

## ความสัมพันธ์ของความเข้มข้นซีรั่มรีซิสตินกับดัชนีมวลกายของเด็กอ้วน ในจังหวัดมหาสารคาม (อายุ 13-15).

### The Relationship of Serum Resistin Concentration and Body Mass Index in Obese Children (aged 13-15).

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#### บทคัดย่อ

การวิจัยนี้เพื่อหาระดับความเข้มข้นของรีซิสติน และหาความสัมพันธ์ระหว่างระดับความเข้มข้นของรีซิสตินกับตัวชี้วัดที่เกี่ยวข้องในเด็กอ้วน เช่น ค่าดัชนีมวลกาย ค่าระดับน้ำตาลในเลือด และค่าไตรกลีเซอไรด์ อาสาสมัครที่เป็นนักเรียนอ้วน (ค่าดัชนีมวลกาย มากกว่า  $\bar{X} + 2$  SD กิโลกรัมต่อเมตร<sup>2</sup>) จำนวน 96 คน สุ่มโดยความสมัครใจ ซึ่งสุ่ม 5 โรงเรียนจากทั้งหมด 18 โรงเรียนในจังหวัดมหาสารคาม โดยการจับฉลาก และระเบียบวิธีวิจัยได้รับการพิจารณารับรองจริยธรรมจากคณะกรรมการพิจารณาจริยธรรมงานวิจัย ของมหาวิทยาลัยมหาสารคาม นักเรียนทั้งหมดรวมทั้งผู้ปกครองได้รับทราบและตกลงเข้าร่วมการวิจัยครั้งนี้ นักเรียนที่เข้าร่วมในงานวิจัยได้รับการสัมภาษณ์ถึงภาวะสุขภาพและประวัติการเจ็บป่วยในช่วง 1 สัปดาห์ ก่อนการเจาะเลือด รวมทั้งการวัดตัวชี้วัดสัดส่วนของร่างกาย ซึ่งประกอบด้วย ชั่งน้ำหนัก วัดส่วนสูง ค่าดัชนีมวลกาย ปริมาณเนื้อเยื่อไขมันใต้ผิวหนังบริเวณต้นแขนส่วนหน้า และปริมาณเนื้อเยื่อไขมันใต้ผิวหนังบริเวณต้นแขนส่วนหลัง

ผลการศึกษาพบว่าเด็กชาย 33 คนและเด็กหญิง 63 คน มีน้ำหนักเฉลี่ย 73 กิโลกรัม ส่วนสูงเฉลี่ย 1.59 เมตร ค่าดัชนีมวลกายเฉลี่ย 28.68 กิโลกรัมต่อเมตร<sup>2</sup> ปริมาณเนื้อเยื่อไขมันใต้ผิวหนังบริเวณต้นแขนส่วนหน้า 16.79 มิลลิเมตร ปริมาณเนื้อเยื่อไขมันใต้ผิวหนังบริเวณต้นแขนส่วนหลัง 24.44 มิลลิเมตร ปริมาณไตรกลีเซอไรด์ 96.00 มิลลิกรัมต่อเดซิลิตร ค่าระดับน้ำตาลในเลือด 87.00 มิลลิกรัมต่อเดซิลิตร และปริมาณของรีซิสติน 5.76 นาโนกรัมต่อมิลลิลิตร โดยที่น้ำหนัก ส่วนสูง ค่าดัชนีมวลกาย และค่าระดับน้ำตาลในเลือดในเด็กชายมากกว่าเด็กหญิง แต่ปริมาณเนื้อเยื่อไขมันใต้ผิวหนังบริเวณต้นแขนส่วนหน้า ปริมาณเนื้อเยื่อไขมันใต้ผิวหนังบริเวณต้นแขนส่วนหลัง และปริมาณไตรกลีเซอไรด์ของเด็กหญิงมากกว่าเด็กชาย และระดับของรีซิสตินในเด็กหญิงมีค่าระหว่าง 4.59 ถึง 8.34 นาโนกรัมต่อมิลลิลิตร และ 3.71 ถึง 8.34 นาโนกรัมต่อมิลลิลิตร ในเด็กชาย ซึ่งในเด็กหญิงมีระดับของรีซิสติน ( $6.00 \pm 0.87$ ) ที่สูงกว่าเด็กชาย ( $5.29 \pm 0.92$ ) จากการศึกษาความสัมพันธ์ของระดับความเข้มข้นของรีซิสตินกับตัวชี้วัดสัดส่วนของร่างกายและตัวชี้วัดชีวเคมีทางการแพทย์ พบว่า มีความสัมพันธ์กับค่าดัชนีมวลกาย น้ำหนัก ส่วนสูง ปริมาณเนื้อเยื่อไขมันใต้ผิวหนังบริเวณต้นแขนส่วนหน้า ปริมาณเนื้อเยื่อไขมันใต้ผิวหนังบริเวณต้นแขนส่วนหลัง และไตรกลีเซอไรด์ ทั้งในเด็กชายและเด็กหญิง ( $P < 0.05$ ) ซึ่งรีซิสตินกับค่าดัชนีมวลกายมีความสัมพันธ์กันอย่างชัดเจน

