigh tends to take fatty acids from the bloodstream, thus preventing the liver, pancreas, and ectopic fat such as the muscles from being exposed to high fatty acids (Nugraha et al., 2019).

Based on the study analysis, no correlation is found between neither waist circumference nor waist-hip circumference ratio with insulin resistance. This finding is contradictory to a study conducted on adolescents in Korea which shows the results that waist circumference and waist-hip circumference ratio have a significant correlation to HOMA-IR (Lim *et al.*, 2015). Waist circumference and waist-hip circumference ratio can be used as a screening tool to detect the incidence of abdominal obesity which can cause metabolic disorders such as insulin resistance (Fitriyanti, *et al.*, 2019).

However, a study conducted in Manado about the correlation of waist circumference and blood sugar levels shows no correlation between waist circumference and blood sugar levels among teachers at the Middle School and High School Eben Haezar Christian Manado. Another study held in Ngawi also shows no correlation between waist circumference and blood sugar levels in early adulthood (Manungkalit et al., 2015). Several other studies, including a study conducted at the Pusti Pidie Health Center, show no correlation between waist circumference ratio pelvis and blood sugar among Community Health Center's employees (Mulyani and Rita, 2016). The study states that the ratio of the waisthip circumference is not an extremely decisive factor in increasing blood sugar levels as many other factors influence the increase in blood sugar levels. Therefore, other anthropometric measurements need to be carried out (Mulyani and Rita, 2016).

Wrist circumference is a strong predictor of diabetes (Noudeh *et al.*, 2013). Wrist circumference is an easily measured anthropometric parameter that can determine body frame and bone size. Increased bone mass will also be associated with hyperinsulinemia (Fitriyanti, *et al.*, 2019) However, in this study, wrist circumference does not correlate with HOMA-IR. Inconsistent with the study eonducted by Kusmiyati *et al.* in 18 years old

adolescents, which demonstrates a correlation between wrist circumference and fasting insulin and HOMA-IR in both male and female adolescents (Fitriyanti *et al.*, 2019). However, the study conducted by Nabila et al. about the correlation of wrist circumference and the blood glucose level among obese women shows no correlation between wrist circumference with fasting blood glucose (Nabila *et al.*, 2018). Another study conducted at Public Senior High School 6 Semarang also results in no correlation between wrist circumference with fasting blood glucose levels (Arifin and Panunggal, 2014). Factors influencing HOMA-IR values were fasting blood glucose and fasting insulin levels, where higher glucose levels fasting blood means higher the HOMA-IR value in the subject (Mitrea *et al.*, 2013).

The Second to Fourth Digit Ratio (2D:4D) can be used to evaluate prenatal androgen exposure in the postpartum period. The Homeobox genes, HoxA and HoxB, are responsible for urogenital differentiation, prenatal androgen synthesis and fingers development. In animals, prenatal and neonatal androgenic exposure can increase adiposity, insulin resistance, and changes in adipose tissue lipolysis later in adulthood (Yıldız et al., 2015). However, based on this study analysis, the Second to Fourth Digit Ratio (2D:4D) of the right and left hand is not related to HOMA-IR or insulin resistance incidence. This finding is supported by the study conducted in Turkey, on the correlation between Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome. It shows that the Second to Fourth Digit Ratio (2D:4D) is not related to insulin resistance or the incidence of diabetes mellitus in the subject. Researchers state that no available study reports Second to Fourth Digit Ratio (2D:4D) as a predictor of androgen exposure and explains its correlation with metabolic syndrome (Yıldız et al., 2015). Another study conducted by Asuku et al. (2017) regarding the correlation of Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome indicators in Nigeria shows the results that Second to Fourth Digit Ratio (2D:4D) of the right and the left hand has no correlation with fasting blood sugar levels in the subjects. Re there explain the absence of correlation between Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome indicators is caused by the small number of subjects, i.e. 465 subjects, meanwhile this study includes only 120 subjects. This might be their reason for no association found between the Second to Fourth Digit Ratio (2D:4D) and the incidence of insulin resistance.

## **Conflict of interest**

The authors declare no conflict of interest.

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Department of Nutrition Science
Faculty of Medicine, Diponegoro University
JI Prof Soedharto SH, Tembalang. Semarang 50275, Central Java, Indonesia.
Phone/Fax (024) 845-37-08/ HP +62856-4020-4747
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# Anthropometric profile and its correlation to insulin resistance in female students with obesity

<sup>1,2,\*</sup>Dieny, F.F., <sup>1,2</sup>Fitranti, D.Y., <sup>1</sup>Jauharany, F.F., <sup>1,2</sup>Tsani, A.F.A., <sup>1</sup>Faradila, U. and <sup>1</sup>Rose, S.

<sup>1</sup>Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia <sup>2</sup>CENURE (Center of Nutrition Research), Universitas Diponegoro, Semarang, Indonesia

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#### **Abstract**

The prevalence of obesity in adolescent girls is increasing each year. Several anthropometric measurements can be used to detect the incidence of insulin resistance. This study was aimed to observe the correlation of anthropometric profiles with insulin resistance in adolescent girls with obesity. This was an observational study with a total of 120 female students of Universitas Diponegoro (Undip), aged between 18 and 21 years old, who have waist circumference >80 cm. They were chosen by a simple random sampling technique. Anthropometric profile data taken has consisted of waist circumference, hip circumference, waist-hip circumference ratio (WHR), waist-to-height ratio (WHtR), neck circumference, waist circumference, thigh circumference, and 2D:4D digit ratio. Insulin resistance data was determined using the Homeostasis Model Assessment-Insulin Resistance (HOMA-IR.). Bivariate analysis was completed with the Spearman rank test. There was 83.3% of subjects who experienced insulin resistance. High WHtR was found in 98.3% of total subjects as many as 90.8% of subjects were at risk based on WHR values. Based on 2D:4D ratio digits, neck circumference, wrist circumference <50% of subjects were found as at risk. There was no correlation between waist circumference, WHR, wrist circumference, 2D:4D digit ratio with HOMA-IR (p>0.05). However, there was a positive correlation between WHtR, neck circumference, and thigh circumference with HOMA-IR (p<0.05). Anthropometric profiles such as WHtR, neck circumference, and thigh circumference were correlated with insulin resistance in female adolescents with obesity.

## 1. Introduction

Nutritional status in adolescents is very important since adolescence is a transition period from childhood adulthood. This transition causes biological, psychological, and cognitive changes that influence their nutritional status (Brown, 2011). However, nutritional status problems in adolescents are still fairly high, including obesity. The prevalence of central obesity 15 years adolescents and older has increased from 26.6% in 2013 to 31% in 2018 (Badan Penelitian dan Pengembangan Kesehatan, 2018). Obesity incidence will later be associated with degenerative diseases. Women are at higher risk of suffering from degenerative disease, while Indonesian Basic Health Research 2018 results report the prevalence of stroke, diabetes mellitus, heart disease, and hypertension is found higher in women than men (Badan Penelitian dan Pengembangan Kesehatan, 2018). Indonesian Basic Health Research 2018 results

also state that women and people who live in urban areas of all ages have a high prevalence of diabetes mellitus (Badan Penelitian dan Pengembangan Kesehatan, 2018).

Type 2 diabetes mellitus is caused by insulin resistance, a condition in which the patient's body is unable to absorb glucose (Srikanthan *et al.*, 2016). A study in Semarang City showed that 96.1% of adolescents experienced insulin resistance which was measured by Homeostasis Insulin Resistance Assessment Model (HOMA-IR) (Nuraini, *et al.*, 2017). HOMA-IR is a formula for calculating insulin resistance based on fasting blood sugar and insulin levels. Its measurement is simple, inexpensive, often used and has been validated by the clamp method (Sumarni, 2017).

One factor causing insulin resistance is central or abdominal obesity as abdominal fat is more actively undergoing lipolysis (Sumarni, 2017). Recently, several measurements of the body's anthropometric profile that

can describe the incidence of central obesity are reported, where the measurements are done easily. Central obesity in adolescents can be described generally using measurements of waist circumference and hip waist circumference ratio (WHR). Some studies also mention that waist circumference and WHR have a significant correlation with insulin resistance (Sumarni, 2017).

In addition to waist circumference and WHR, other anthropometric profile measurements are also progressively more used, namely Waist-to-Height Ratio (WHtR). WHtR describes central obesity in adolescents with more accurate results than Body Mass Index (BMI) (Ashwell and Gibson, 2016; Saraswati and Sulchan, 2016; Yang *et al.*, 2017). A study in Mexico demonstrates WHtR as a better tool in identifying cardiometabolic obesity in adolescents used to predict hypertension and insulin resistance (Rodea-Montero, *et al.*, 2014). Other studies conducted in Semarang also showed the correlation between WHtR and increasing insulin resistance (Asnelviana, *et al.*, 2017).

Wrist circumference can also be utilized as an indicator. Studies conducted in late adolescents in Indonesia show wrist circumference as one of the anthropometric measurements that can predict obesity and insulin resistance in late adolescents. Wrist circumference reflects bone in the wrist area as well as peripheral fat distribution and metabolism thus it can measure one's body frame and bone size easily (Fitriyanti *et al.*, 2019).

Another measurement of anthropometric profiles that can be used to predict metabolic syndrome in adolescents is the measurement of neck circumference. Some studies show a correlation between neck circumference with insulin resistance (Liang *et al.*, 2014). Neck circumference can represent upper-body subcutaneous adipose tissue that plays a role in predicting insulin resistance and type 2 diabetes (Saneei *et al.*, 2019).

In addition, measurement of thigh circumference can also predict metabolic syndrome in adolescents since it reflects central adiposity (Bando *et al.*, 2017). Results of a study conducted in Korea show that thigh circumference is positively related to insulin resistance (Park *et al.*, 2012). Several studies also explain that thigh circumference is a good indicator in determining type 2 diabetes mellitus 2 (Jung *et al.*, 2013; Ting *et al.*, 2018).

