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Prediction of Insulin Resistance in Late Adolescent Based on Anthropometric Index

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ABSTRACT

The study aimed to evaluate the role of neck circumference for predicting insulin resistance in adolescent compared with waist circumference and waist hip ratio. A cross sectional study was conducted by measuring anthropometric parameters (neck circumference, waist circumference, hip circumference) and biochemical parameter (fasting plasma glucose, fasting insulin, and HOMA-IR) involving 80 late adolescents. Statistical analysis used in this study were Pearson and Spearman correlation, multivariate linear regression. Neck circumference positively correlated with fasting insulin and HOMA-IR in both gender, while neck circumference only positively correlated with fasting plasma glucose in men. In addition, multivariate linier regression showed that a higher regression coefficient of waist circumference associated with a higher risk of insulin resistance (fasting insulin (β=0.11; $p<0.05$), HOMA-IR (β=0.05; $p<0.05$)) compared to neck circumference and waist hip ratio. Neck circumference, waist circumference, and waist hip ratio is an anthropometry indicators that could be used to predict insulin resistance. However, waist circumference is better than neck circumference and waist-hip ratio for predicting insulin resistance in adolescent.

Keywords: insulin resistance, neck circumference, predictor, waist circumference, waist hip ratio

INTRODUCTION

Body fat composition and body fat distribution are related to metabolic dysfunction (Silva *et al*. 2014; Stabe *et al*. 2013). Body fat distribution related to visceral fat and subcutaneous fat will have an impact on insulin resistance (Dai *et al*. 2016). The high prevalence of obesity in adolescents may lead to insulin resistance and becomes a serious issue (Caprio *et al*. 2017; Dewi 2007). Insulin resistance plays a role in the development of dyslipidemia, type 2 diabetes mellitus, metabolic syndrome, and cardiovascular disease (Silva *et al*. 2014; Dewi 2007; Stabe *et al*. 2013).

The most commonly used anthropometric indexes to determine obesity which correlated with various adverse health outcomes is the Body Mass Index (BMI), waist circumference, and waist-hip ratio (Silva *et al*. 2014; Junge *et al*. 2017). In determining obesity, BMI cannot account for the actual composition and distribution of body fat, while the use of waist circumference and waist-to-hip ratio has limitations in distinguishing the distribution of visceral fat and subcutaneous fat (Gomez-Arbelaez *et al*. 2016; Kelishadi *et al*. 2017). The results of waist circumference can vary due to the variance of time of measurement, the last food consumed, breathing, health conditions, and errors in determining the measuring point (Joshipura *et al*. 2016; Stabe *et al*. 2013).

Neck circumference is one of the new anthropometric meassurement, inexpensive, simple, practical, non-invasive, comfortable indicators, and it can be used to determine obesity and the risk of comorbidity (Gomez-Arbelaez *et al*. 2016; Joshipura *et al*. 2016; Junge *et al*. 2017). Obesity causes build-up of subcutaneous fat depots in the neck resulting larger neck circumference (Dai *et al*. 2016; Joshipura *et al*. 2016). Fat depots around the neck is unique place that can depict the upper subcutaneous adipose tissue of the body (Hingorjo *et al*. 2016; Ma *et al*. 2016), it also has greater lipolysis activity which increase free fatty acids, oxidative stress, and insulin resistance (Joshipura *et al*. 2016; Ma *et al*. 2016).

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Several studies showed that neck circumference was correlated with obesity and insulin resistance (Gomez-Arbelaez *et al*. 2016; Junge, *et al*. 2017). Study on 669 children aged 8-14 years showed that neck circumference had a positive and significant correlation with fasting blood glucose, fasting insulin, and Homeostasis Model Assessment for Insulin Resistance (HOMA-IR) (Gomez-Arbelaez *et al*. 2016). Furthermore, Junge *et al*. (2017) showed that neck circumference was positively and significantly correlated with fasting insulin levels and insulin resistance in 1542 children aged 5-18 years. This study aimed to compare the neck circumference, waist circumference, and waist-hip ratio to predict the insulin resistance in late adolescents in Semarang City.

METHODS

Design, location, and time

This study was an observasional study using a cross-sectional design which was conducted in Diponegoro University, Semarang from February-March 2018.

Sampling

A total of 80 subjects aged 17-21 years were selected using simple random sampling. Participants were recruited from five different faculties in the college. The inclusion criteria of participantss: subjects without enlargement of the thyroid gland, never had previously pregnant and diagnosed or treated with type 1/type 2 diabetes mellitus, and were not pregnant and not an athletes. This study was approved by The Ethics Committee of the Medical Faculty of the Diponegoro University (ethical approval number: 41/ EC/FK-RSDK/I/2018).