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จากการวิจัยทำให้ทราบถึงบทบาททางสรีระวิทยาของรีซิสตินในเด็ก ซึ่งรีซิสตินไม่ใช่ตัวหลักในการเชื่อมโยงระหว่างโรคอ้วนกับภาวะดื้อต่ออินซูลิน เนื่องจากรีซิสตินอาจมีความสัมพันธ์กับการเติบโตของเด็กในช่วงพัฒนาการของวัยรุ่นขณะจะเข้าสู่ช่วงวัยหนุ่มสาว โดยที่ฮอร์โมนกระตุ้นการเจริญเติบโตมีผลชักนำให้มีการแสดงออกของ mRNA ของรีซิสติน และฮอร์โมนกระตุ้นการเจริญเติบโตมีผลกระตุ้นให้มีการเจริญเติบโตและพัฒนาของร่างกาย นอกจากนี้จากการวิจัยนี้ยังพบความสัมพันธ์ระหว่างรีซิสตินและค่าดัชนีมวลกายที่คล้ายกับข้อมูลที่พบในผู้ใหญ่

## Abstract

This research aims to determine the serum resistin concentration level in obese children and the relationship between serum resistin concentration and related parameters such as Body Mass Index (BMI), bicep skinfold thickness, tricep skinfold thickness and triglyceride level. The purposively selected volunteers were ninety-six students with BMI over  $\bar{X} + 2$  SD kg/m<sup>2</sup> which were drawn from five secondary schools as a simple randomized unit from the entire 18 schools as the sample frame by lottery in Mahasarakham province. This protocol was ethical consideration approved by the ethics committee of Mahasarakham University. All subjects and their parents understood, consented and enrolled in this research. Thus selected students were interviewed for history of illness as healthy period during one week before blood collection, fasting blood sugar (FBS), triglyceride, serum resistin and other related biomedical parameters were determined, and anthropometric parameters measured included as height, weight, BMI, left mid-arm circumference, tricep and bicep skin fold thickness.

This study found that: 33 boys and 63 girls students had average weight 73 kg, Height 1.59 m, BMI 28.68 kg/m<sup>2</sup>, Bicep 16.79 mm, Tricep 24.44 mm, TG 96.00 mg/dL, Resistin 5.76 ng/ml, FBS 87.00 mg/dL. The weight, height, BMI and FBS of boys was found to be higher than girls, but bicep, tricep skinfold thickness and TG of girls were higher than boys. Resistin was detected in girls ranging from 4.59 ng/ml to 8.34 ng/ml and in boys 3.71 ng/ml to 8.34 ng/ml. In girls resistin levels were higher ( $6.00 \pm 0.87$ ) than boys ( $5.29 \pm 0.92$ ). The relationship of serum resistin concentration was positively related to each anthropometric and biochemical parameter. The BMI, weight, height, bicep skinfold thickness, tricep skinfold thickness and triglyceride in both boys and girls are significantly different statistically ( $P < 0.05$ ). The association of serum resistin with the marker BMI was strongly significant.