Recently, it has been reported that there are other anthropometric measurements as indicators in predicting metabolic syndrome disease, namely The Ratio of Second to Fourth Digit Length (2D:4D) (Purwaningsih, 2016). The Ratio of the length of the index finger and

ring finger (2D:4D) can describe the exposure to the hormone estrogen and prenatal testosterone. A study has shown that a low digit ratio is associated with high testosterone levels in men, while a high digit ratio is associated with low testosterone levels in women (Kumar et al., 2016). The size of digit ratio occurs since the end of the first trimester of fetal development (Oyeyemi et al., 2014). Inappropriate exposure to androgen hormone can cause Polycystic Ovary Syndrome (PCOS), causing infertility in premenopausal women. Women who experience PCOS often have metabolic diseases such as hypertension and insulin resistance (White et al., 2017). The Study states that digit ratio is correlated with obesity, which is a risk factor for metabolic disease (Gölge et al., 2016). There aren't many studies showing the relationship between digit ratio with insulin resistance.

In this study, the portrayal and correlation of anthropometric profiles (waist circumference, WHR, WHtR, wrist circumference, neck circumference, thigh circumference, and second to fourth digit ratio) and insulin resistance in female adolescents with obesity were studied.

## 2. Materials and methods

## 2.1 Experimental design, location, and time

This is an observational study and is included within the scope of community nutrition science. This research was conducted in Universitas Diponegoro Semarang, Indonesia at 10 Faculties from June until August 2019. There were 1,260 female students who participated in a screening program. The entire study was approved by the Health Study Ethics Committee (KEPK) Faculty of Medicine, Universitas Diponegoro/Central General Hospital dr. Kariadi No. 373/EC/KEPK/FK UNDIP/VIII/2019.

## 2.2 Samplings

Subjects of this study were 120 students from Universitas Diponegoro who were selected through simple random sampling, according to the following inclusion criteria: aged 18-21 years old, had 80 cm or more waist circumference, had intact fingers on both hands, were not currently consuming drugs that could affect the blood glucose and insulin levels, were willing to do fasting for at least 8 hours, did not smoke and/or consume alcohol, were not sick or in the care of a doctor, did not do heavy physical activity or exercise, were not pregnant and breastfeeding were willing to be the subject of study by filling out informed consent. The exclusion criteria in this study were the subject's withdrawal from the study, the subject's moved to another university, and the subjects passed away within the study period.

## 2.3 Data collected

Independent variables in this study were the anthropometric profile consisting of waist circumference, waist-hip circumference ratio (WHR), Waist-Height Ratio (WHtR), neck circumference, wrist circumference, thigh circumference, and the ratio of index finger length and ring finger (2D:4D). The dependent variable in this study was insulin resistance.

Waist circumference data were obtained from waist circumference measurements measured at the midpoint between the iliac crest and costal margins (lower ribs) using a medical measuring tape with 0.1 cm precision. Subjects used minimal clothing (Yang *et al.*, 2017). Subjects were considered at risk when waist circumference was 80 cm or more (Saklayen, 2018).

WHR data was obtained from the waist circumference to hip circumference ratio. Measurement of pelvic circumference was done by medical measuring tape with 0.1 cm precision. The Pelvic circumference is measured by determining the widest points on the buttock (Fitriyanti, *et al.*, 2019). Subjects are categorized as risky when WHR was more than 0.85 (Saklayen, 2018).

Data on the ratio of waist circumference and height (WHtR) was obtained from measurements of the height and waist circumference of the subject. Height was measured using a microtoise with 0.01 cm precision. The subject stands without using footwear and accessories above the head. Subjects were considered at risk when WHtR was 0.5 or more (Zhang et al., 2016).

Neck circumference was measured by medical measuring tape with 0.1 cm precision. Its measurements in women were one by subject's upright head position and forward-facing eyes, and then horizontally measured just below the protruding larynx.

Wrist circumference data were measured using medical measuring tape with 0.1 cm precision. Its measurement was done by placing the medical measuring tape horizontally on the distal side of the ulna protrusion, around the wrist. Wrist circumference measurement results were divided into 3 categories: small if subjects whose height less than 155 cm had wrist circumference less than 14 cm, subjects whose height 155-163 cm had wrist circumference 15.2 cm, subjects whose height more than 163 cm had wrist circumference less than 15.9 cm; moderate if subjects whose height less than 155 cm had wrist circumference 14-14.6 cm, subjects whose height 155-163 cm had wrist circumference 15.2-15.9 cm, subjects whose height more than 163 cm had wrist circumference 15.9-16.5 cm; large if subjects whose height less than 155 cm had wrist

circumference more 14.6 cm, subjects whose height 155-163 cm had wrist circumference of more than 15.9 cm, subjects had height more than 163 cm have wrist circumference of more than 16.5 cm (Nabila, et al., 2018).

Thigh circumference was measured by a medical measuring tape. Subjects were standing and wearing as few clothes as possible. Thigh circumference was measured 10 cm above the upper right patella. After that certain point was marked, the tape is placed horizontally and encircles the thigh (Bando *et al.*, 2017).

2D:4D ratio digit data is measured by a caliper with 0.001 mm precision. Measurements were made with the position of the palm open (Wu et al., 2013). The length of the index finger or second finger is the length of the finger measured from the midpoint of the second metacarpophalangeal joint and the most distal point of the second finger. The length of the ring finger or the fourth finger is the length of the finger measured from the midpoint of the fourth metacarpophalangeal joint and the most distal point of the fourth finger. 2D:4D ratio digit data was obtained from the length of the second finger divided by the length of the fourth finger. The ratio digits were considered high when the result shows more than 0.9811 for the right hand and more than 0.9821 for the left hand (Balci et al., 2018). Anthropometric data were collected by trained personnel.

Insulin resistance data was determined using HOMA -IR values. Measurement of Homeostasis Insulin Resistance Assessment Model (HOMA-IR) based on fasting blood glucose and fasting insulin level with the following formula (Matthews *et al.*, 1985; Levy, *et al.*, 1998; Torréns *et al.*, 2004):

Fasting Insulin 
$$\left(\frac{mU}{L}\right)$$
x Fasting Blood Glucose  $\left(\frac{mmol}{L}\right)$ 

The threshold of HOMA-IR value for adolescents is less than 1.65 (Rocco *et al.*, 2011). Blood sampling was collected by health workers. This blood sampling was in collaboration with the Sarana Medika laboratory.

## 2.4 Data analysis

Data normality test was performed through Kolmogorov-Smirnov test. We used univariate analysis to describe each variable. Bivariate analysis was completed by the Spearman Rank test. Bivariate analysis was performed to see whether there was a correlation between anthropometric profiles and insulin resistance.

## 3. Results

Table 1 described the anthropometric profile of the

Table 1. Characteristics of subjects.

Variable	Median	Minimum	Maximum
Body weight (kg)	66.6	47.8	107.4
Body height (cm)	157.4	100.5	171.4
Waist circumference (cm)	85.75	80.5	114
Hip circumference (cm)	103.5	30	170
Neck circumference (cm)	32.5	14.5	39
Wrist circumference (cm)	15	13.5	17.5
Thigh circumference (cm)	57.4	31	78.4
Waist Height to Ratio (WHtR)	0.55	0.49	0.95
Waist-hip circumference ratio (WHR)	0.84	0.6	3.33
2D:4D digit ratio of the right hand	0.98	0.84	1.09
2D:4D digit ratio of the left hand	0.99	0.52	0.6
HOMA-IR	2.33	0.54	18.32

subjects. The median body weight was 66.6 kg. The median waist circumference and pelvic circumferences were 85.75 cm and 103.5 cm, respectively, while the median WHR was 0.84±0.23. Based on Table 1, the median neck circumference, wrist circumference, WHtR was 32.5 cm, 15 cm, and 0.55 cm, respectively. The characteristic of the subjects could also be seen in Table 2. Table 2 showed that all subjects (100%) had less than 80 cm waist circumference which meant they were at risk of developing metabolic syndrome. Another anthropometric profile showed that 98.3% of subjects (n = 118) had high WHtR values. Based on WHR, as many as 90.8% of the subjects (n = 108) were at risk. A total of 83.3% of subjects (n = 100) also experienced insulin resistance as seen from the HOMA-IR value >1.65. However, anthropometric profiles, specifically neck circumference, wrist circumference, 2D:4D digit ratio of the right hand; 2D:4D digit ratio of the left hand, showed that less than 50% of subjects are at risk (10.8%; 21.7%;

Table 2. Frequency distribution of the subjects

Category	n	%
Waist circumference		
At risk >80 cm	120	100
Neck circumference		
At risk ≥35.5 cm	13	10.8
Under risk <35.5 cm	107	89.2
Wrist circumference		
At risk ≥16 cm	26	21.7
Under risk <16 cm	94	78.3
Waist Height to Ratio (WHtR)		
At risk ≥0.5	118	98.3
Under risk < 0.5	2	1.7
Waist-hip circumference ratio (WHR)		
At risk ≥0.8	109	90.8
Under risk < 0.8	11	9.2
2D:4D digit ratio of the right hand		
At risk	47	39.2
Under risk	73	60.8
2D:4D digit ratio of the left hand		
At risk	53	44.2
Under risk	67	55.8
HOMA-IR		
Normal	20	16.7
Resistance	100	83.3

39.2%; 44.2% respectively).

The correlation of anthropometric profile and insulin resistance incidence determined by HOMA-IR was shown in Table 3. Anthropometric profiles having a significant correlation with HOMA-IR were neck circumference (r = 0.271; p = 0.003), WHtR (r = 0.33; p < 0.001) and thigh circumference (r = 0.224; p = 0.014). Based on the analysis, the higher the value of the neck circumference, thigh circumference, and WHtR, the higher the HOMA-IR score. Table 3 also show that waist circumference had no correlation with HOMA-IR (r = 0.151; p = 0.1). There was also no correlation between wrist circumference and HOMA-IR (r = 0.12; p = 0.19). In addition, there was no correlation between WHR and HOMA-IR in the study subjects (r = -0.019; p = 0.836). Based on the analysis, other anthropometric profiles having no correlation with HOMA-IR were 2D:4D righthand digit ratios (r = 0.139; p = 0.129) and 2D:4D left hand digit ratios (r = 0.169; p = 0.065).