Data Collection

The primary collected data included subject identity, anthropometric measurements (body weight, height, neck circumference, waist circumference, and hip circumference), and biochemical measurements (fasting blood glucose and fasting insulin). Body Mass Index (BMI) was calculated by dividing body weight (kg) by height (m^2). In this study, BMI was referred to WHO reference standard for Asian population.

Neck circumference was measured using flexible tape with the standardized position: "Frankfort plane" head, facing forward, and the arms hanging loosely. The measurement was performed at the level of the thyroid cartilage for females and above the laryngeal prominence (adam's apple) for males.

The posture at the time the waist circumference measurement was the body stands firmly with the loosely hanging arms, the feet close together, and relaxes. The approximate midpoint of waist circumference measurement was between the lower limit of the rib and the upper limit of the iliac. Hip circumference was measured by determining the widest point on the buttocks. Subjects were assigned to wear minimize clothes and stand in a relaxed abdominal position. Waist-hip ratio was calculated by dividing the waist circumference to the hip circumference.

The 8-10 hours fasting venous blood was drawn by trained laboratory staff. Fasting plasma glucose (FPG) was analysed using the hexokinase method conducted at the certified laboratory of Diponegoro National Hospital, Semarang, Indonesia; while fasting insulin was analysed using the Enzyme Linked Immunosorbent Assay (ELISA) method conducted at the certified GAKY Laboratory of the Faculty of Medicine, Diponegoro University Semarang, Indonesia. Insulin resistance was determined using the HOMA-IR which was calculated by the formula: fasting insulin (µIU/ml) x FPG (mg/dl)/405.

Data analysis

Descriptive analysis were performed using frequencies and percentages to describe subjects characteristics based on gender including age, nutrition status, anthropometric measurements, and biochemical parameters. The Pearson's correlation coefficients and Spearman correlation were used to analyse the relationship between circumferences measure (neck circumference, waist circumference, and waist-hip ratio) and biochemical parameters (FPG, fasting insulin, and HOMA-IR) separated by gender. Multivariate linear regression analysis were applied to assess the quantitative associations between circumferences measure and biochemical parameter adjusted by gender and age. Receiver Operating Curve (ROC) was used to assess the accuracy of the cut-off point for insulin resistance prediction.

RESULTS AND DISCUSSION

Anthropometric measures and biochemical parameters

Numerous hormones, body fat mass, and lean body mass affect the metabolism in human body. The pattern of fat deposition is controlled by genes and varies between males and females

(Lysen & Israel 2018). A total of 80 subjects consist of 51 females and 29 males who have characteristics of age, nutritional status, anthropometric measurements, and biochemical parameters according to gender are presented in Table 1. The mean age of adolescents was 18.44 years. The percentage of obesity and underweight were higher in males than females.

The mean values of BMI, neck circumference, waist circumference, and hip circumference were higher in males than females, while the mean value of waist-hip ratio was higher in females than males. The difference of the anthropometric measurements between males and females might be caused by the difference of adipose tissue activity, fat distribution, and morphology according to gender (Straznicky *et al*. 2017).

Males tend to have higher neck circumference than females particularly in healthy and normal body weight (Ferretti *et al*. 2015). The previous study by Li *et al.* (2014) which measured neck fat by computer tomography in patients aged 35-75 years showed that man tend to have higher neck circumference, less adipose tissue, and more visceral fat than woman. During the process of puberty, accumulation of fat mass in truncal area, visceral fat, and liver fat in boys increases the waist circumference, while accumulation of gluteofemoral fat in girls increases the waist-hip ratio (Kautzky-Willer *et al*. 2016).

The mean value of fasting plasma glucose was higher in males than females, while the mean values of fasting insulin and HOMA-IR were higher in females than males. Gender differences play a diverse role in the pathogenesis of insulin resistance in adolescents. In the puberty phase, females tend to have body fat mass and subcutaneous fat increment, while males tend to gain lean body mass. Increase of body fat mass and decrease of lean body mass are associated with insulin resistance in adolescents (Newbern *et al*. 2014). In addition, sex hormone plays a role in distribution, function, and fat deposition, also inflammatory response and the development of insulin resistance (Kautzky-Willer *et. al* .2016).

