

Predictors of Insulin Resistance in Indonesian Adolescents with Obesity

Hasanuddin Nuru, Noppawan Piaseu*, Rutja Phuphaibul, Umaporn Suthutvoravut

Abstract: Insulin resistance commonly results from obesity with excessive adipose tissue, increasing body mass index and waist circumference. This cross-sectional correlational study aimed to examine factors influencing insulin resistance in Indonesian adolescents with obesity. A total of 134 adolescents with obesity aged 13-15 years were recruited from five randomly selected junior high schools in a southern city in Indonesia. Participants were classified into insulin resistance (n =67) and non-insulin resistance (n =67) based on the homeostasis model assessment of insulin resistance. Data were collected using a demographic questionnaire, the Adolescent Sedentary Activity Questionnaire, and had a nutritional assessment comprised of waist circumference, body mass index, snacking calories, fasting blood glucose and plasma insulin. Data were analyzed using descriptive statistics, and univariate and multivariate logistic regression.

The univariate logistic regression indicated that waist circumference, body mass index, family history of obesity or diabetes, frequency of breakfast, snacking calories, sedentary behavior, and father's income and mother's education were significantly associated with insulin resistance. The multivariate logistic regression model predicting insulin resistance included waist circumference, family history of obesity or diabetes, and sedentary behavior >5 hours/day. These three variables together explained 76.7% variance of the insulin resistance. Nurses' roles should include monitoring health education and assessment of adolescents and their families, and promoting physical activity in schools, and particularly for those adolescents with obesity and family history of obesity or diabetes.

Pacific Rim Int J Nurs Res 2017; 21(4) 280-290

Keywords: Adolescents, Diabetes, Homeostasis model, Indonesia, Insulin resistance, Obesity, Predictive factors

Introduction

Obesity in adolescents is a substantial epidemiological and clinical significance issue.¹ Obesity has broad range of adverse health effects including type 2 diabetes, insulin resistance (IR), hypertension, metabolic syndrome, and also psychological disturbances such as low self-esteem and depression.² It affects not only deleterious individual health, but

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also increasing healthcare cost at public and national levels.³ A previous study⁴ revealed that the most common cause of morbidity in adolescents with obesity is IR.

IR is defined as inability to control hepatic glucose production and enhance glucose clearance in target tissues.⁵ The homeostasis model assessing insulin resistance (HOMA-IR) has been commonly used as an indirect measure of IR in adolescents.⁶ It was estimated that 52.1% of adolescents with obesity in the United States, while 11.7%–81% in European countries and 38% in Indonesia suffered with IR.^{7,8} Obesity is therefore a key predictor of IR, closely associated with increasing body mass index (BMI) and visceral fat, resulting in increased prevalence of type 2 diabetes mellitus both in childhood and later in adulthood.^{4,9} However, studies investigating social determinants of IR in Indonesian adolescents with obesity are scarce.⁸ Thus, this study aimed to identify factors determining IR in this population.

Literature review and theoretical framework

Obesity in adolescents is defined by BMI according to age and sex-specific growth chart at two levels: BMI >95th percentile indicating “obesity” and BMI >97th percentile indicating “severe obesity”, as recommended by the Centers for Disease Control and Prevention (CDC).¹⁰ Obesity is influenced by multidimensional factors that can be described through a social ecological framework.^{11,12} This framework is recognized as the most capable approach to describe how individuals interact with different factors that influence their behaviors in the context of multiple environments involving the intrapersonal, interpersonal, organizational, community, and public policy arenas.^{11,12} An adolescent’s food consumption behaviors, particularly snacking and breakfast skipping

and physical activity, are commonly influenced by their parents.¹² Parental socioeconomic status is therefore considered as interpersonal factors affecting an adolescent’s weight status, BMI, and waist circumference which are considered their intrapersonal factors affecting insulin resistance. This study particularly focused on intrapersonal and interpersonal levels that built up an integrative framework to determine insulin resistance as measured by HOMA IR¹³ in adolescents with obesity.