Resistin physiology of children needs to be understood, as resistin seem not to be the major link between obesity and insulin resistance, but it may be related to the maturation of children during pubertal development, ability of growth hormone to induce resistin mRNA expression, and the growth-promoting action of growth hormone. Resistin was found to have a relationship with BMI similarly to other data obtained in adults.

**คำสำคัญ:** รีซิสติน, ค่าดัชนีมวลกาย และฮอร์โมนกระตุ้นเจริญเติบโต

**Keywords:** Resistin, Body mass index (BMI) and Growth hormone.

## INTRODUCTION

Excess body weight is the sixth most important risk factor contributing to the overall burden of disease worldwide and about 110 million of children are now classified as overweight or obese (Haslam and James, 2005 and Strok et al., 2005). Childhood obesity is associated with substantial co-morbidity and late sequelae, including hypertension, liver disease and cardiovascular complications especially type 2 diabetes mellitus (T2DM) (Wieland et al., 2006). T2DM is considered one of the major metabolic diseases of 21<sup>st</sup> century. The excessive intake of food, sedentary life style and lack of physical activity are responsible for the growing epidemic of obesity, together with the increasing rate of T2DM in many parts of the world (Zimmet et al., 2001).

The seminal proposal by Steppan et al. (2001) suggested resistin to be a hormone that links obesity to diabetes. Resistin serum levels were increased in obesity and resistin gene expression was induced during adipocyte differentiation. However, the biologic activity of resistin is poorly understood. Resistin, a peptide hormone produced by mature adipocytes in the rodent, regulates insulin sensitivity in both skeletal muscle and hepatic tissue (Steppan et al., 2001). In vitro study indicated that the expression of the resistin was associated with increased serum fatty acids and muscle triglycerides, impaired skeletal muscle glucose metabolism, and glucose intolerance (Pravenec et al., 2003). Adenovirus-mediated chronic "hyper-resistinemia" leads to whole-body insulin resistance involving impaired insulin signaling in skeletal muscle, liver, and adipose tissue, resulting in glucose intolerance, hyperinsulinemia, and hypertriglyceridemia (Sato et al., 2004). Only recently has the novel feature of

resistin as a pro-inflammatory molecule emerged. Several previous studies have highlighted the associations between resistin and inflammatory factors, such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), Interleukin-6 (IL-6) and C-reactive protein (Shetty et al., 2004). Silswal et al. (2005) recently demonstrated that human resistin stimulates the synthesis and secretion of pro-inflammatory cytokines TNF- $\alpha$  and IL-12 in macrophages via a nuclear factor-(NF)-kappa B-dependent pathway.

Serum resistin levels were found to be elevated in rodent models of obesity such as ob/ob-, db/db-mice, or diet-induced obesity, while others and more recent studies found resistin expression and secretion decreased in a variety of obese rodent models. There is slightly more existed evidence of increased resistin expression associated with insulin resistance in rodents, pointing towards a potential role of resistin in obesity associated insulin resistance. The putative involvement of resistin in obesity and/or insulin resistance in human is largely controversial. Although some studies report positive correlations between resistin and obesity or insulin resistance, others have not revealed yet (Conneely et al., 2004 and Banerjee et al., 2004). The physiological range of serum resistin levels have so far not been identified making interpretation of clinical studies difficult to investigate serum resistin level and investigate the relationship between resistin concentration and related parameter in obesity children. Because children are relatively free from co-morbidity compared with adults, we examined the role of serum resistin levels as a marker of students obesity or insulin resistance, with this has not been studies in children Thailand to date. For this used, we extensively evaluated a new in-house immunoassay to determine of resistin serum levels in obesity children.