Correlation between neck circumference, waist circumference, waist-hip ratio, and biochemical parameters

Body fat distribution can be assessed by anthropometric measurements. Neck circumference, waist circumference, and waist-hip ratio in the assessment of body fat distribution are the alternative ways to predict glucose homeostasis, metabolic disorders, and the risk of cardiovascular disease (Silva *et al*. 2014; Joshipura *et al*. 2016; Stabe *et al*. 2013). The correlation between neck circumference, waist circumference, waist-hip ratio and biochemical parameters according to gender were presented in Table 2. In this study,

Table 1. Subjects characteristic according to gender

	Total (n=80)	Males (n=29)	Females (n=51)	p
Age	18.44±0.65[a]	18.38±0.677[a]	18.47±0.644[a]	0.55[c]
Nutritional Status				
Obesity	23 (28.8%)	9 (31%)	14 (27.5%)	
Overweight	19 (23.8%)	4 (13.8%)	15 (29.4%)	0.44[d]
Normal	20 (25%)	9 (31%)	11 (21.6%)	
Underweight	18 (22.5%)	7 (24.1%)	11 (21.6%)	
Anthropometric measurements				
BMI (kg/m^2)	23.22±5.078[a]	23.31±5.676[a]	23.17±4.763[a]	0.98[c]
NC (cm)	31 (27.35-39.30)[b]	33.3 (29.70-39.30)[b]	30 (27.35-36.50)[b]	0.00[e]
WC (cm)	75.82±10.275[a]	77.58±11.752[a]	74.82±9.309[a]	0.25[c]
HC (cm)	89.21±11.419[a]	96.90±10.423[a]	84.84±9.562[a]	0.00[c]
WHR	0.85±0.067[a]	0.79±0.048[a]	0.88±0.056[a]	0.00[c]
Biochemical parameters				
FPG (mg/dl)	86 (70-327)[b]	89 (77-103)[b]	85 (70-327)[b]	0.00[e]
Fasting Insulin (µIU/ml)	6.88 (0.32-22.94)[b]	6.41 (1.96-22.94)[b]	7.24 (0.32-22.32)[b]	0.57[e]
HOMA-IR	1.51 (0.06-5.61)[b]	1.34 (0.39-5.61)[b]	1.52 (0.06-4.7)[b]	0.73[e]

[a]Mean±SD; [b]Median(min-max); [c]Independent t test; [d]Chi-square test, [e]Mann-Whitney test; BMI: Body Mass Index; NC: Neck Circumference; WC: Waist Circumference; HC: Hip Circumference; WHR: Waist-Hip Ratio; FPG: Fasting Plasma Glucose

Table 2. Correlation between neck circumference, waist circumference, waist-hip ratio and biochemical parameters

	Males			Females		
	NC (cm)	WC (cm)	WHR	NC (cm)	WC (cm)	WHR
NC (cm)	1[a]	0.73[a]	0.44[a*]	1[a]	0.58[a**]	0.30[a*]
WC (cm)	0.73[a**]	1[b]	0.78[b**]	0.58[a**]	1[b]	0.43[b**]
WHR	0.44[a*]	0.78[b**]	1[b]	0.30[a*]	0.43[b**]	1[b]
FPG (mg/dl)	0.27[a]	0.38[a*]	0.17[a]	-0.01[a]	0.05[a]	-0.08
Insulin (µIU/ml)	0.72[a**]	0.88[a**]	0.64[a**]	0.28[a*]	0.32[a*]	0.25[a]
HOMA-IR	0.73[a**]	0.87[a**]	0.62[a**]	0.29[a*]	0.33[a*]	0.25[a]

[a]Spearman; [b]R Pearson; *p<0.05; **p<0.001; BMI: Body Mass Index; NC: Neck Circumference; WC: Waist Circumference; HC: Hip Circumference; WHR: Waist-Hip Ratio; FPG: Fasting Plasma Glucose

there was positive correlation between neck circumference, waist circumference, waist-hip ratio and all biochemical parameters in males; while in females, neck circumference, waist circumference, and waist-hip ratio showed positive correlation with fasting insulin and HOMA-IR.

The present study indicated statistically significant positive correlation between waist circumference and fasting plasma glucose (r=0.38, p<0.05), waist circumference and fasting insulin (r=0.88, p<0.001), and waist circumference and HOMA-IR (r=0.87, p<0.001) in males. This study was in line with the previous study in 15,542 children and adolescents aged 5-18 years which showed statistically significant positive correlation between waist circumference and fasting insulin (r=0.59, p<0.001); and waist circumference and HOMA-IR (r=0.58, p<0.001), and the neck circumference also showed positive correlation with fasting insulin and insulin resistance (Junge *et al*. 2017).