Intrapersonal factors in this study can be categorized into three groups: 1) biological factors consisting of gender and family history of diabetes,^{14,15} 2) behavioral factors including breakfast skipping and sedentary behavior,^{14,16-18} and 3) nutritional factors including snacking, severity of obesity as measured by body mass index and waist circumference.^{14,19-23} Snacking refers to calorie intake from consumption of foods and drinks between meals, normally contributing to 10–20% of daily calorie intake.²¹ However, excessive consumption of snacks containing fructose results in visceral adiposity, hepatic lipogenesis, increased free fatty acid and ultimately insulin resistance.²² Severity of obesity is closely associated with visceral adiposity and IR in adolescents.²³ **Interpersonal factors** refer to parental socioeconomic status including education, income and occupation of parents (Figure 1) and adolescent financial dependency on parents. Parents with low income, education attainment, and occupation have increased risk for obesity, affecting IR through adiposity.²⁴⁻²⁷

Considering evidence from the literature and the social ecological framework, it was hypothesized that intrapersonal factors (gender, family history of diabetes or obesity, breakfast skipping, sedentary behavior, snacking, BMI, WC) and interpersonal factors (parents’ income, occupation and income) are associated with IR, and all these factors predict IR in adolescents with obesity.

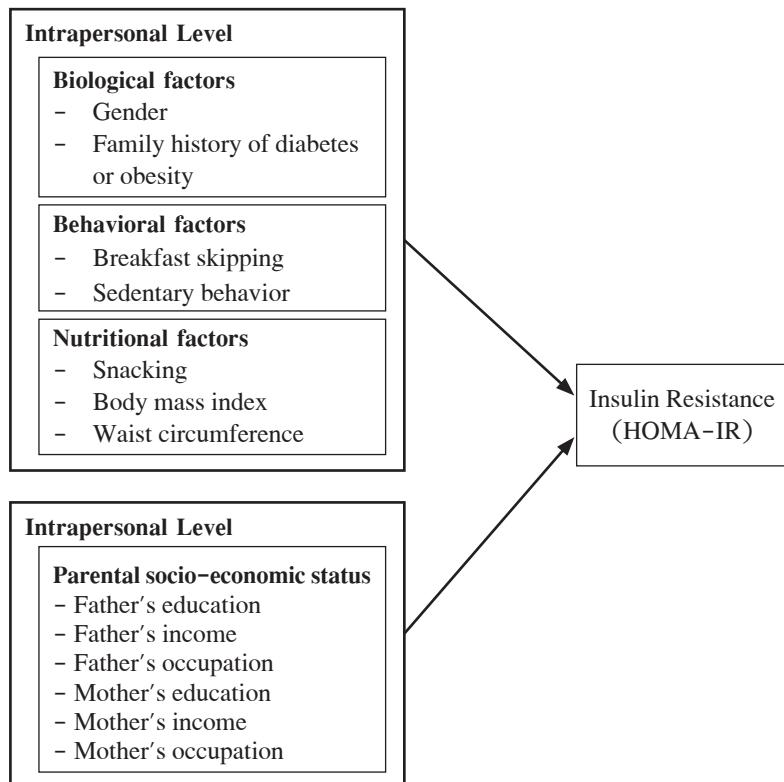


Figure 1 A conceptual framework of the study

Methods

Design: A cross-sectional correlational design was used.

Sample and settings: The participants consisted of 134 Indonesian adolescents with obesity aged 13–15 years who were in grades 7–9 at five randomly selected private and public junior high schools in central Makassar City, South Sulawesi, Indonesia. Convenience sampling was based on the following inclusion criteria: 1) BMI >95th percentile based on age and sex; 2) living with their parents, and 3) not taking any medication affecting their nutritional status.

The sample size was determined according to Kelsey²⁸, using OpenEpi sample size calculation online software, with a level of significance (α) of .05 and power ($1-\beta$) of .80. Initially, the sample size was 112.

To allow for incomplete data, 40% was added, calculating a required sample of 157 participants. There were 159 potential participants who met the inclusion criteria; however, 19 of them did not have permission from their parents. A total of 140 participants were then classified into two groups based on the HOMA-IR criteria. Six were excluded due to data incompleteness, therefore the final participant was 134 consisting of 67 participants with insulin resistance and 67 participants with no insulin resistance (Figure 2).

Ethical considerations: This study was approved by the Institutional Review Board for Research Ethics, Faculty of Medicine, Ramathibodi Hospital, Mahidol University (ID 12-58-21). Permissions for data collection were obtained from school administrators and the participants' parent. Information was provided to participants including research purposes, details of