### General Objective

The investigation of serum resistin concentration level will be illustrated baseline for obesity children in Mahasarakham Province, Thailand.

### Specific Objectives

1. Investigation of serum resistin concentration level in obesity children.
2. To study the relationship between resistin concentration and related parameter such as Body Mass Index (BMI), bicep skinfold thickness, tricep skinfold thickness and triglyceride.

## MATERIALS AND METHODS

### Subject

The purposive volunteer as ninety-six students with BMI over  $\bar{X} + 2$  SD kg/m<sup>2</sup> which were drew from five secondary schools randomized from entire 18 schools in Mahasarakham province. All subjects and their parents were understood consented and to enroll agreed in this study. The specimens and data collecting were done during March 1, 2008 to June 30, 2008. All subjects were examined history illness interviewed as healthy inclusive 1 week before blood collected.

This research protocol was approved by the ethics committee of the Mahasarakham University.

### Collection of serum

The collection of blood specimens, was taking by medical assistance professional scientist staffs of Mahasarakham hospital. Blood samples were took after 12 hour fasting as fasting blood sugar, triglyceride, serum resistin and other related biomedical parameter. All of the blood samples were

immediately proceeding for fasting blood sugar, triglyceride and serum resistin were divided into aliquots and stored at  $-80^{\circ}\text{C}$  until serum resistin be assayed.

### Anthropometrical measurements

Anthropometric parameters measured included height, weight, left mid-arm circumferences, tricep, bicep skin fold thickness and the body mass index (BMI). BMI calculated as the body weight divided by height squared (kilograms per-square meter) was used as a marker of obesity.

### Biochemical measurements and tests

Plasma biochemical parameters were also measured after overnight fasting including fasting blood sugar (FBS) and triglycerides was performed using routine laboratory procedures by Mahasarakham hospital professional staff.

### Serum resistin

Radio immunometric assay was used to determine serum resistin levels. The measurement was performed with commercial kits, Human Resistin ELISA Kit (LINCO Research, Inc, St., Charles, Missouri, USA).

### Statistical methods

The data were analyzed as normal distribution data were expressed as mean and standard deviation. The relations between indexes were assessed by Pearson correlation. Some of parameters, such as age, FBS, and triglyceride, show a non-normal distribution, nonparametric statistical were applied for all. (Descriptive statistics by medians and quartiles, correlations according to Spearman sing rank test). Under 95% confidential interval.

## RESULTS

The investigation of serum resistin concentration level and relationship between serum resistin levels and related parameter (BMI, bicep skinfold thickness, tricep skinfold thickness and triglyceride) of obesity children in Mahasarakham Province, Thailand.

### The serum resistin levels and parameters data of the obesity children.

Ninety-six obesity children individual participated in this study, included 33 boys and 63 girls. The anthropometric measurement and mean values of biochemical parameters of the obesity children are shown in Table 1.

Subjects were measured weight, height, BMI, bicep, tricep skinfold thickness, triglyceride and resistin. Serum resistin levels were found higher in girls ( $6.00 \pm 0.87$  ng/ml) than boys ( $5.29 \pm 0.92$  ng/ml); concentrations ranged from 3.71 mg/dL to 8.22 mg/dL and 4.59 mg/dL to 8.34 mg/dL in girls (Figure 1). Fasting blood sugar were found normal level, as all subject did not get T2DM (as Thai medical DM council; cut of point  $< 126$  mg/dL). BMI levels were found high both sex, the mean value in boy  $29.54 \pm 5.25$  kg/m<sup>2</sup> and  $28.23 \pm 4.11$  kg/m<sup>2</sup> in girl.