Table 3. Correlation of Anthropometric Profile and HOMA-IR.

r	р
0.151	0.100
0.271	$0.003^{*}$
0.120	0.190
0.224	0.014*
0.330	<0.001*
-0.019	0.836
0.139	0.129
0.169	0.065
	0.151 0.271 0.120 0.224 0.330 -0.019 0.139

Correlation test: Rank-Spearman, \*Significant (p<0.05)

#### 4. Discussion

Late adolescents, especially women, have the risk of experiencing the metabolic syndrome. Based on this study results, 83.3% of subjects experience insulin resistance determined by HOMA-IR. Since 2007, the Genome Wide Association Studies (GWAS) have identified around 88 loci associated with the risk of developing type 2 diabetes mellitus where most of the

loci are related to insulin secretion and pancreatic betacell function, causing insulin resistance associated with obesity (Brown and Walker, 2016). A study conducted in Semarang City also showed that 96.1% of subjects experienced insulin resistance determined by HOMA-IR (Nuraini *et al.*, 2017).

More than 50% of subjects of this study have high WHtR and WHR values. The study conducted in Jepara shows that 26.94% of adolescents experience abdominal obesity as seen from WHtR values of above 0.45 (Azizah and Sulchan, 2016). Another study conducted at the Faculty of Medicine Universitas Riau demonstrates that 44.1% of students experience central obesity as seen in the ratio waist-hip circumference (Jannah *et al.*, 2015). For women of reproductive age, fat storage is centralized in certain areas to protect important reproductive organs. This increases the risk of high WHR in women (Jannah *et al.*, 2015).

Based on the analysis, neck circumference has a significant correlation with Homeostasis Assessment for Insulin Resistance (HOMA-IR), where the greater the neck circumference of the subject, the higher HOMA-IR value. A Study in China shows that neck circumference has a significant correlation with insulin resistance assessed by HOMA-IR (Liang et al., 2014). Previous case studies in Public Senior High School 2 Semarang and Public Junior High School 9 Semarang also stated that neck circumference has a significant correlation with fasting blood sugar (Mayasari and Wirawanni, 2014).

Neck circumference is an easy anthropometric measurement. It can reflect the central obesity index and is associated with several cardiovascular risk factors such as dyslipidemia, hypertension, hyperuricemia, and insulin resistance. It is also considered an estimation of upper-body subcutaneous adipose tissue which plays a role in predicting insulin resistance and type-2 diabetes (Nabila *et al.*, 2018). The release of excess free fatty acids associated with upper-body subcutaneous fat, explicitly the neck, can be one mechanism to explain the correlation between neck circumference and insulin resistance (Ebbert and Jensen, 2013).

Lipolytic function and releasing rate of free fatty acids in upper body subcutaneous fat is found higher than lower body subcutaneous fat. Excessive free fatty acids in muscles and other tissues induce the body to use more free fatty acids as energy. They will also inhibit glucose oxidation, causing insulin resistance (Ebbert and Jensen, 2013). Increased free fatty acids also play a role in increasing VLDL production and inhibition of insulin clearance which induces insulin resistance. In addition, neck circumference is also positively correlated with A

total fat body and visceral fat which are related to biological parameters of insulin resistance. Two perivascular ectopic fat depots are also found in the neck region. Adipokine secretion, such as leptin, adiponectin, and interleukin-6, from perivascular ectopic fat depots, causes metabolic dysfunction including insulin resistance (Saneei *et al.*, 2019).

Subjects with large neck circumferences have a greater risk for obesity (Saneei *et al.*, 2019). Subcutaneous fat has a major role in the association of insulin resistance and obesity (Yuliani *et al.*, 2017). Insulin resistance is an important complication of obesity that causes hyperglycemia and impaired glycemic parameters (Saneei *et al.*, 2019).

Waist to Height Ratio (WHtR) is a good predictor in determining insulin resistance in an individual with obesity (Jamar *et al.*, 2017). Based on the analysis, WHtR has a correlation with HOMA-IR, where the greater the WHtR score, the greater the value of HOMA-IR. A study conducted in Australia on the correlation of WHtR and metabolic syndrome in adolescents and children with obesity, results in a correlation between WHtR and HOMA-IR (Nambiar *et al.*, 2013). Other studies conducted in Korea also find that high WHtR values in obese adolescents would affect the incidence of insulin resistance measured by HOMA-IR (Lim *et al.*, 2015).

WHtR plays a role in measuring central obesity which is often associated with metabolic disorders. An increase in fat tissue will promote an increase in adipokine secretion. This can increase insulin resistance. The most important adipokines are TNF- $\alpha$  which plays a role in inducing insulin resistance through glucose transporter 4 (GLUT-4) and increasing the release of free fatty acids. Increased transfer of free fatty acids to muscles results in increased intracellular fatty acid metabolites such as diacylglycerol, ceramide, and acetyl-CoA. These metabolites will activate the serine pathway or threonine kinase that reduces the ability to activate insulin receptors. Hence, it can cause insulin resistance when occurs in the long term it can damage visceral adipocyte  $\beta$  cells (Asnelviana *et al.*, 2017).

Based on the statistical test results, we find a correlation between thigh circumference and insulin resistance as measured by HOMA-IR. This finding is in line with the study conducted in Korea which shows the result that thigh circumference is positively related to HOMA-IR. The greater the thigh circumference, the greater the risk of insulin resistance (Park *et al.*, 2012). Another study in Korea explains that the measurement of thigh circumference is an indicator of diabetes marker (Jung *et al.*, 2013). The study conducted in Taiwan also

shows the left thigh circumference is a significant predictor of determining type 2 diabetes mellitus 2 (Ting et al., 2018). Large thigh circumference not only indicates greater muscle mass but also an increase in femoral subcutaneous fat mass. Lower muscle mass and subcutaneous fat in the thigh are associated with insulin resistance which results in hyperglycemia and diabetes (Ting et al., 2018). Subcutaneous fat in the thighs is a metabolism of circulating fatty acids that are circulating because there is a difference in lipolysis activity between subcutaneous fat in the abdomen and thighs. Subcutaneous fat in the thigh is wasting the metabolism of circulatory fatty acids as there is a difference between lipolysis activity of abdominal and thigh subcutaneous fat. Subcutaneous fat of the thigh tends to take fatty acids from the bloodstream, thus preventing the liver, pancreas, and ectopic fat such as the muscles from being exposed to high fatty acids (Nugraha et al., 2019).

Based on the study analysis, no correlation is found between neither waist circumference nor waist-hip circumference ratio with insulin resistance. This finding is contradictory to a study conducted on adolescents in Korea which shows the results that waist circumference and waist-hip circumference ratio have a significant correlation to HOMA-IR (Lim *et al.*, 2015). Waist circumference and waist-hip circumference ratio can be used as a screening tool to detect the incidence of abdominal obesity which can cause metabolic disorders such as insulin resistance (Fitriyanti, *et al.*, 2019).

However, a study conducted in Manado about the correlation of waist circumference and blood sugar levels shows no correlation between waist circumference and blood sugar levels among teachers at the Middle School and High School Eben Haezar Christian Manado. Another study held in Ngawi also shows no correlation between waist circumference and blood sugar levels in early adulthood (Manungkalit et al., 2015). Several other studies, including a study conducted at the Pusti Pidie Health Center, show no correlation between waist circumference ratio pelvis and blood sugar among Community Health Center's employees (Mulyani and Rita, 2016). The study states that the ratio of the waisthip circumference is not an extremely decisive factor in increasing blood sugar levels as many other factors influence the increase in blood sugar levels. Therefore, other anthropometric measurements need to be carried out (Mulyani and Rita, 2016).

Wrist circumference is a strong predictor of diabetes (Noudeh *et al.*, 2013). Wrist circumference is an easily measured anthropometric parameter that can determine body frame and bone size. Increased bone mass will also be associated with hyperinsulinemia (Fitriyanti, *et al.*,

2019) However, in this study, wrist circumference does not correlate with HOMA-IR. Inconsistent with the study in 18 years old adolescents, which demonstrated a correlation between wrist circumference and fasting insulin and HOMA-IR in both male and female adolescents (Fitriyanti et al., 2019). However, the study conducted by Nabila et al. about the correlation of wrist circumference and the blood glucose level among obese shows correlation between women no circumference with fasting blood glucose (Nabila et al., 2018). Another study conducted at Public Senior High School 6 Semarang also results in no correlation between wrist circumference with fasting blood glucose levels (Arifin and Panunggal, 2014). Factors influencing HOMA-IR values were fasting blood glucose and fasting insulin levels, where higher glucose levels fasting blood means higher the HOMA-IR value in the subject (Mitrea et al., 2013).

The Second to Fourth Digit Ratio (2D:4D) can be used to evaluate prenatal androgen exposure in the postpartum period. The Homeobox genes, HoxA and HoxB, are responsible for urogenital differentiation, prenatal androgen synthesis and fingers development. In animals, prenatal and neonatal androgenic exposure can increase adiposity, insulin resistance, and changes in adipose tissue lipolysis later in adulthood (Yıldız et al., 2015). However, based on this study analysis, the Second to Fourth Digit Ratio (2D:4D) of the right and left hand is not related to HOMA-IR or insulin resistance incidence. This finding is supported by the study conducted in Turkey, on the correlation between Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome. It shows that the Second to Fourth Digit Ratio (2D:4D) is not related to insulin resistance or the incidence of diabetes mellitus in the subject. Researchers state that no available study reports Second to Fourth Digit Ratio (2D:4D) as a predictor of androgen exposure and explains its correlation with metabolic syndrome (Yıldız et al., 2015). Another study conducted by Asuku et al. (2017) regarding the correlation of Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome indicators in Nigeria shows the results that Second to Fourth Digit Ratio (2D:4D) of the right and the left hand does not correlate with fasting blood sugar levels in the subjects. Researchers explain the absence of correlation between Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome indicators is caused by the small number of subjects, i.e. 465 subjects, meanwhile this study includes only 120 subjects. This might be their reason for no association found between the Second to Fourth Digit Ratio (2D:4D) and the incidence of insulin resistance.

### **Conflict of interest**

The authors declare no conflict of interest.

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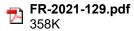
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# Anthropometric profile and its correlation to insulin resistance in female students with obesity

<sup>1,2,\*</sup>Dieny, F.F., <sup>1,2</sup>Fitranti, D.Y., <sup>1</sup>Jauharany, F.F., <sup>1,2</sup>Tsani, A.F.A., <sup>1</sup>Faradila, U. and <sup>1</sup>Rose, S.