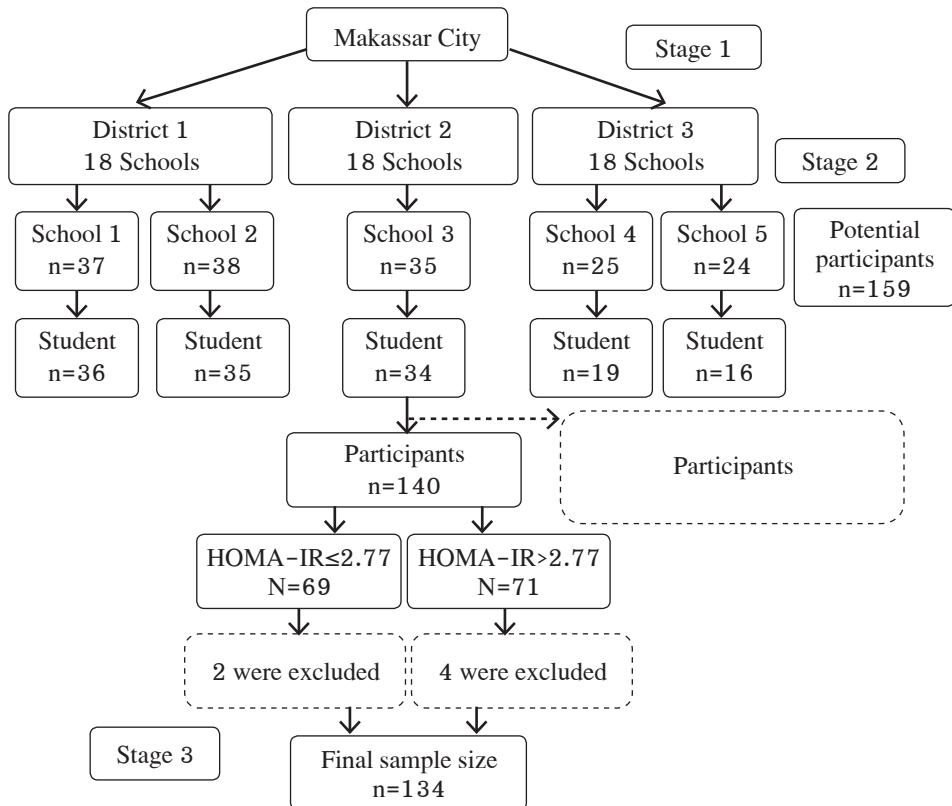


Figure 2 Sampling procedure

the study, confidentiality, risks and benefits. Assents were obtained from all participants and consents from their parents. Participant rights were protected throughout the study.

Instruments

The Demographic Questionnaire was developed by the principal investigator (PI) and consisted of 16 questions on age, gender, family history of diabetes or obesity, and Parental socioeconomic status as classified into three parts: 1) father's education and mother's education categorized into 3 levels (primary or middle school; high school or diploma; and university or higher); 2) father's income and mother's income categorized into 3 levels: low (< 150 USD), middle (150–375 USD) and high (>375 USD) and 3)

father's occupation and mother's occupation categorized into 2 levels (employed and unemployed).²⁶

The Adolescent Sedentary Activity Questionnaire (ASAQ) was developed by Hardy et al.²⁹, and measures a comprehensive range of sedentary activity time, among school-aged children, out of school hours. The questionnaire, translated to Indonesian with author permission, and using the forward-backward technique, was slightly modified and consisted of 11 questions for weekdays and 12 questions for weekends. The participants were asked to complete how long they spent for daily activities including: 1) small screen recreation (SSR); 2) studying; 3) traveling; 4) cultural activities; and 5) social activities. Those who were inactive less than 2 hours/day, between 2–5 hours/day, and more than 5 hours/day were classified as having "light", "moderate", and "severe" sedentary behavior,

respectively.³⁰ The content was validated by five experts obtaining the scale content validity index (S-CVI) at .91. In a 1-week interval, the test-retest reliability from a pilot-test with 30 adolescents with obesity was .94.

Additionally, the **Breakfast Skipping Questionnaire of just one question** commonly used to identify frequency of breakfast skipping³¹ was “How many times do you have breakfast within a week?”. Response items including “twice a week or less or never”, and “3 times a week or more” were categorized as “breakfast skipping”, and “no breakfast skipping”, respectively. The intraclass correlation coefficient (ICC) was 0.66 and Kappa was 0.69 in the original questionnaire.³¹ In this study, test-retest reliability was 0.81.

