

Association of resistin level with acanthosis nigricans in obese adolescents

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Abstract

Background Childhood obesity is associated with increased risk of cardiovascular diseases and metabolic syndrome, such as insulin resistance. Clinically, insulin resistance may be manifested as acanthosis nigricans. Resistin has a biological activity that is important in glucose and lipid metabolisms and closely related to the incidence of insulin resistance.

Objective To find out the association of resistin level with scale of acanthosis nigricans in adolescents obesity.

Methods A cross-sectional study was conducted on 53 obese adolescents with acanthosis nigricans in senior high schools in Padang, West Sumatera. Degree of acanthosis nigricans was assessed using scale of Burke and then plasma resistin level was performed with ELISA. Data were analyzed using ANOVA and post-hoc test.

Result The mean of resistin level in obese adolescents was 14.21 (SD 7.43) ng/dL. High resistin level was found in scale of acanthosis nigricans 2,3 and 4 ($P=0.0001$). Obese adolescents with severe degree of acanthosis nigricans has higher resistin level compared to milder acanthosis nigricans.

Conclusion In obese adolescents, the higher degree of acanthosis nigricans, the higher level of plasma resistin. [Paediatr Indones. 2016;56:32-6.]

Keyword: resistin, acanthosis nigricans, obesity

Obesity has become a leading public health concern. Over 1 billion people are now overweight or obese, and the prevalence of these conditions is rising rapidly.¹ In the year 1988 to 1994 by the National Health and Nutrition Examination Survey (NHANES) in the United States, approximately 30% of obese adolescents had metabolic syndrome, which is closely related to an increased risk of atherosclerotic coronary heart disease, diabetes mellitus (DM) type 2.² Insulin resistance can be characterized clinically by the presence of acanthosis nigricans. Acanthosis nigricans (AN) is a skin condition characterized by darkening and thickening of the skin caused by papillomatosis and hyperkeratosis.³

Stacking excessive adipose tissue in obesity will cause chronic inflammation which occurs in increased production of proinflammatory cytokines such as tumor necrosis factor (TNF)- α , interleukin (IL)-1, IL-6 and resistin.^{4,5} Resistin is a protein secreted in adipose tissue by preadipocytes primarily on monocytes of resistin stromal.^{6,7} This component has potential link between obesity and glucose regulation. In mice, resistin can induce insulin resistance, whereas

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its implications in the control of insulin sensitivity in human is still a matter of debate. Several studies of clinical studies have shown that plasma resistin levels are associated with BMI.⁶⁻⁸

The purpose of this study was to determine the average levels of resistin in obese adolescents with acanthosis nigricans and to find out the relationships between acanthosis nigricans degree with resistin levels.

Methods

A cross sectional study of 53 obese adolescent was conducted in three senior high schools in Padang, from May 2014 to Agustus 2014. Ethical approval was obtained from the Medical Ethics Committee, Andalas University Medical School.

Inclusion criteria were obese adolescents who have acanthosis nigricans, willing to retrace the study, and got permission from the parents. Adolescents who had treatment for diabetes mellitus were excluded. The subjects were chosen proporsively. The diagnosis of obesity was upheld by $BMI \geq 95^{\text{th}}$ percentile of BMI curve CDC 2000. The degree of acanthosis nigricans were determined using a scale of acanthosis by Burke (**Table 1**).

Blood samples were obtained for resistin in the morning after an overnight fasting. Samples for resistin obtained with venous blood sampling as much as 5 mL by trained laboratory personnels using disposable syringe. Blood was inserted into the tube without anticoagulant, allowed to set for 30 minutes and then centrifuged at 1000 rev/min for 15 min,

Table 1. The scale of acanthosis nigricans by Burke⁹

Score	Description
0	Absent: not detectable at close inspection
1	Present: clearly present on close visual inspection, not visible to the casual observer, extent not measurable.
2	Mild: limited to the base of the skull, does not extend to the lateral margins of the neck (usually, 3 inches in breadth)
3	Moderate: extending to the lateral margins of the neck (posterior border of the sternocleidomastoid) (usually 3-6 inches), should not be visible when the participant is viewed from the front
4	Severe: extending anteriorly (6 inches), visible when the participant is viewed from the front.

the serum obtained and stored at -20°C. Serum level of resistin were assayed by an enzyme-linked immunosorbent assay (ELISA) with resistin kit from R & D Systems Inc. (USA). Normal resistin levels ranged from 0.156 to 10 ng /mL, with a sensitivity of 0.026 ng/mL.

All data were recorded, tabulated, and analyzed using SPSS version 14.0. Numerical data analyzed by analysis of variance (ANOVA), with P value of < 0.05 was considered as statistically significant.

Results

From 53 subjects participating in the study, 25 were males and 28 were females. The characteristic of subjects are shown in **Table 2**. Most obese adolescents (39%) had second scale of acanthosis nigricans (AN). Mean resistin levels in males was higher than in females, but it was statistically not significant (**Table 3**). The mean resistin levels in obese adolescents with first scale of AN was still within normal limits. The higher scales of acanthosis nigricans, the higher the levels of resistin ($P=0.001$) (**Table 4**). Post hoc analysis of resistin levels showed significant differences between groups scale of acanthosis nigricans 1 with 2, 3, and 4, with P value of < 0.05 (**Table 5**). There was a tendency of increased BMI with increased levels of resistin. The statistical test found no correlation

Table 2. Subject characteristics

Characteristics	
Mean age (SD), year	16 (0.62)
Gender, n	
Male	25
Female	28
Mean body weight (SD), kg	90.28 (12.70)
Mean body height (SD), cm	163.32 (7.96)
Mean BMI (SD), kg/m ²	33.89 (4.31)
Acanthosis nigricans scale, n	
Scale 1	13
Scale 2	21
Scale 3	9
Scale 4	10