<sup>1</sup>Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia <sup>2</sup>CENURE (Center of Nutrition Research), Universitas Diponegoro, Semarang, Indonesia

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#### **Abstract**

The prevalence of obesity in adolescent girls is increasing each year. Several anthropometric measurements can be used to detect the incidence of insulin resistance. This study was aimed to observe the correlation of anthropometric profiles with insulin resistance in adolescent girls with obesity. This was an observational study with a total of 120 female students of Universitas Diponegoro (Undip), aged between 18 and 21 years old, who have waist circumference >80 cm. They were chosen by a simple random sampling technique. Anthropometric profile data taken has consisted of waist circumference, hip circumference, waist-hip circumference ratio (WHR), waist-to-height ratio (WHtR), neck circumference, waist circumference, thigh circumference, and 2D:4D digit ratio. Insulin resistance data was determined using the Homeostasis Model Assessment-Insulin Resistance (HOMA-IR.). Bivariate analysis was completed with the Spearman rank test. There was 83.3% of subjects who experienced insulin resistance. High WHtR was found in 98.3% of total subjects as many as 90.8% of subjects were at risk based on WHR values. Based on 2D:4D ratio digits, neck circumference, wrist circumference <50% of subjects were found as at risk. There was no correlation between waist circumference, WHR, wrist circumference, 2D:4D digit ratio with HOMA-IR (p>0.05). However, there was a positive correlation between WHtR, neck circumference, and thigh circumference with HOMA-IR (p<0.05). Anthropometric profiles such as WHtR, neck circumference, and thigh circumference were correlated with insulin resistance in female adolescents with obesity.

## 1. Introduction

Nutritional status in adolescents is very important since adolescence is a transition period from childhood adulthood. This transition causes biological, psychological, and cognitive changes that influence their nutritional status (Brown, 2011). However, nutritional status problems in adolescents are still fairly high, including obesity. The prevalence of central obesity 15 years adolescents and older has increased from 26.6% in 2013 to 31% in 2018 (Badan Penelitian dan Pengembangan Kesehatan, 2018). Obesity incidence will later be associated with degenerative diseases. Women are at higher risk of suffering from degenerative disease, while Indonesian Basic Health Research 2018 results report the prevalence of stroke, diabetes mellitus, heart disease, and hypertension is found higher in women than men (Badan Penelitian dan Pengembangan Kesehatan, 2018). Indonesian Basic Health Research 2018 results

also state that women and people who live in urban areas of all ages have a high prevalence of diabetes mellitus (Badan Penelitian dan Pengembangan Kesehatan, 2018).

Type 2 diabetes mellitus is caused by insulin resistance, a condition in which the patient's body is unable to absorb glucose (Srikanthan *et al.*, 2016). A study in Semarang City showed that 96.1% of adolescents experienced insulin resistance which was measured by Homeostasis Insulin Resistance Assessment Model (HOMA-IR) (Nuraini, *et al.*, 2017). HOMA-IR is a formula for calculating insulin resistance based on fasting blood sugar and insulin levels. Its measurement is simple, inexpensive, often used and has been validated by the clamp method (Sumarni, 2017).

One factor causing insulin resistance is central or abdominal obesity as abdominal fat is more actively undergoing lipolysis (Sumarni, 2017). Recently, several measurements of the body's anthropometric profile that

can describe the incidence of central obesity are reported, where the measurements are done easily. Central obesity in adolescents can be described generally using measurements of waist circumference and hip waist circumference ratio (WHR). Some studies also mention that waist circumference and WHR have a significant correlation with insulin resistance (Sumarni, 2017).

In addition to waist circumference and WHR, other anthropometric profile measurements are also progressively more used, namely Waist-to-Height Ratio (WHtR). WHtR describes central obesity in adolescents with more accurate results than Body Mass Index (BMI) (Ashwell and Gibson, 2016; Saraswati and Sulchan, 2016; Yang *et al.*, 2017). A study in Mexico demonstrates WHtR as a better tool in identifying cardiometabolic obesity in adolescents used to predict hypertension and insulin resistance (Rodea-Montero, *et al.*, 2014). Other studies conducted in Semarang also showed the correlation between WHtR and increasing insulin resistance (Asnelviana, *et al.*, 2017).

Wrist circumference can also be utilized as an indicator. Studies conducted in late adolescents in Indonesia show wrist circumference as one of the anthropometric measurements that can predict obesity and insulin resistance in late adolescents. Wrist circumference reflects bone in the wrist area as well as peripheral fat distribution and metabolism thus it can measure one's body frame and bone size easily (Fitriyanti *et al.*, 2019).

Another measurement of anthropometric profiles that can be used to predict metabolic syndrome in adolescents is the measurement of neck circumference. Some studies show a correlation between neck circumference with insulin resistance (Liang *et al.*, 2014). Neck circumference can represent upper-body subcutaneous adipose tissue that plays a role in predicting insulin resistance and type 2 diabetes (Saneei *et al.*, 2019).

In addition, measurement of thigh circumference can also predict metabolic syndrome in adolescents since it reflects central adiposity (Bando *et al.*, 2017). Results of a study conducted in Korea show that thigh circumference is positively related to insulin resistance (Park *et al.*, 2012). Several studies also explain that thigh circumference is a good indicator in determining type 2 diabetes mellitus 2 (Jung *et al.*, 2013; Ting *et al.*, 2018).

Recently, it has been reported that there are other anthropometric measurements as indicators in predicting metabolic syndrome disease, namely The Ratio of Second to Fourth Digit Length (2D:4D) (Purwaningsih, 2016). The Ratio of the length of the index finger and

ring finger (2D:4D) can describe the exposure to the hormone estrogen and prenatal testosterone. A study has shown that a low digit ratio is associated with high testosterone levels in men, while a high digit ratio is associated with low testosterone levels in women (Kumar et al., 2016). The size of digit ratio occurs since the end of the first trimester of fetal development (Oyeyemi et al., 2014). Inappropriate exposure to androgen hormone can cause Polycystic Ovary Syndrome (PCOS), causing infertility in premenopausal women. Women who experience PCOS often have metabolic diseases such as hypertension and insulin resistance (White et al., 2017). The Study states that digit ratio is correlated with obesity, which is a risk factor for metabolic disease (Gölge et al., 2016). There aren't many studies showing the relationship between digit ratio with insulin resistance.

In this study, the portrayal and correlation of anthropometric profiles (waist circumference, WHR, WHtR, wrist circumference, neck circumference, thigh circumference, and second to fourth digit ratio) and insulin resistance in female adolescents with obesity were studied.

## 2. Materials and methods

## 2.1 Experimental design, location, and time

This is an observational study and is included within the scope of community nutrition science. This research was conducted in Universitas Diponegoro Semarang, Indonesia at 10 Faculties from June until August 2019. There were 1,260 female students who participated in a screening program. The entire study was approved by the Health Study Ethics Committee (KEPK) Faculty of Medicine, Universitas Diponegoro/Central General Hospital dr. Kariadi No. 373/EC/KEPK/FK UNDIP/VIII/2019.

## 2.2 Samplings

Subjects of this study were 120 students from Universitas Diponegoro who were selected through simple random sampling, according to the following inclusion criteria: aged 18-21 years old, had 80 cm or more waist circumference, had intact fingers on both hands, were not currently consuming drugs that could affect the blood glucose and insulin levels, were willing to do fasting for at least 8 hours, did not smoke and/or consume alcohol, were not sick or in the care of a doctor, did not do heavy physical activity or exercise, were not pregnant and breastfeeding were willing to be the subject of study by filling out informed consent. The exclusion criteria in this study were the subject's withdrawal from the study, the subject's moved to another university, and the subjects passed away within the study period.

## 2.3 Data collected

Independent variables in this study were the anthropometric profile consisting of waist circumference, waist-hip circumference ratio (WHR), Waist-Height Ratio (WHtR), neck circumference, wrist circumference, thigh circumference, and the ratio of index finger length and ring finger (2D:4D). The dependent variable in this study was insulin resistance.

Waist circumference data were obtained from waist circumference measurements measured at the midpoint between the iliac crest and costal margins (lower ribs) using a medical measuring tape with 0.1 cm precision. Subjects used minimal clothing (Yang *et al.*, 2017). Subjects were considered at risk when waist circumference was 80 cm or more (Saklayen, 2018).

WHR data was obtained from the waist circumference to hip circumference ratio. Measurement of pelvic circumference was done by medical measuring tape with 0.1 cm precision. The Pelvic circumference is measured by determining the widest points on the buttock (Fitriyanti, *et al.*, 2019). Subjects are categorized as risky when WHR was more than 0.85 (Saklayen, 2018).

Data on the ratio of waist circumference and height (WHtR) was obtained from measurements of the height and waist circumference of the subject. Height was measured using a microtoise with 0.01 cm precision. The subject stands without using footwear and accessories above the head. Subjects were considered at risk when WHtR was 0.5 or more (Zhang et al., 2016).

Neck circumference was measured by medical measuring tape with 0.1 cm precision. Its measurements in women were one by subject's upright head position and forward-facing eyes, and then horizontally measured just below the protruding larynx.

Wrist circumference data were measured using medical measuring tape with 0.1 cm precision. Its measurement was done by placing the medical measuring tape horizontally on the distal side of the ulna protrusion, around the wrist. Wrist circumference measurement results were divided into 3 categories: small if subjects whose height less than 155 cm had wrist circumference less than 14 cm, subjects whose height 155-163 cm had wrist circumference 15.2 cm, subjects whose height more than 163 cm had wrist circumference less than 15.9 cm; moderate if subjects whose height less than 155 cm had wrist circumference 14-14.6 cm, subjects whose height 155-163 cm had wrist circumference 15.2-15.9 cm, subjects whose height more than 163 cm had wrist circumference 15.9-16.5 cm; large if subjects whose height less than 155 cm had wrist

circumference more 14.6 cm, subjects whose height 155-163 cm had wrist circumference of more than 15.9 cm, subjects had height more than 163 cm have wrist circumference of more than 16.5 cm (Nabila, et al., 2018).

Thigh circumference was measured by a medical measuring tape. Subjects were standing and wearing as few clothes as possible. Thigh circumference was measured 10 cm above the upper right patella. After that certain point was marked, the tape is placed horizontally and encircles the thigh (Bando *et al.*, 2017).