Body mass index (BMI) was used to determine the severity of obesity according to age and a sex-specific growth chart. Body weight was measured in light clothing to the nearest 0.1 kg on a digital weighing scale and height was measured without shoes to the nearest 0.1 cm with specificity 0.8–0.92 and sensitivity 0.92.¹⁷ Participants were divided into obesity (BMI >95th percentile) and severe obesity (BMI >97th percentile) based on the recommendation of CDC.¹⁰

Waist circumference (WC) was measured using percentiles of age and gender following the cut off points used in Malaysian adolescents.³² Non-stretchable nylon tape was used to measure waist circumferences to the nearest 0.1 cm in a horizontal plane at the level of the middle between the lower margin of the last rib and the iliac crest. The WC was measured twice and the average was recorded in each participant. Participants were classified into “central obesity” (WC >90th percentile) and “severe central obesity” (WC ≥95th percentile).³² In the training session of research assistants for this study, inter-rater reliability with the expert in nutrition assessment was .93 and intra-rater reliability was .95.

Snacking was measured as daily calorie intake from snack and drinks between meals using one-day food record with 24-hour recall. The data were then analyzed in percentage of daily calories from snack

using Nutrisurvey software³³ according to Recommended Dietary Allowance (RDA) for Indonesian adolescents.³⁴ Participants were classified into “very good” (<10% of daily calories from snack), “good” (10–20 % of daily calories from snack), and “poor” (>20 % of daily calories from snack).²¹

Insulin resistance was measured by fasting glucose and fasting insulin using the Enzyme-linked Immunosorbent Assay (ELISA) method in the laboratory certificated by the National Accreditation Committee, then calculated for HOMA-IR by the formula: [fasting glucose (mmol/l) × fasting insulin (μIU/l)]/22.5.³⁵ Participants were classified into two groups based on the HOMA-IR cut off point: “normal” (HOMA-IR ≤ 2.77) and “insulin resistance” (HOMA-IR >2.77).³⁵

Data Collection

The PI coordinated with school administrators for research permission and provided information on study purposes and procedures to prospective participants. After consents were obtained, the participants completed all self-administered questionnaires lasting approximately 20 minutes. The participants had their body weight, height, and waist circumference measured by a research assistant trained by the PI. Two nurses were trained and served as research assistants. The PI then made participant appointments and informed them of 10-hour fasting before blood test for insulin and glucose in the morning of the next day. The participants had their blood drawn by a qualified technician at Hasanuddin University Medical Research Centre (HUM-RC), and received a small gift from the PI as appreciation for their time and cooperation during the study.

Data Analysis

Demographic data were analyzed using descriptive statistics. Univariate Logistic Regression was used to

examine associations of intrapersonal factors (gender, family history of diabetes or obesity, breakfast skipping, sedentary behavior, snacking, BMI, WC) and interpersonal factors (father and mother education, income, occupation) with insulin resistance (HOMA-IR) in the participants. Multivariate logistic regression was used to examine intrapersonal factors and interpersonal factors together predicting insulin resistance in the participants.

Results

Most participants were male (61.2%). Univariate logistic regression analysis revealed that a family history of obesity or diabetes, breakfast skipping, severe sedentary behavior, poor snacking, more body mass index, excessive waist circumference, low income of father, and a less educated mother were significantly associated with insulin resistance (Table 1). Multiple

logistic regression analysis with forward method was applied to obtain adjusted odds ratio. Results revealed that three out of eight factors (sedentary behavior, waist circumference, and family history of obesity and diabetes) together predicted insulin resistance, with the overall percentage of predicted insulin resistance of 76.7% (Table 2). A participant with severe central obesity (waist circumference $\geq 95^{\text{th}}$ percentile) was 26.5 times more likely to have insulin resistance than those with waist circumference less than the 95th percentile (95% CI 4.598–152.136); a person with family history of obesity and diabetes was 9 times more likely to have insulin resistance than those with no family history (95% CI 2.396–34.082) and a person with severe sedentary behavior (> 5 hours/day) was 25.5 times more likely to have insulin resistance than those who had moderate sedentary behavior (2–5 hours) (95% CI 6.253–103.994) when controlling for other variables.

Table 1 Univariate Logistic Regression examining factors associated with HOMA-IR in participants

Factors	Insulin Resistance n (%)	No Insulin Resistance n (%)	OR	95%CI	p-value
Intrapersonal factors:					
Family history of obesity or diabetes					
Yes	52(77.6)	25(37.3)	5.824	2.728–12.433	<.001
No*	15(22.4)	42(62.7)			
Breakfast skipping					
No*	7(10.4)	34(50.7)			
Yes	60(89.6)	33(49.3)	8.831	3.527–22.109	<.001
Sedentary behavior					
Moderate*	7(10.4)	54(80.6)			
Severe	60(89.6)	13(19.4)	35.604	13.234–95.788	<.001
Snacking					
Good to very good*	13(19.4)	33(49.3)	4.032	1.863–8.725	<.001
Poor	54(80.6)	34(50.7)			
BMI group					
Obesity*	11(16.4)	22(32.8)			
Severe obesity	56(83.6)	45(67.2)	2.489	1.093–5.670	.030
WC group					
Central obesity*	2(3.0)	44(65.7)			
Severe central obesity	65(97.0)	23(34.3)	62.174	3.946–277.174	<.001

Table 1 Univariate Logistic Regression examining factors associated with HOMA-IR in participants (Cont.)