Overweight and obesity associated with fat deposition in abdomen, waist, hip, and neck then result in enlargement of waist circumference, hip circumference, and neck circumference (Joshipura *et al*. 2016). The study conducted in Brazilian adolescents aged 10-19 years, neck circumference was found to be positively associated with waist circumference in puberty boys and girls. The correlation between neck circumference and the risk of cardiovascular disease is similar to correlation between BMI, waist circumference, hip circumference, waist-hip ratio, waist-height ratio and the risk of cardiovascular disease (Silva *et al*. 2014).

Regression between anthropometric parameters and biochemical parameters

Multivariate linear regression analysis were used to assess the most influenced anthropometric measurements towards insulin resistance. Table 3 showed the multivariate linear regression

Table 3. The association between neck circumference, waist circumference and waist-hip ratio with fasting plasma glucose, fasting insulin, and HOMA-IR

Dependent variables	Independent variables	B	β standardized	t	P
FPG (mg/dl)	NC (cm)	-1.47	-0.14	-0.07	0.47
	WC (cm)	0.67	0.25	1.32	0.18
	WHR	-12.04	-0.02	-0.16	0.86
Fasting insulin (µIU/ml)	NC (cm)	0.33	0.20	1.17	0.24
	WC (cm)	0.17	0.38	2.44	0.01
	WhR	7.66	0.11	0.76	0.44
HOMA-IR	NC (cm)	0.04	0.11	0.65	0.51
	WC (cm)	0.05	0.46	2.98	0.00
	WhR	1.51	0.09	0.63	0.52

Multivariate linear regression. NC: Neck Circumference; WC: Waist Circumference; WHR: Waist-Hip Ratio; FPG: Fasting Plasma Glucose analysis between neck circumference, waist circumference, waist-hip ratio and fasting plasma glucose, fasting insulin, HOMA-IR.

This study showed that neck circumference did not significantly correlated with insulin resistance ($p>0.05$). The previous study which conducted the enlargement of neck circumference in 1053 adults aged 18-60 years in Brazil revealed the increasing chance of insulin resistance by 1.2 times both male and female (Stabe *et al*. 2013).

All independent variables did not significantly correlated with fasting plasma glucose ($p>0.05$). Waist circumference was found to be significantly correlated to fasting insulin and HOMA-IR ($p<0.05$). The enlargement by 1 cm of waist circumference increased both fasting insulin by 0.17 μIU/ml and HOMA-IR by 0.05.

Waist circumference is one of simple anthropometrics used to evaluated abdominal obesity in clinical study or large epidemiological population based studies (Luo *et al*. 2016). Waist circumference may not only be associated both intra-abdominal and subcutaneous adipose tissue, but also used to be screening tools for identifying visceral adiposity (Stabe *et al*. 2013; Luo *et al*. 2016). Abdominal obesity is one of important risks of metabolic disorder in insulin resistance and metabolic syndrome (Luo *et al*. 2016).

The optimal neck circumference, waist circumference, and waist-hip ratio cut-off point for insulin resistance prediction

Adipose tissue not only the primary site of energy storage but also active endocrine organ involved in regulating the body's metabolism and immunity (Luo *et al*. 2016; Zhao *et al*. 2018). Directly measured by gold standard methods (dual energy X-ray absorptiometry (DEXA), bioimpedance, hydro densitometry, Magnetic Resonance Imaging (MRI) and computer tomography (CT)) may provide accurate results, but those methods are not practical and expensive (Hatipoglu *et al*. 2010). Therefore, we considered the anthropometric measurement as a tool in measuring body fat distribution which is simpler and easier to use than the gold standard methods. The optimal cut-off point, sensitivity, specificity, and AUC values of neck circumference in predicting insulin resistance are presented in Table 4.

Waist circumference was better than waist-hip ratio and neck circumference in predicting insulin resistance, particularly in male. The optimal waist circumference cut-off point was ≥85.6 cm in men has a sensitivity value of 100% and a specificity of 96%. A high sensitivity value is suitable for screening to obtain adolescents suspected of having insulin resistance, while a high specificity value is used to obtain adolescents suspected of not experiencing insulin resistance. The AUC value of waist circumference in men to predict insulin resistance was 99% (95% CI 0.95-1.00). Statistically, the AUC value of 99% is classified as very good (Dahlan 2009).

Biochemical measurements in identifying insulin resistance are expensive and not practical for screening tools, mainly in individuals settled in low income countries (Gomez-Arbelaez *et al*. 2016). Therefore, neck circumference is one of anthropometric measurements which effective, simple, cheap, and easy for predicting adolescents with insulin resistance risk. Furthermore, neck circumference can be implemented for screening comorbidity in large scale (Joshipura *et al*. 2016).