2D:4D ratio digit data is measured by a caliper with 0.001 mm precision. Measurements were made with the position of the palm open (Wu et al., 2013). The length of the index finger or second finger is the length of the finger measured from the midpoint of the second metacarpophalangeal joint and the most distal point of the second finger. The length of the ring finger or the fourth finger is the length of the finger measured from the midpoint of the fourth metacarpophalangeal joint and the most distal point of the fourth finger. 2D:4D ratio digit data was obtained from the length of the second finger divided by the length of the fourth finger. The ratio digits were considered high when the result shows more than 0.9811 for the right hand and more than 0.9821 for the left hand (Balci et al., 2018). Anthropometric data were collected by trained personnel.

Insulin resistance data was determined using HOMA -IR values. Measurement of Homeostasis Insulin Resistance Assessment Model (HOMA-IR) based on fasting blood glucose and fasting insulin level with the following formula (Matthews *et al.*, 1985; Levy, *et al.*, 1998; Torréns *et al.*, 2004):

Fasting Insulin 
$$\left(\frac{mU}{L}\right)$$
x Fasting Blood Glucose  $\left(\frac{mmol}{L}\right)$ 

The threshold of HOMA-IR value for adolescents is less than 1.65 (Rocco *et al.*, 2011). Blood sampling was collected by health workers. This blood sampling was in collaboration with the Sarana Medika laboratory.

## 2.4 Data analysis

Data normality test was performed through Kolmogorov-Smirnov test. We used univariate analysis to describe each variable. Bivariate analysis was completed by the Spearman Rank test. Bivariate analysis was performed to see whether there was a correlation between anthropometric profiles and insulin resistance.

## 3. Results

Table 1 described the anthropometric profile of the

Table 1. Characteristics of subjects.

Variable	Median	Minimum	Maximum
Body weight (kg)	66.6	47.8	107.4
Body height (cm)	157.4	100.5	171.4
Waist circumference (cm)	85.75	80.5	114
Hip circumference (cm)	103.5	30	170
Neck circumference (cm)	32.5	14.5	39
Wrist circumference (cm)	15	13.5	17.5
Thigh circumference (cm)	57.4	31	78.4
Waist Height to Ratio (WHtR)	0.55	0.49	0.95
Waist-hip circumference ratio (WHR)	0.84	0.6	3.33
2D:4D digit ratio of the right hand	0.98	0.84	1.09
2D:4D digit ratio of the left hand	0.99	0.52	0.6
HOMA-IR	2.33	0.54	18.32

subjects. The median body weight was 66.6 kg. The median waist circumference and pelvic circumferences were 85.75 cm and 103.5 cm, respectively, while the median WHR was 0.84±0.23. Based on Table 1, the median neck circumference, wrist circumference, WHtR was 32.5 cm, 15 cm, and 0.55 cm, respectively. The characteristic of the subjects could also be seen in Table 2. Table 2 showed that all subjects (100%) had less than 80 cm waist circumference which meant they were at risk of developing metabolic syndrome. Another anthropometric profile showed that 98.3% of subjects (n = 118) had high WHtR values. Based on WHR, as many as 90.8% of the subjects (n = 108) were at risk. A total of 83.3% of subjects (n = 100) also experienced insulin resistance as seen from the HOMA-IR value >1.65. However, anthropometric profiles, specifically neck circumference, wrist circumference, 2D:4D digit ratio of the right hand; 2D:4D digit ratio of the left hand, showed that less than 50% of subjects are at risk (10.8%; 21.7%;

Table 2. Frequency distribution of the subjects

Category	n	%
Waist circumference		
At risk >80 cm	120	100
Neck circumference		
At risk ≥35.5 cm	13	10.8
Under risk <35.5 cm	107	89.2
Wrist circumference		
At risk ≥16 cm	26	21.7
Under risk <16 cm	94	78.3
Waist Height to Ratio (WHtR)		
At risk ≥0.5	118	98.3
Under risk < 0.5	2	1.7
Waist-hip circumference ratio (WHR)		
At risk ≥0.8	109	90.8
Under risk < 0.8	11	9.2
2D:4D digit ratio of the right hand		
At risk	47	39.2
Under risk	73	60.8
2D:4D digit ratio of the left hand		
At risk	53	44.2
Under risk	67	55.8
HOMA-IR		
Normal	20	16.7
Resistance	100	83.3

39.2%; 44.2% respectively).

The correlation of anthropometric profile and insulin resistance incidence determined by HOMA-IR was shown in Table 3. Anthropometric profiles having a significant correlation with HOMA-IR were neck circumference (r = 0.271; p = 0.003), WHtR (r = 0.33; p < 0.001) and thigh circumference (r = 0.224; p = 0.014). Based on the analysis, the higher the value of the neck circumference, thigh circumference, and WHtR, the higher the HOMA-IR score. Table 3 also show that waist circumference had no correlation with HOMA-IR (r = 0.151; p = 0.1). There was also no correlation between wrist circumference and HOMA-IR (r = 0.12; p = 0.19). In addition, there was no correlation between WHR and HOMA-IR in the study subjects (r = -0.019; p = 0.836). Based on the analysis, other anthropometric profiles having no correlation with HOMA-IR were 2D:4D righthand digit ratios (r = 0.139; p = 0.129) and 2D:4D left hand digit ratios (r = 0.169; p = 0.065).

Table 3. Correlation of Anthropometric Profile and HOMA-IR.

r	р
0.151	0.100
0.271	$0.003^{*}$
0.120	0.190
0.224	0.014*
0.330	<0.001*
-0.019	0.836
0.139	0.129
0.169	0.065
	0.151 0.271 0.120 0.224 0.330 -0.019 0.139

Correlation test: Rank-Spearman, \*Significant (p<0.05)

#### 4. Discussion

Late adolescents, especially women, have the risk of experiencing the metabolic syndrome. Based on this study results, 83.3% of subjects experience insulin resistance determined by HOMA-IR. Since 2007, the Genome Wide Association Studies (GWAS) have identified around 88 loci associated with the risk of developing type 2 diabetes mellitus where most of the

loci are related to insulin secretion and pancreatic betacell function, causing insulin resistance associated with obesity (Brown and Walker, 2016). A study conducted in Semarang City also showed that 96.1% of subjects experienced insulin resistance determined by HOMA-IR (Nuraini *et al.*, 2017).

More than 50% of subjects of this study have high WHtR and WHR values. The study conducted in Jepara shows that 26.94% of adolescents experience abdominal obesity as seen from WHtR values of above 0.45 (Azizah and Sulchan, 2016). Another study conducted at the Faculty of Medicine Universitas Riau demonstrates that 44.1% of students experience central obesity as seen in the ratio waist-hip circumference (Jannah *et al.*, 2015). For women of reproductive age, fat storage is centralized in certain areas to protect important reproductive organs. This increases the risk of high WHR in women (Jannah *et al.*, 2015).

Based on the analysis, neck circumference has a significant correlation with Homeostasis Assessment for Insulin Resistance (HOMA-IR), where the greater the neck circumference of the subject, the higher HOMA-IR value. A Study in China shows that neck circumference has a significant correlation with insulin resistance assessed by HOMA-IR (Liang et al., 2014). Previous case studies in Public Senior High School 2 Semarang and Public Junior High School 9 Semarang also stated that neck circumference has a significant correlation with fasting blood sugar (Mayasari and Wirawanni, 2014).

Neck circumference is an easy anthropometric measurement. It can reflect the central obesity index and is associated with several cardiovascular risk factors such as dyslipidemia, hypertension, hyperuricemia, and insulin resistance. It is also considered an estimation of upper-body subcutaneous adipose tissue which plays a role in predicting insulin resistance and type-2 diabetes (Nabila *et al.*, 2018). The release of excess free fatty acids associated with upper-body subcutaneous fat, explicitly the neck, can be one mechanism to explain the correlation between neck circumference and insulin resistance (Ebbert and Jensen, 2013).

Lipolytic function and releasing rate of free fatty acids in upper body subcutaneous fat is found higher than lower body subcutaneous fat. Excessive free fatty acids in muscles and other tissues induce the body to use more free fatty acids as energy. They will also inhibit glucose oxidation, causing insulin resistance (Ebbert and Jensen, 2013). Increased free fatty acids also play a role in increasing VLDL production and inhibition of insulin clearance which induces insulin resistance. In addition, neck circumference is also positively correlated with A

total fat body and visceral fat which are related to biological parameters of insulin resistance. Two perivascular ectopic fat depots are also found in the neck region. Adipokine secretion, such as leptin, adiponectin, and interleukin-6, from perivascular ectopic fat depots, causes metabolic dysfunction including insulin resistance (Saneei *et al.*, 2019).

Subjects with large neck circumferences have a greater risk for obesity (Saneei *et al.*, 2019). Subcutaneous fat has a major role in the association of insulin resistance and obesity (Yuliani *et al.*, 2017). Insulin resistance is an important complication of obesity that causes hyperglycemia and impaired glycemic parameters (Saneei *et al.*, 2019).

Waist to Height Ratio (WHtR) is a good predictor in determining insulin resistance in an individual with obesity (Jamar *et al.*, 2017). Based on the analysis, WHtR has a correlation with HOMA-IR, where the greater the WHtR score, the greater the value of HOMA-IR. A study conducted in Australia on the correlation of WHtR and metabolic syndrome in adolescents and children with obesity, results in a correlation between WHtR and HOMA-IR (Nambiar *et al.*, 2013). Other studies conducted in Korea also find that high WHtR values in obese adolescents would affect the incidence of insulin resistance measured by HOMA-IR (Lim *et al.*, 2015).

WHtR plays a role in measuring central obesity which is often associated with metabolic disorders. An increase in fat tissue will promote an increase in adipokine secretion. This can increase insulin resistance. The most important adipokines are TNF- $\alpha$  which plays a role in inducing insulin resistance through glucose transporter 4 (GLUT-4) and increasing the release of free fatty acids. Increased transfer of free fatty acids to muscles results in increased intracellular fatty acid metabolites such as diacylglycerol, ceramide, and acetyl-CoA. These metabolites will activate the serine pathway or threonine kinase that reduces the ability to activate insulin receptors. Hence, it can cause insulin resistance when occurs in the long term it can damage visceral adipocyte  $\beta$  cells (Asnelviana *et al.*, 2017).