### The correlation of serum resistin level and parameters.

In the study (Table 2), serum resistin concentration was positively related to each of the analyzed anthropometric and biochemical parameters, most statisticals significantly with BMI, weight, height, bicep skinfold thickness, tricep skinfold thickness and triglyceride in both boys and girls ( $P < 0.05$ ), could be observed after all participants were included and

the Spearman's rank correlation test conducted. The association of serum resistin with markers of obesity such as weight and BMI was strongly significant in both groups. No significant correlation ( $P > 0.05$ ) and, consequently, a relatively low power for an association was found between serum resistin levels and fasting blood sugar in boys, but significant relationship in girls. However, a potential association between resistin and obesity.

## Discussion and Conclusion

The present study concerns association between serum resistin concentration and related parameter such as BMI, bicep skinfold thickness, tricep skinfold thickness and triglyceride in obesity children, and determined serum resistin levels in obesity adolescent. These results it assumed that resistin with markers of obesity such as weight and BMI was strongly significant correlation.

The serum resistin levels were significantly correlated with BMI and were significantly correlated with bicep skinfold thickness, tricep skinfold thickness and triglyceride (TG). At a given BMI, a high bicep and triceps skinfold thickness are associated with peripheral obesity. The distribution of body fat could play a role in determination of resistin plasma levels as proposed by Mc-Ternan et al. (2002), who found higher resistin mRNA expression in abdominal fat than in thigh. Resistin correlates positively with body fat mass and negatively with waist-to-hip ratio in humans (Yannakoulia et al., 2003). Blood resistin concentrations were significantly higher in obese than in lean patients and were positively related to anthropometric parameters (Lee et al., 2003 and Silha et al., 2003). Serum resistin levels were found to be elevated in rodent models of obesity such as ob/ob-, db/db mice,

or diet-induced obesity, while others and more recent studies found resistin expression and secretion decreased in a variety of obese rodent models. There is slightly more consistent evidence of increased resistin expression associated with insulin resistance in rodents Conneely et al., 2004 and Banerjee et al., 2004), pointing towards a potential role of resistin in obesity associated insulin resistance. Azuma et al. (2003) found that serum resistin level were higher in obese than in lean individuals and that resistin levels were significantly correlated with BMI. Schaffler et al. (2004) also found a positive correlation between serum resistin levels and BMI in healthy individuals. Therefore, we investigated relationship between serum resistin levels and BMI was strongly mutual inclusive relationship as other researcher above mentioned.

In our group of subject, serum resistin levels were found in higher girl than boy. Similar observations were made in several previous studies such as Gerber et al. (2008) found that resistin was significantly correlated with BMI higher in girls than in boys. Positive association between resistin and BMI was observed only in women by Vilarrasa et al. (2005).

The finding of serum resistin is markedly up-regulated by growth hormone. The rapidity with which resistin mRNA levels in white adipose tissue are increased suggests that growth hormone has a direct effect on resistin transcription (Delhanty et al., 2002). Holdaway et al., (2004) shown twenty-four-hour continuous infusion of growth hormone (1 mg/kg/day) caused marked (720-950%) increases the level of resistin mRNA in rat epididymal and subcutaneous white adipose tissue when compared to controls (Delhanty et al., 2002). The ability of growth hormone to induce resistin mRNA expression may be due to the growth-promoting action of growth hormone.

In summary, the findings are a first step to the understanding of resistin physiology in children and found that resistin may not be the main link between obesity and insulin resistance in children, because of it may be related to the maturation of children during pubertal development (Gerber et al., 2008) or ability of growth hormone to induce resistin mRNA expression may be due to the growth-promoting action of growth hormone (Holdaway et al., 2004). But resistin was found relationship with BMI as similar with data obtained in adults. (Azuma et al., 2003 and Fujinami et al., 2004).

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**Table 1.** The anthropometric measurement and mean values of biochemical parameters of the obesity children.