Subcutaneous fat at the upper part of the body measured by neck circumference may associate with the risk of comorbidity (Stabe *et al*. 2013; Silva *et al*. 2014). Visceral fat is main site to release free fatty acid may account for increasing risk comorbidity by neck circumference enlargement. Circulation free fatty acid is also secreted by subcutaneous fat, particularly in obesity. Obesity has subcutaneous fat 2-3 times higher than normal weight individuals (Namazi *et al*. 2018). Subcutaneous fat at the upper part of the body has lipolytic activity bigger than subcutaneous fat at the lower body part and visceral fat (Silva *et al*. 2014; Stabe *et al*. 2013; Joshipura *et al*. 2016; Pandzic Jaksic *et al*. 2018). Free fatty acid concentration is directly associated with insulin resistance, oxidative stress, production of very low density lipoprotein (VLDL) in hepar, and it is endothelial dysfunction consequence (Stabe *et al*. 2013; Joshipura *et al*. 2016; Kelishadi *et al*. 2017; Namazi *et al*. 2018).

Result of the assessment of CT scan and MRI show that neck circumference is positively correlated with visceral fat accumulation. Li *et al*. (2014) previously measured with neck fat with CT scan showed that neck circumference is positively and is significantly correlated to visceral fat both in male and female. Neck has two perivascular fat depots surrounding bilateral carotid vessel (Namazi *et al*. 2018). Perivascular fat is metabolically active adipokine which consist of cytokines and hormones associated with meta-

Table 4. The optimal neck circumference, waist circumference, and waist-hip ratio cut off point for predicting insulin resistance

	Cut-off point (cm)	Se (%)	Sp (%)	AUC (95% CI)	p
Neck circumference					
Male	≥35.3	75	80	0.88 (0.71-1.00)	0.01
Female	≥30.1	75	55.3	0.58 (0.21-0.95)	0.58
Waist circumference					
Male	≥85.6	100	96	0.99 (0.95-1.00)	0.00
Female	≥75.5	50	53.2	0.59 (0.26-0.92)	0.52
Waist-hip ratio					
Male	≥0.84	75	96	0.99 (0.95-1.00)	0.00
Female	≥0.91	75	73.9	0.61 (0.29-0.94)	0.61

Receiver operating curve analysis. Se: Sensitivity, Sp: Specivity, AUC: Area Under Curve, CI: Confidence Interval

bolic disregulation (Namazi *et al*. 2018; Meiliana & Wijaya 2013; Pandzic Jaksic *et al*. 2018).

Prospective cohort by which was conducted in adult aged 24-64 years in Beijing China showed that neck circumference associated with cardio metabolic risk, and the enlargement of neck circumference indicated the incidence of later life cardiovascular events and high mortality of cardiovascular disease (Dai *et al*. 2016).

The latest evidence shows that waist circumference is good predictor for some chronic disease, but waist circumference has limitation (Namazi *et al*. 2018). The interesting point of neck circumference as screening tools is easy and stable due to not being affected by abdominal distention or breathing movements. Compared with waist circumference, neck circumference measurement is not necessarily required multiple measurements which are responsible for the precision and reability. Neck circumference measurement provides comfortable aspects for both examiner and patient, mainly for children with obesity or overweight who feel embarrassed when having waist circumference measurements (Junge *et al*. 2017; Hatipoglu *et al*. 2010; Silva *et al*. 2014; Namazi *et al*. 2018; Stabe *et al*. 2013). Therefore, neck circumference is simple, convenient, and fast as screening tool which can be used for public health services and epidemiology study in large scale for identifying insulin resistance and other metabolic risk.

Our study has few limitations because it was cross sectional study which could not show the causality of association. Furthermore, the small number of samples might affect the statistical analysis result, and we did not have any information regarding to the exercise habits which might also affect the size of neck circumference.

CONCLUSION

Neck circumference, waist circumference, and waist-hip ratio are anthropometric measurements that can be used for predicting insulin resistance in adolescents.Waist circumference is a stronger predictor for insulin resistance than neck circumference and waist-hip ratio.

Neck circumference, waist circumference, and waist-hip ratio can be implemented as simple tools for identifying insulin resistance in asymptomatic adolescents, and are acceptable to both patients and health practitioners in public health services. Further studies are needed to identify the relationship between anthropometric measurements and insulin resistance state of overweight and obesity in different age in the population.

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