Based on the statistical test results, we find a correlation between thigh circumference and insulin resistance as measured by HOMA-IR. This finding is in line with the study conducted in Korea which shows the result that thigh circumference is positively related to HOMA-IR. The greater the thigh circumference, the greater the risk of insulin resistance (Park *et al.*, 2012). Another study in Korea explains that the measurement of thigh circumference is an indicator of diabetes marker (Jung *et al.*, 2013). The study conducted in Taiwan also

shows the left thigh circumference is a significant predictor of determining type 2 diabetes mellitus 2 (Ting et al., 2018). Large thigh circumference not only indicates greater muscle mass but also an increase in femoral subcutaneous fat mass. Lower muscle mass and subcutaneous fat in the thigh are associated with insulin resistance which results in hyperglycemia and diabetes (Ting et al., 2018). Subcutaneous fat in the thighs is a metabolism of circulating fatty acids that are circulating because there is a difference in lipolysis activity between subcutaneous fat in the abdomen and thighs. Subcutaneous fat in the thigh is wasting the metabolism of circulatory fatty acids as there is a difference between lipolysis activity of abdominal and thigh subcutaneous fat. Subcutaneous fat of the thigh tends to take fatty acids from the bloodstream, thus preventing the liver, pancreas, and ectopic fat such as the muscles from being exposed to high fatty acids (Nugraha et al., 2019).

Based on the study analysis, no correlation is found between neither waist circumference nor waist-hip circumference ratio with insulin resistance. This finding is contradictory to a study conducted on adolescents in Korea which shows the results that waist circumference and waist-hip circumference ratio have a significant correlation to HOMA-IR (Lim *et al.*, 2015). Waist circumference and waist-hip circumference ratio can be used as a screening tool to detect the incidence of abdominal obesity which can cause metabolic disorders such as insulin resistance (Fitriyanti, *et al.*, 2019).

However, a study conducted in Manado about the correlation of waist circumference and blood sugar levels shows no correlation between waist circumference and blood sugar levels among teachers at the Middle School and High School Eben Haezar Christian Manado. Another study held in Ngawi also shows no correlation between waist circumference and blood sugar levels in early adulthood (Manungkalit et al., 2015). Several other studies, including a study conducted at the Pusti Pidie Health Center, show no correlation between waist circumference ratio pelvis and blood sugar among Community Health Center's employees (Mulyani and Rita, 2016). The study states that the ratio of the waisthip circumference is not an extremely decisive factor in increasing blood sugar levels as many other factors influence the increase in blood sugar levels. Therefore, other anthropometric measurements need to be carried out (Mulyani and Rita, 2016).

Wrist circumference is a strong predictor of diabetes (Noudeh *et al.*, 2013). Wrist circumference is an easily measured anthropometric parameter that can determine body frame and bone size. Increased bone mass will also be associated with hyperinsulinemia (Fitriyanti, *et al.*,

2019) However, in this study, wrist circumference does not correlate with HOMA-IR. Inconsistent with the study in 18 years old adolescents, which demonstrated a correlation between wrist circumference and fasting insulin and HOMA-IR in both male and female adolescents (Fitriyanti et al., 2019). However, the study conducted by Nabila et al. about the correlation of wrist circumference and the blood glucose level among obese shows correlation between women no circumference with fasting blood glucose (Nabila et al., 2018). Another study conducted at Public Senior High School 6 Semarang also results in no correlation between wrist circumference with fasting blood glucose levels (Arifin and Panunggal, 2014). Factors influencing HOMA-IR values were fasting blood glucose and fasting insulin levels, where higher glucose levels fasting blood means higher the HOMA-IR value in the subject (Mitrea et al., 2013).

The Second to Fourth Digit Ratio (2D:4D) can be used to evaluate prenatal androgen exposure in the postpartum period. The Homeobox genes, HoxA and HoxB, are responsible for urogenital differentiation, prenatal androgen synthesis and fingers development. In animals, prenatal and neonatal androgenic exposure can increase adiposity, insulin resistance, and changes in adipose tissue lipolysis later in adulthood (Yıldız et al., 2015). However, based on this study analysis, the Second to Fourth Digit Ratio (2D:4D) of the right and left hand is not related to HOMA-IR or insulin resistance incidence. This finding is supported by the study conducted in Turkey, on the correlation between Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome. It shows that the Second to Fourth Digit Ratio (2D:4D) is not related to insulin resistance or the incidence of diabetes mellitus in the subject. Researchers state that no available study reports Second to Fourth Digit Ratio (2D:4D) as a predictor of androgen exposure and explains its correlation with metabolic syndrome (Yıldız et al., 2015). Another study conducted by Asuku et al. (2017) regarding the correlation of Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome indicators in Nigeria shows the results that Second to Fourth Digit Ratio (2D:4D) of the right and the left hand does not correlate with fasting blood sugar levels in the subjects. Researchers explain the absence of correlation between Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome indicators is caused by the small number of subjects, i.e. 465 subjects, meanwhile this study includes only 120 subjects. This might be their reason for no association found between the Second to Fourth Digit Ratio (2D:4D) and the incidence of insulin resistance.

### **Conflict of interest**

The authors declare no conflict of interest.

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# Anthropometric profile and its correlation to insulin resistance in female students with obesity

<sup>1,2,\*</sup>Dieny, F.F., <sup>1,2</sup>Fitranti, D.Y., <sup>1</sup>Jauharany, F.F., <sup>1,2</sup>Tsani, A.F.A., <sup>1</sup>Faradila, U. and <sup>1</sup>Rose, S.

<sup>1</sup>Department of Nutrition Science, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia <sup>2</sup>CENURE (Center of Nutrition Research), Universitas Diponegoro, Semarang, Indonesia

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#### **Abstract**

The prevalence of obesity in adolescent girls is increasing each year. Several anthropometric measurements can be used to detect the incidence of insulin resistance. This study was aimed to observe the correlation of anthropometric profiles with insulin resistance in adolescent girls with obesity. This was an observational study with a total of 120 female students of Universitas Diponegoro (Undip), aged between 18 and 21 years old, who have waist circumference >80 cm. They were chosen by a simple random sampling technique. Anthropometric profile data taken has consisted of waist circumference, hip circumference, waist-hip circumference ratio (WHR), waist-to-height ratio (WHtR), neck circumference, waist circumference, thigh circumference, and 2D:4D digit ratio. Insulin resistance data was determined using the Homeostasis Model Assessment-Insulin Resistance (HOMA-IR.). Bivariate analysis was completed with the Spearman rank test. There was 83.3% of subjects who experienced insulin resistance. High WHtR was found in 98.3% of total subjects as many as 90.8% of subjects were at risk based on WHR values. Based on 2D:4D ratio digits, neck circumference, wrist circumference <50% of subjects were found as at risk. There was no correlation between waist circumference, WHR, wrist circumference, 2D:4D digit ratio with HOMA-IR (p>0.05). However, there was a positive correlation between WHtR, neck circumference, and thigh circumference with HOMA-IR (p<0.05). Anthropometric profiles such as WHtR, neck circumference, and thigh circumference were correlated with insulin resistance in female adolescent with obesity.

## 1. Introduction

Nutritional status in adolescents is very important since adolescence is a transition period from childhood adulthood. This transition causes biological, psychological and cognitive changes that influence their nutritional status (Brown, 2011). However, nutritional status problems in adolescents are still fairly high, including obesity. The prevalence of central obesity 15 years adolescents and older has increased from 26.6% in 2013 to 31% in 2018 (Badan Penelitian dan Pengembangan Kesehatan, 2018). Obesity incidence will later be associated with degenerative diseases. Women are at higher risk of suffering from degenerative disease, while Indonesian Basic Health Research 2018 results report the prevalence of stroke, diabetes mellitus, heart disease, and hypertension is found higher in women than men (Badan Penelitian dan Pengembangan Kesehatan, 2018). Indonesian Basic Health Research 2018 results

also state that women and people who live in urban areas of all ages have a high prevalence of diabetes mellitus (Badan Penelitian dan Pengembangan Kesehatan, 2018).

Type 2 diabetes mellitus is caused by insulin resistance, a condition in which the patient's body is unable to absorb glucose (Srikanthan *et al.*, 2016). A study in Semarang City showed that 96.1% of adolescents experienced insulin resistance which was measured by Homeostasis Insulin Resistance Assessment Model (HOMA-IR) (Nuraini, *et al.*, 2017). HOMA-IR is a formula for calculating insulin resistance based on fasting blood sugar and insulin levels. Its measurement is simple, inexpensive, often used and has been validated by the clamp method (Sumarni, 2017).

One factor causing insulin resistance is central or abdominal obesity as abdominal fat is more actively undergoing lipolysis (Sumarni, 2017). Recently, several measurements of the body's anthropometric profile that can describe the incidence of central obesity are reported, where the measurements are done easily. Central obesity in adolescents can be described generally using measurements of waist circumference and hip waist circumference ratio (WHR). Some studies also mention that waist circumference and WHR have a significant correlation with insulin resistance (Sumarni, 2017).

In addition to waist circumference and WHR, other anthropometric profile measurements are also progressively more used, namely Waist-to-Height Ratio (WHtR). WHtR describes central obesity in adolescents with more accurate results than Body Mass Index (BMI) (Ashwell and Gibson, 2016; Saraswati and Sulchan, 2016; Yang *et al.*, 2017). A study in Mexico demonstrates WHtR as a better tool in identifying cardiometabolic obesity in adolescents used to predict hypertension and insulin resistance (Rodea-Montero, *et al.*, 2014). Other studies conducted in Semarang also showed the correlation between WHtR and increasing insulin resistance (Asnelviana, *et al.*, 2017).

Wrist circumference can also be utilized as an indicator. Studies conducted in late adolescents in Indonesia show wrist circumference as one of the anthropometric measurements that can predict obesity and insulin resistance in late adolescents. Wrist circumference reflects bone in the wrist area as well as peripheral fat distribution and metabolism thus it can measure one's body frame and bone size easily (Fitriyanti *et al.*, 2019).

Another measurement of anthropometric profiles that can be used to predict metabolic syndrome in adolescents is the measurement of neck circumference. Some studies show a correlation between neck circumference with insulin resistance (Liang *et al.*, 2014). Neck circumference can represent upper-body subcutaneous adipose tissue that plays a role in predicting insulin resistance and type 2 diabetes (Saneei *et al.*, 2019).

In addition, measurement of thigh circumference can also predict metabolic syndrome in adolescents since it reflects central adiposity (Bando *et al.*, 2017). Results of a study conducted in Korea show that thigh circumference is positively related to insulin resistance (Park *et al.*, 2012). Several studies also explain that thigh circumference is a good indicator in determining type 2 diabetes mellitus 2 (Jung *et al.*, 2013; Ting *et al.*, 2018).