Table 3. Resistin level by gender

Gender	n	Mean resistin level (SD), ng/mL	P value
Male	25	14.82 (8.14)	0.582
Female	28	13.68 (6.83)	

Table 4. Description of resistin levels based on the scale of acanthosis nigricans

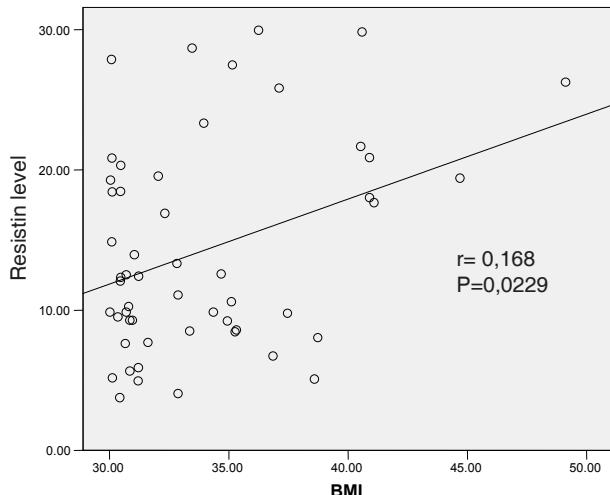
Acanthosis nigricans scale	Mean resistin level (SD), ng/mL	P value
Scale 1	6.79 (2.05)	0.0001
Scale 2	12.47 (3.56)	
Scale 3	17.38 (5.22)	
Scale 4	24 (6.45)	

another study on native American children found more females had acanthosis nigricans.¹³ A study in the United States shows the value of HOMA-IR were significantly higher in adolescents with acanthosis nigricans than youth without acanthosis nigricans.¹⁴ Another study observed that children with acanthosis nigricans showed significantly higher BMI and waist

Table 5. The P-value for the average resistin levels between the two groups of acanthosis nigricans scale

	Scale 1	Scale 2	Scale 3	Scale 4
Scale 1		0.003	0.000	0.000
Scale 2	0.003		0.035	0.000
Scale 3	0.000	0.035		0.003
Scale 4	0.000	0.000	0.003	

between the two variables ($r = 0.168$, $P = 0.0229$) (Figure 1).

**Figure 1.** Correlation between resistin levels with BMI

Discussion

Acanthosis nigricans is pathognomonic for insulin resistance. Screening for acanthosis nigricans in clinics and schools to identify individuals at high risk of type 2 diabetes has important implications in the development of intervention strategies against diabetes.¹⁰ Most subjects in this study was acanthosis nigricans scale 2 (39.6%). A study in Padang showed that most obese adolescents had acanthosis nigricans scale 2 and 3.¹¹ A previous study on Hispanic obese children revealed that acanthosis was found more in boys,¹² while

circumference. These results confirm the relationship between adiposity and insulin resistance.¹⁵ Several studies have noted that the incidence of acanthosis nigricans increased with increased risk of diabetes mellitus. A previous study found that obese youth with acanthosis nigricans had 1.97 times greater likelihood of developing type 2 diabetes mellitus.³ Type 2 diabetes is reaching 15% in patients with acanthosis nigricans and only 4% in patients without acanthosis nigricans. Acanthosis nigricans may be an independent risk factor for this disease.³

Resistin is an adipocytokine protein produced by adipose tissue, the levels are increased in patients with obesity and is closely related to the incidence of insulin resistance. Resistin is suspected as a liaison between adipocytes and insulin resistance in insulin-stimulated glucose way uptake inhibition. Several studies support that high levels of resistin induces insulin resistance and contributes to the failure of insulin sensitivity. Resistin showed its role in hemostasis toward glucose and insulin action, antagonistic towards insulin.¹⁶ The mean levels of resistin in this study was 14.21 (SD 7.43) ng/mL with a normal standard of 0.156 to 10 ng/mL. Resistin levels in boys was 14.82 (SD 8.14) ng/mL and in girls was 13.68 (SD 6.83) ng/mL. A study on obese children aged 12.6 (SD 3.4) years in Germany revealed the mean resistin level in girls was 6.79 (SD 2.67) ng/mL, while its level among boys was 5.74 (SD 2.62) ng/mL, with a standard value of 5 ng /mL.¹⁷ Similarly, previous studies revealed a significant higher levels of resistin in obesity compared to non obesity.^{18,19} Another study obtained a different result that there is no significant difference in resistin

levels between obese and non-obese children.²⁰ In this study we found no correlation between resistin levels and BMI ($r=0.168$). This was similar to the results of a study conducted in Iran.²¹

Elevated levels of resistin in this study have been obtained in acanthosis nigricans scale 2. The study of Lestari R (2010) obtained a mean HOMA-IR was higher in subjects with higher degree of acanthosis nigricans, especially in the group of acanthosis nigricans scale 3 and 4.¹¹ In this study, the higher degree of acanthosis nigricans, the higher mean of resistin levels.

A study in Cairo found that resistin levels were higher in obese children with acanthosis nigricans, hypertension, and insulin resistance. There is a significant positive correlation between resistin levels with insulin resistance, but there was no significant correlation between resistin levels with BMI, body fat percentage, and number of waist circumference. This study describes the relationship between resistin levels and insulin resistance in obese children, but cannot prove whether high or low levels of resistin is associated with insulin resistance.¹⁵

We conclude that there is a significant correlation between resistin levels with acanthosis nigricans scale in obese adolescents.

Conflict of interest

None declared.

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