Parameter	Boy	Girl
	mean $\pm$ SD (range)	mean $\pm$ SD (range)
Weight (kg)	79.34 $\pm$ 18.52 (52.30 – 126.30)	70.47 $\pm$ 12.88 (49.40 - 108.10)
Height (m)	1.63 $\pm$ 0.08 (1.48 - 1.80)	1.58 $\pm$ 0.06 (1.43 - 1.70)
BMI (kg/m <sup>2</sup> )	29.54 $\pm$ 5.25 (20.67 – 45.83)	28.23 $\pm$ 4.11 (21.56 – 39.23)
Bicep (mm)	16.53 $\pm$ 6.29 (4.50 - 26.67)	16.92 $\pm$ 5.82 (4.50 - 29.33)
Tricep (mm)	24.00 $\pm$ 7.47 (7.00 – 39.00)	24.66 $\pm$ 5.71 (11.43 – 40.83)
FBS (mg/dL)	89.00 $\pm$ 3.50 (78.00 – 114.00)	86.00 $\pm$ 5.50 (77.00 - 162.00)
TG (mg/dL)	100.00 $\pm$ 42.75 (26.00 - 329.00)	92.00 $\pm$ 33.00 (33.00 - 404.00)
Resistin (ng/ml)	5.29 $\pm$ 0.92 (3.71 – 8.22)	6.00 $\pm$ 0.87 (4.59 – 8.34)

FBS = Fasting blood sugar

TG = Triglyceride

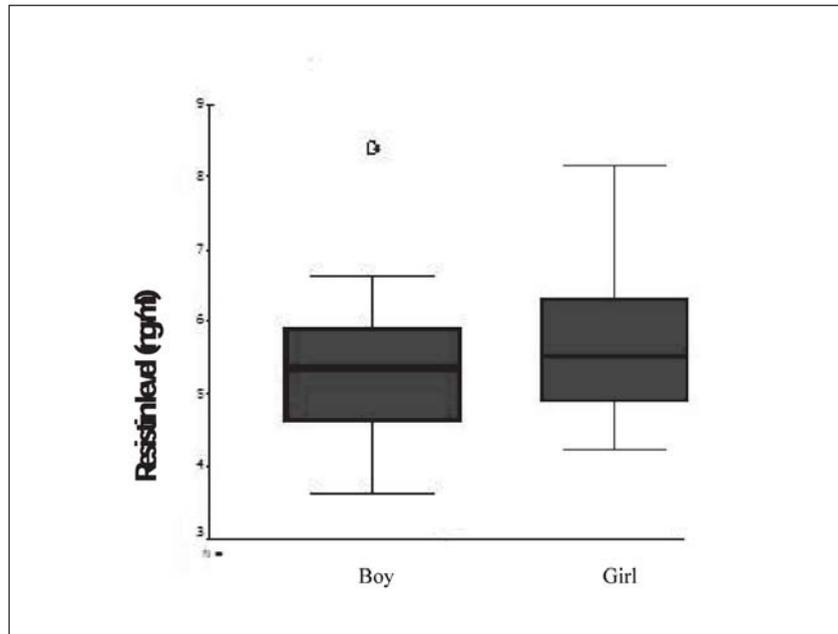


Figure 1. The mean value of serum resistin concentration in boys and girls.

Table 2. Correlation between serum resistin level and related parameters.

Parameter	Boy		girl	
	r	p-value	r	p-value
BMI	1.00	< 0.001**	1.00	< 0.001**
Weight	0.92	< 0.001**	0.92	< 0.001**
Height	0.41	0.019*	0.28	0.026*
Bicep	0.69	< 0.001**	0.68	< 0.001**
Tricep	0.76	< 0.001**	0.75	< 0.001**
TG	0.47	0.006*	0.29	0.021*

\* Spearson correlation coefficient is significant at the 0.05 level

\*\* Spearson correlation coefficient is significant at the 0.01 level