Recently, it has been reported that there are other anthropometric measurements as indicators in predicting metabolic syndrome disease, namely The Ratio of Second to Fourth Digit Length (2D:4D) (Purwaningsih, 2016). The Ratio of the length of the index finger and

ring finger (2D:4D) can describe the exposure to the hormone oestrogen and prenatal testosterone. A study has shown that a low digit ratio is associated with high testosterone levels in men, while a high digit ratio is associated with low testosterone levels in women (Kumar et al., 2016). The size of digit ratio occurs since the end of the first trimester of foetal development (Oyeyemi et al., 2014). Inappropriate exposure to androgen hormone can cause Polycystic Ovary Syndrome (PCOS), causing infertility in premenopausal women. Women who experience PCOS often have metabolic diseases such as hypertension and insulin resistance (White et al., 2017). The Study states that digit ratio is correlated with obesity, which is a risk factor for metabolic disease (Gölge et al., 2016). There aren't many studies showing the relationship between digit ratio with insulin resistance.

In this study, the portrayal and correlation of anthropometric profiles (waist circumference, WHR, WHtR, wrist circumference, neck circumference, thigh circumference, and second to fourth digit ratio) and insulin resistance in female adolescents with obesity were studied.

## 2. Materials and methods

## 2.1 Experimental design, location, and time

This is an observational study and is included within the scope of community nutrition science. This research was conducted in Universitas Diponegoro Semarang, Indonesia at 10 Faculties from June until August 2019. There were 1,260 female students who participated in a screening program. The entire study was approved by the Health Study Ethics Committee (KEPK) Faculty of Medicine, Universitas Diponegoro/Central General Hospital dr. Kariadi No. 373/EC/KEPK/FK UNDIP/VIII/2019.

## 2.2 Samplings

Subjects of this study were 120 students from Universitas Diponegoro who were selected through simple random sampling, according to the following inclusion criteria: aged 18-21 years old, had 80 cm or more waist circumference, had intact fingers on both hands, were not currently consuming drugs that could affect the blood glucose and insulin levels, were willing to do fasting for at least 8 hours, did not smoke and/or consume alcohol, were not sick or in the care of a doctor, did not do heavy physical activity or exercise, were not pregnant and breastfeeding were willing to be the subject of study by filling out informed consent. The exclusion criteria in this study were the subject's withdrawal from the study, the subject's moved to another university, and the subjects passed away within the study period.

## 2.3 Data collected

Independent variables in this study were the anthropometric profile consisting of waist circumference, waist-hip circumference ratio (WHR), Waist-Height Ratio (WHtR), neck circumference, wrist circumference, thigh circumference, and the ratio of index finger length and ring finger (2D:4D). The dependent variable in this study was insulin resistance.

Waist circumference data were obtained from waist circumference measurements measured at the midpoint between the iliac crest and costal margins (lower ribs) using a medical measuring tape with 0.1 cm precision. Subjects used minimal clothing (Yang *et al.*, 2017). Subjects were considered at risk when waist circumference was 80 cm or more (Saklayen, 2018).

WHR data was obtained from the waist circumference to hip circumference ratio. Measurement of pelvic circumference was done by medical measuring tape with 0.1 cm precision. The Pelvic circumference is measured by determining the widest points on the buttock (Fitriyanti, *et al.*, 2019). Subjects are categorized as risky when WHR was more than 0.85 (Saklayen, 2018).

Data on the ratio of waist circumference and height (WHtR) was obtained from measurements of the height and waist circumference of the subject. Height was measured using a microtoise with 0.01 cm precision. The subject stands without using footwear and accessories above the head. Subjects were considered at risk when WHtR was 0.5 or more (Zhang *et al.*, 2016).

Neck circumference was measured by medical measuring tape with 0.1 cm precision. Its measurements in women were one by subject's upright head position and forward-facing eyes, and then horizontally measured just below the protruding larynx.

Wrist circumference data were measured using medical measuring tape with 0.1 cm precision. Its measurement was done by placing the medical measuring tape horizontally on the distal side of the ulna protrusion, around the wrist. Wrist circumference measurement results were divided into 3 categories: small if subjects whose height less than 155 cm had wrist circumference less than 14 cm, subjects whose height 155-163 cm had wrist circumference 15.2 cm, subjects whose height more than 163 cm had wrist circumference less than 15.9 cm; moderate if subjects whose height less than 155 cm had wrist circumference 14-14.6 cm, subjects whose height 155-163 cm had wrist circumference 15.2-15.9 cm, subjects whose height more than 163 cm had wrist circumference 15.9-16.5 cm; large if subjects whose height less than 155 cm had wrist circumference more 14.6 cm, subjects whose height 155-163 cm had wrist circumference more than 15.9 cm, subjects had height more than 163 cm have wrist circumference more than 16.5 cm (Nabila, et al., 2018).

Thigh circumference was measured by a medical measuring tape. Subjects were standing and wearing as few clothes as possible. Thigh circumference was measured 10 cm above the upper right patella. After that certain point was marked, the tape is placed horizontally and encircles the thigh (Bando *et al.*, 2017).

2D:4D ratio digit data is measured by a calliper with 0.001 mm precision. Measurements were made with the position of the palm open (Wu et al., 2013). The length of the index finger or second finger is the length of the finger measured from the midpoint of the second metacarpophalangeal joint and the most distal point of the second finger. The length of the ring finger or the fourth finger is the length of the finger measured from the midpoint of the fourth metacarpophalangeal joint and the most distal point of the fourth finger. 2D:4D ratio digit data was obtained from the length of the second finger divided by the length of the fourth finger. The ratio digits were considered high when the result shows more than 0.9811 for the right hand and more than 0.9821 for the left hand (Balci et al., 2018). Anthropometric data collected by trained were personnel.

Insulin resistance data was determined using HOMA -IR values. Measurement of Homeostasis Insulin Resistance Assessment Model (HOMA-IR) based on fasting blood glucose and fasting insulin level with the following formula (Matthews *et al.*, 1985; Levy, *et al.*, 1998; Torréns *et al.*, 2004):

$$\frac{Fasting\ Insulin\ \left(\frac{mU}{L}\right)x\ Fasting\ Blood\ Glucose\ \left(\frac{mmol}{L}\right)}{22.5}$$

The threshold of HOMA-IR value for adolescents is less than 1.65 (Rocco *et al.*, 2011). Blood sampling was collected by health workers. This blood sampling was in collaboration with Sarana Medika laboratory.

## 2.4 Data analysis

Data normality test was performed through Kolmogrov-Smirnov test. We used univariate analysis to describe each variable. Bivariate analysis was completed by the Spearman Rank test. Bivariate analysis was performed to see whether there was a correlation between anthropometric profiles and insulin resistance.

#### 3. Results

Table 1 described the anthropometric profile of the subjects. The median body weight was 66.6 kg. The

Table 1. Characteristics of subjects.

Variable	Median	Minimum	Maximum
Body weight (kg)	66.6	47.8	107.4
Body height (cm)	157.4	100.5	171.4
Waist circumference (cm)	85.75	80.5	114
Hip circumference (cm)	103.5	30	170
Neck circumference (cm)	32.5	14.5	39
Wrist circumference (cm)	15	13.5	17.5
Thigh circumference (cm)	57.4	31	78.4
Waist Height to Ratio (WHtR)	0.55	0.49	0.95
Waist-hip circumference ratio (WHR)	0.84	0.6	3.33
2D:4D digit ratio of the right hand	0.98	0.84	1.09
2D:4D digit ratio of the left hand	0.99	0.52	0.6
HOMA-IR	2.33	0.54	18.32

median waist circumference and pelvic circumferences were 85.75 cm and 103.5 cm, respectively, while the median WHR was 0.84±0.23. Based on Table 1, the median neck circumference, wrist circumference, WHtR was 32.5 cm, 15 cm, and 0.55 cm, respectively. The characteristic of the subjects could also be seen in Table 2. Table 2 showed that all subjects (100%) had less than 80 cm waist circumference which meant they were at risk of developing metabolic syndrome. Another anthropometric profile showed that 98.3% of subjects (n = 118) had high WHtR values. Based on WHR, as many as 90.8% of the subjects (n = 108) were at risk. A total of 83.3% of subjects (n = 100) also experienced insulin resistance as seen from the HOMA-IR value >1.65. However, anthropometric profiles, specifically neck circumference, wrist circumference, 2D:4D digit ratio of right hand; 2D:4D digit ratio of left hand, showed that less than 50% of subjects are at risk (10.8%; 21.7%; 39.2%; 44.2% respectively).

Table 2. Frequency distribution of the subjects

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Table 2. Frequency distribution of the subjects		
Category	n	%
Waist circumference		
At risk >80 cm	120	100
Neck circumference		
At risk ≥35.5 cm	13	10.8
Under risk <35.5 cm	107	89.2
Wrist circumference		
At risk ≥16 cm	26	21.7
Under risk <16 cm	94	78.3
Waist Height to Ratio (WHtR)		
At risk ≥0.5	118	98.3
Under risk < 0.5	2	1.7
Waist-hip circumference ratio (WHR)		
At risk ≥0.8	109	90.8
Under risk < 0.8	11	9.2
2D:4D digit ratio of the right hand		
At risk	47	39.2
Under risk	73	60.8
2D:4D digit ratio of the left hand		
At risk	53	44.2
Under risk	67	55.8
HOMA-IR		
Normal	20	16.7
Resistance	100	83.3

The correlation of anthropometric profile and insulin resistance incidence determined by HOMA-IR was shown in Table 3. Anthropometric profiles having a significant correlation with HOMA-IR were neck circumference (r = 0.271; p = 0.003), WHtR (r = 0.33; p < 0.001) and thigh circumference (r = 0.224; p = 0.014). Based on the analysis, the higher the value of the neck circumference, thigh circumference, and WHtR, the higher the HOMA-IR score. Table 3 also show that waist circumference had no correlation with HOMA-IR (r = 0.151; p = 0.1). There was also no correlation between wrist circumference and HOMA-IR (r = 0.12; p = 0.19). In addition, there was no correlation between WHR and HOMA-IR in the study subjects (r = -0.019; p = 0.836). Based on the analysis, other anthropometric profiles having no correlation with HOMA-IR were 2D:4D righthand digit ratios (r = 0.139; p = 0.129) and 2D:4D left hand digit ratios (r = 0.169; p = 0.065).