Factors	Insulin Resistance n (%)	No Insulin Resistance n (%)	OR	95%CI	p-value
Interpersonal factors					
Father's income					
Low	12(17.9)	5(7.5)	4.000	1.210-13.244	.023
Middle	37(55.2)	32(47.7)	1.927	0.909-4.087	.087 ^{ns}
High*	18(26.9)	30(44.8)			
Mother's education					
Primary-High School	43(64.2)	28(41.8)	2.496	1.244-5.008	.010
University/higher*	24(35.8)	39(58.2)			

OR=Odd ratio, CI=Confident interval; ns= No statistical significance

*Reference group

Discussion

It was evident in this study that intrapersonal factors, particularly severe sedentary behaviors, excessive waist circumference, and family history of obesity or diabetes, had association with insulin resistance stronger than other intrapersonal factors and the interpersonal factors, and the findings were consistent with previous studies.^{5,16,19} These three factors were therefore highly associated with insulin resistance.

Multivariate logistic regression revealed that the best predictors of insulin resistance were severe sedentary behavior, excessive waist circumference, and family history of obesity and diabetes with overall predictive power at 76.7% (Table 2). According to social ecological framework,^{11,12} these three factors were at intrapersonal level, indicating that the intrapersonal factors including nutritional, biological, and behavioral factors strongly influenced insulin resistance.

Table 2 Multivariate Logistic Regression examining factors predicting HOMA-IR in the participants

Factors	Insulin Resistance n (%)	No Insulin Resistance n (%)	B	OR	95%CI	p-value
WC group						
Central obesity*	2(3.0)	44(65.7)				
Severe central obesity	65(97.0)	23(34.3)	3.275	26.449	4.598-152.136	<.001
Family history						
Yes	52(77.6)	25(37.3)	2.201	9.036	2.396-34.082	<.001
No*	15(22.4)	42(62.7)				
Sedentary behavior						
Moderate*	7(10.4)	54(80.6)				
Severe	60(89.6)	13(19.4)	3.239	25.500	6.253-103.994	<.001

Nagelkerke R²=.767; -2LL=71.143; x²=114.620; df=4; p<.001

WC=Waist circumference, OR=Odd ratio, CI=Confident interval

*Reference group

The strongest predictor of insulin resistance in this study was severe sedentary behavior for more than 5 hours /day. It was evident that most of the participants with insulin resistance (89.6%) spent time for sedentary behavior more than 5 hours/day (**Table 1**) particularly watching TV, playing games, getting access to the internet. Sedentary behavior, therefore, plays a major role in reducing energy expenditure and increasing insulin resistance. This finding supports the mutual interaction of the participants and their environment, and is similar to findings of other studies indicating that sitting activities for a long period of time and low physical activity have direct association with insulin resistance and cardiovascular risks in overweight adolescents.^{36, 37}

The second predictor of insulin resistance was severe central obesity. The increased waist circumference in the participants with insulin resistance may be partly due to poor quality of snack, breakfast skipping and sedentary behavior. A previous study revealed that the risk of insulin resistance among persons with overweight and obesity increases significantly with increased waist circumference.³⁷ This could be explained by a mechanism through releasing the pro-inflammatory adipokines and releasing non-esterified free fatty acids from visceral fat to the portal system, inducing lipotoxicity and insufficient phosphorylation in the insulin type 1 receptor substrate presenting in adipocytes and myocytes and finally leading to insulin signaling alteration and insulin resistance.²³

Family history of obesity or diabetes was the third predictor of insulin resistance. This is consistent with a previous study³⁸ reporting that genetic transmission from parents with obesity is clearly shown to be associated with higher secretion of insulin in both male and female offspring. According to the social ecological framework, it was evident in this study that within the intrapersonal factors, the biological factor may have less influence on insulin resistance than behavioral and nutritional factors.