Table 3. Correlation of Anthropometric Profile and HOMA-IR.

0.151 0.271	0.100
0.271	*
0.2/1	$0.003^{*}$
0.120	0.190
0.224	0.014*
0.330	<0.001*
-0.019	0.836
0.139	0.129
0.169	0.065
	0.224 0.330 -0.019 0.139

Correlation test: Rank-Spearman, \*Significant (p<0.05)

#### 4. Discussion

Late adolescents, especially women, have the risk of experiencing the metabolic syndrome. Based on this study results, 83.3% of subjects experience insulin resistance determined by HOMA-IR. Since 2007, the Genome Wide Association Studies (GWAS) have identified around 88 loci associated with the risk of developing type 2 diabetes mellitus where most of the loci are related to insulin secretion and pancreatic betacell function, causing insulin resistance associated with

obesity (Brown and Walker, 2016). A study conducted in Semarang City also showed that 96.1% of subjects experienced insulin resistance determined by HOMA-IR (Nuraini *et al.*, 2017).

More than 50% of subjects of this study have high WHtR and WHR values. The study conducted in Jepara shows that 26.94% of adolescents experience abdominal obesity as seen from WHtR values of above 0.45 (Azizah and Sulchan, 2016). Another study conducted at the Faculty of Medicine Universitas Riau demonstrates that 44.1% of students experience central obesity as seen in the ratio waist-hip circumference (Jannah *et al.*, 2015). For women of reproductive age, fat storage is centralized in certain areas to protect important reproductive organs. This increases the risk of high WHR in women (Jannah *et al.*, 2015).

Based on the analysis, neck circumference has a significant correlation with Homeostasis Model Assessment for Insulin Resistance (HOMA-IR), where the greater the neck circumference of the subject, the higher HOMA-IR value. A Study in China shows that neck circumference has a significant correlation with insulin resistance assessed by HOMA-IR (Liang et al., 2014). Previous case studies in Public Senior High School 2 Semarang and Public Junior High School 9 Semarang also stated that neck circumference has a significant correlation with fasting blood sugar (Mayasari and Wirawanni, 2014).

Neck circumference is an easy anthropometric measurement. It can reflect the central obesity index and is associated with several cardiovascular risk factors such as dyslipidemia, hypertension, hyperuricemia, and insulin resistance. It is also considered an estimation of upper-body subcutaneous adipose tissue which plays a role in predicting insulin resistance and type-2 diabetes (Nabila *et al.*, 2018). The release of excess free fatty acids associated with upper-body subcutaneous fat, explicitly the neck, can be one mechanism to explain the correlation between neck circumference and insulin resistance (Ebbert and Jensen, 2013).

Lipolytic function and releasing rate of free fatty acids in upper body subcutaneous fat is found higher than lower body subcutaneous fat. Excessive free fatty acids in muscles and other tissues induce the body to use more free fatty acids as energy. They will also inhibit glucose oxidation, causing insulin resistance (Ebbert and Jensen, 2013). Increased free fatty acids also play a role in increasing VLDL production and inhibition of insulin clearance which induces insulin resistance. In addition, neck circumference is also positively correlated with A total fat body and visceral fat which are related to biological parameters of insulin resistance. Two

perivascular ectopic fat depots are also found in the neck region. Adipokine secretion, such as leptin, adiponectin, and interleukin-6, from perivascular ectopic fat depots, causes metabolic dysfunction including insulin resistance (Saneei *et al.*, 2019).

Subjects with large neck circumferences have a greater risk for obesity (Saneei *et al.*, 2019). Subcutaneous fat has a major role in the association of insulin resistance and obesity (Yuliani *et al.*, 2017). Insulin resistance is an important complication of obesity that causes hyperglycaemia and impaired glycemic parameters (Saneei *et al.*, 2019).

Waist to Height Ratio (WHtR) is a good predictor in determining insulin resistance in individual with obesity (Jamar *et al.*, 2017). Based on the analysis, WHtR has a correlation with HOMA-IR, where the greater the WHtR score, the greater the value of HOMA-IR. A study conducted in Australia on the correlation of WHtR and metabolic syndrome in adolescents and children with obesity, results in a correlation between WHtR and HOMA-IR (Nambiar *et al.*, 2013). Other studies conducted in Korea also find that high WHtR values in obese adolescents would affect the incidence of insulin resistance measured by HOMA-IR (Lim *et al.*, 2015).

WHtR plays a role in measuring central obesity which is often associated with metabolic disorders. An increase in fat tissue will promote an increase in adipokine secretion. This can increase insulin resistance. The most important adipokines is TNF- $\alpha$  which plays a role in inducing insulin resistance through glucose transporter 4 (GLUT-4) and increasing the release of free fatty acids. Increased transfer of free fatty acids to muscles results in increased intracellular fatty acid metabolites such as diacylglycerol, ceramide, and acetyl-CoA. These metabolites will activate the serine pathway or threonine kinase that reduces the ability to activate insulin receptors. Hence, it can cause insulin resistance when occurs in the long term it can damage visceral adipocyte  $\beta$  cells (Asnelviana *et al.*, 2017).

Based on the statistical test results, we find a correlation between thigh circumference and insulin resistance as measured by HOMA-IR. This finding is in line with the study conducted in Korea which shows the result that thigh circumference is positively related to HOMA-IR. The greater the thigh circumference, the greater the risk of insulin resistance (Park *et al.*, 2012). Another study in Korea explains that the measurement of thigh circumference is an indicator of diabetes marker (Jung *et al.*, 2013). The study conducted in Taiwan also shows the left thigh circumference is a significant predictor of determining type 2 diabetes mellitus 2 (Ting *et al.*, 2018). Large thigh circumference not only

indicates greater muscle mass but also an increase in femoral subcutaneous fat mass. Lower muscle mass and subcutaneous fat in the thigh are associated with insulin resistance which results in hyperglycaemia and diabetes (Ting et al., 2018). Subcutaneous fat in the thighs is metabolism of circulating fatty acids that are circulating because there is a difference in lipolysis activity between fat in the abdomen and subcutaneous Subcutaneous fat in the thigh is wasting the metabolism of circulatory fatty acids as there is a difference between lipolysis activity of abdominal and thigh subcutaneous fat. Subcutaneous fat of the thigh tends to take fatty acids from the bloodstream, thus preventing the liver, pancreas, and ectopic fat such as the muscles from being exposed to high fatty acids (Nugraha et al., 2019).

Based on the study analysis, no correlation is found between neither waist circumference nor waist-hip circumference ratio with insulin resistance. This finding is contradictory to a study conducted on adolescents in Korea which shows the results that waist circumference and waist-hip circumference ratio have a significant correlation to HOMA-IR (Lim *et al.*, 2015). Waist circumference and waist-hip circumference ratio can be used as a screening tool to detect the incidence of abdominal obesity which can cause metabolic disorders such as insulin resistance (Fitriyanti, *et al.*, 2019).

However, a study conducted in Manado about the correlation of waist circumference and blood sugar levels shows no correlation between waist circumference and blood sugar levels among teachers at the Middle School and High School Eben Haezar Christian Manado. Another study held in Ngawi also shows no correlation between waist circumference and blood sugar levels in early adulthood (Manungkalit et al., 2015). Several other studies, including a study conducted at the Pusti Pidie Health Center, show no correlation between waist circumference ratio pelvis and blood sugar among Community Health Center's employees (Mulyani and Rita, 2016). The study states that the ratio of the waisthip circumference is not an extremely decisive factor in increasing blood sugar levels as many other factors influence the increase in blood sugar levels. Therefore, other anthropometric measurements need to be carried out (Mulyani and Rita, 2016).

Wrist circumference is a strong predictor of diabetes (Noudeh *et al.*, 2013). Wrist circumference is an easily measured anthropometric parameter that can determine body frame and bone size. Increased bone mass will also be associated with hyperinsulinemia (Fitriyanti, *et al.*, 2019) However, in this study, wrist circumference does not correlate with HOMA-IR. Inconsistent with the study conducted by Kusmiyati *et al.* in 18 years old

adolescents, which demonstrates a correlation between wrist circumference and fasting insulin and HOMA-IR in both male and female adolescents (Fitriyanti *et al.*, 2019). However, the study conducted by Nabila et al. about the correlation of wrist circumference and the blood glucose level among obese women shows no correlation between wrist circumference with fasting blood glucose (Nabila *et al.*, 2018). Another study conducted at Public Senior High School 6 Semarang also results in no correlation between wrist circumference with fasting blood glucose levels (Arifin and Panunggal, 2014). Factors influencing HOMA-IR values were fasting blood glucose and fasting insulin levels, where higher glucose levels fasting blood means higher the HOMA-IR value in the subject (Mitrea *et al.*, 2013).

The Second to Fourth Digit Ratio (2D:4D) can be used to evaluate prenatal androgen exposure in the postpartum period. The Homeobox genes, HoxA and HoxB, are responsible for urogenital differentiation, prenatal androgen synthesis and fingers development. In animals, prenatal and neonatal androgenic exposure can increase adiposity, insulin resistance, and changes in adipose tissue lipolysis later in adulthood (Yıldız et al., 2015). However, based on this study analysis, the Second to Fourth Digit Ratio (2D:4D) of the right and left hand is not related to HOMA-IR or insulin resistance incidence. This finding is supported by the study conducted in Turkey, on the correlation between Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome. It shows that the Second to Fourth Digit Ratio (2D:4D) is not related to insulin resistance or the incidence of diabetes mellitus in the subject. Researchers state that no available study reports Second to Fourth Digit Ratio (2D:4D) as a predictor of androgen exposure and explains its correlation with metabolic syndrome (Yıldız et al., 2015). Another study conducted by Asuku et al. (2017) regarding the correlation of Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome indicators in Nigeria shows the results that Second to Fourth Digit Ratio (2D:4D) of the right and the left hand has no correlation with fasting blood sugar levels in the subjects. Researchers explain the absence of correlation between Second to Fourth Digit Ratio (2D:4D) and metabolic syndrome indicators is caused by the small number of subjects, i.e. 465 subjects, meanwhile this study includes only 120 subjects. This might be their reason for no association found between the Second to Fourth Digit Ratio (2D:4D) and the incidence of insulin resistance.

## **Conflict of interest**

The authors declare no conflict of interest.

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