Other intrapersonal factors including breakfast skipping, snacking, severity of obesity and interpersonal

factors including father's income and mother's education were not included as predictors of insulin resistance. These variables may be correlated with the three other predicted variables. In addition, areas on why these factors were no longer significant in multiple logistic regression model was that waist circumference, indicating visceral fat as a major determinant of insulin resistance, was already influenced by these factors. In addition, interpersonal factors as social determinants may not have a direct influence on insulin resistance.¹²

Limitations

Causal relationship was limited due to this cross-sectional design and potential recall bias. Confounding of correlations among behavioral and nutritional factors also needed to be taken into account.

Conclusions and Implications for Nursing Practice

The findings in this study support the social ecological framework. Intrapersonal factors strongly influenced insulin resistance in adolescents with obesity, particularly behavioral, nutritional, and biological factors. Sedentary behavior, waist circumference and family history of obesity or diabetes were major predictors of insulin resistance; it is therefore necessary that nurses play roles in developing strategies for behavioral modification within family and school contexts with aims to promote physical activity and reduce waist circumference particularly for obese adolescents with family history of obesity or diabetes.

Acknowledgments

This study was supported by the Ministry of Research and Technology, Indonesia and the International Nursing Program, Mahidol University, Thailand. Gratitude is conveyed to the adolescents for their participation.

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ปัจจัยทำนายภาวะต้ออินสูลินในวัยรุ่นอ้วนชาวอินโดเนเซีย

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บทคัดย่อ: ภาวะต้ออินสูลินเป็นผลจากโรคอ้วน ที่มีการสะสมของไขมันในร่างกาย ด้ัชนมีมวลกายและเส้นรอบเอวเกินเกณฑ์ การศึกษาเชิงความลึกพื้นที่แบบตัดขวางในครั้งนี้มีวัตถุประสงค์เพื่อศึกษาปัจจัยทำนายภาวะต้ออินสูลินในวัยรุ่นอ้วนชาวอินโดเนเซีย ตัวอย่างเป็นวัยรุ่นที่อ้วน อายุ 13-15 ปี จำนวน 134 คน จากโรงเรียน 5 แห่งที่สุ่มได้ในจังหวัดทางภาคใต้ของอินโดเนเซีย แบ่งเป็นกลุ่มที่มีภาวะต้ออินสูลิน (67 คน) และไม่มีภาวะต้ออินสูลิน (67 คน) ตามเกณฑ์การประเมินภาวะต้ออินสูลินเก็บรวมข้อมูลโดยใช้แบบสอบถามข้อมูลส่วนบุคคล แบบสอบถามพฤติกรรมแบบนิ่งและการประเมินภาวะโภชนาการได้แก่ เส้นรอบเอว ดัชนีมวลกาย พลังงานที่ได้รับจากขนมขบเคี้ยว ระดับน้ำตาลและอินสูลินในเลือด วิเคราะห์ข้อมูลด้วยสถิติบรรยาย และการวิเคราะห์ผลโดยอิสติทิด ผลการศึกษาพบว่า เส้นรอบเอว ดัชนีมวลกาย ประวัติโรคอ้วนหรือเบาหวานในครอบครัว ความถี่ของการรับประทานอาหารเช้า พลังงานที่ได้รับจากขนมขบเคี้ยว พฤติกรรมแบบนิ่ง รายได้ของบิดา การศึกษาของมารดา มีความลึกพื้นที่ กับภาวะต้ออินสูลินอย่างมีนัยสำคัญทางสถิติ ผลการวิเคราะห์ผลโดยอิสติทิดแบบพหุ พบร่วมกับเส้นรอบเอวที่ 95 เปอร์เซ็นไทล์ขึ้นไปการมีประวัติโรคอ้วนหรือเบาหวานในครอบครัวและพฤติกรรมแบบนิ่งมากกว่า 5 ชั่วโมงต่อวัน ร่วมกันทำนายภาวะต้ออินสูลินได้ร้อยละ 76.7 อย่างมีนัยสำคัญทางสถิติพยาบาล ความมีบทบาทในการติดตามประเมินเส้นรอบเอวและส่งเสริมกิจกรรมทางกายในโรงเรียนโดยเฉพาะในวัยรุ่นที่อ้วนและมีประวัติโรคอ้วนหรือเบาหวานในครอบครัว

Pacific Rim Int J Nurs Res 2017; 21(4) 280-290

คำสำคัญ: วัยรุ่น การประเมินภาวะต้ออินสูลิน อินโดเนเซีย ภาวะต้ออินสูลิน โรคอ้วน ปัจจัยทำนาย

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