

Serum levels of leptin in obese Thai children

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- Objective** : *To study the leptin levels in obese Thai children and evaluate the relationship between leptin and body mass index in obese children*
- Design** : *Descriptive study*
- Setting** : *Pediatric Endocrine Unit, Faculty of Medicine, King Chulalongkorn Memorial Hospital*
- Material and Method** : *Forty obese children were divided into 4 groups according to gender and puberty. Serum leptin concentrations were measured by ELISA commercial test kit. Body mass index (BMI) defined as weight in kilograms divided by the square of height in meters (Kg/m^2) was calculated. Statistical analyses were performed using SPSS. All values are means \pm SD*
- Results** : *Serum leptin levels in obese girls were marginally significantly higher than in boys (53.8 ± 21.3 , 41.7 ± 22.0 ng/mL). Also in obese pubertal children, girls had a higher serum leptin level than boys (55.8 ± 23.9 and 31.3 ± 16.7 ng/mL, $p = 0.02$). In addition, the level of serum leptin significantly correlated with body mass index in obese girls ($r = 0.594$, $p = 0.003$) but not in obese boys.*

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Conclusion : *Control of leptin production in obese children may be sex different, and through unknown mechanism it may trigger the onset of puberty in obese girls.*

Key words : *Leptin, Obesity, Body mass index (BMI).*

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- วัตถุประสงค์** : เพื่อศึกษาระดับซีรั่ม leptin ในเด็กไทยอ้วน และความสัมพันธ์ระหว่างซีรั่ม leptin และดัชนีมวลกายในเด็กไทยอ้วน
- ชนิดของการวิจัย** : การวิจัยเชิงพรรณนา
- สถานที่ทำการวิจัย** : หน่วยต่อมไร้ท่อ ภาควิชากุมารเวชศาสตร์ โรงพยาบาลจุฬาลงกรณ์
- วัสดุและวิธีการ** : ทำการศึกษาในเด็กไทยอ้วนจำนวน 40 คน แบ่งออกเป็น 4 กลุ่มตามเพศและอายุเพื่อศึกษาระดับซีรั่ม leptin ด้วยวิธี ELISA และดัชนีมวลกาย (BMI) จากน้ำหนัก/ส่วนสูง (เมตร)² และคำนวณค่าทางสถิติโดยใช้โปรแกรม SPSS แสดงผลเป็นค่า Means \pm SD
- ผลการศึกษา** : พบว่าระดับซีรั่ม leptin ในเด็กอ้วนเพศหญิงมีค่าสูงกว่าในเด็กอ้วนเพศชายคือ 53.8 ± 21.3 และ 41.7 ± 22.0 ng/mL ตามลำดับ โดยเฉพาะอย่างยิ่ง เด็กอ้วนเพศหญิงที่เข้าสู่วัยรุ่นแล้ว จะมีระดับซีรั่ม leptin สูงกว่าในเด็กอ้วนเพศชายที่เข้าสู่วัยรุ่นอย่างมีนัยสำคัญทางสถิติคือ 55.8 ± 23.9 และ 31.3 ± 16.7 ($p = 0.002$) ตามลำดับ นอกจากนี้ยังพบว่าระดับซีรั่ม leptin ในเด็กอ้วนเพศหญิง มีความสัมพันธ์อย่างมีนัยสำคัญทางสถิติกับดัชนีมวลกาย (BMI) คือ $r = 0.594$, $p = 0.003$ แต่ไม่มีนัยสำคัญในเด็กอ้วนเพศชาย
- สรุปผลการศึกษา** : ความแตกต่างของเพศในเด็กอ้วนจะมีผลต่อการสร้างซีรั่ม leptin และอาจเป็นตัวกระตุ้นทำให้เกิดการเข้าสู่ภาวะวัยสาวในเด็กอ้วนเพศหญิงได้ แต่ยังไม่ทราบกลไกที่ชัดเจน
- คำสำคัญ** : leptin , โรคอ้วน, ดัชนีมวลกาย

Obesity in children and adolescents is increasingly prevalent. Leptin, a product of the ob gene located on chromosome 7q31.3, is a 16-Kda protein secreted by differentiated adipocytes. It acts on the hypothalamus by suppressing food intake and stimulating energy expenditure.^(1,2) In human subjects, a high correlation between the body fat content and serum concentrations of leptin has been found.⁽³⁾ In addition, level of serum leptin was reported to be higher in obese subjects than in those with normal weight. This renders a state of leptin resistance in obese subjects.⁽⁴⁾

Aims of this study were to measure serum concentrations of leptin in Thai obese children, and also to evaluate the relationship between leptin and body mass index (BMI), sex and puberty in children.

Material and Method

Forty obese children were divided into 4 groups according to sex and puberty : group I prepubertal girls (N=10 ; age 7.5 ± 1.8 yr.), group II pubertal girls (N=10 ; age 12.1 ± 1.4 yr.), group III prepubertal boys (N=10 ; age 8.0 ± 1.6 yr.) and group IV pubertal boys (N=10 ; age 13.4 ± 1.2 yr.). Puberty was defined when girls had breast tanner stage II or over and boys had testicular volume more than 4 mL.

Body mass index (BMI) was defined as weight in kilograms divided by the square of height in meters (Kg/m^2) was calculated. Fasting blood samples were obtained in the morning. After clotting, the sera were separated and stored at -70°C until analysis.

Serum concentrations of leptin were measured by ELISA commercial test kit, which is an enzyme-linked immunosorbent assay based on "two-step" sandwich type (Human Leptin ELISA, Diagnostic Systems Laboratories, Inc, Texas, USA). The limit of sensitivity was 0.05 ng/mL, the maximal intra-assay coefficient of variation was 6.2 % and the maximal inter-assay coefficient of variation was 5.3 %.

Statistical analyses were performed using SPSS. All values are means \pm SD.

Results

Table 1 shows clinical characteristic of all subjects under this study. Leptin concentrations were higher in prepubertal boys than in prepubertal girls (52.2 ± 22.5 ng/mL, 51.7 ± 19.4 ng/mL, respectively). A mean concentration of serum leptin in obese girls was higher than that in obese boys (53.8 ± 21.3 ng/mL, 41.7 ± 22.0 ng/mL, $p= 0.06$) Pubertal girls had higher concentrations of leptin than pubertal boys (55.8 ± 23.9 and 31.3 ± 16.7 ng/mL, $p= 0.02$)

Table 1. The clinical characteristics of the 40 obese children.

	CA (yr)	BA (yr)	BMI (kg/m ²)	Leptin (ng/mL)
Prepubertal girls (N=10)	7.5 ± 1.8	9.3 ± 2.2	26.5 ± 3.0	51.7 ± 19.4
Pubertal girls (N=10)	12.1 ± 1.4	13.9 ± 2.1	31.7 ± 8.1	55.8 ± 23.9
Prepubertal boys (N=10)	8.0 ± 1.6	9.3 ± 2.3	28.8 ± 3.7	52.2 ± 22.5
Pubertal boys (N=10)	13.4 ± 1.2	15.3 ± 1.3	29.9 ± 3.5	31.3 ± 16.7

CA = chronological age, BA = bone age, BMI = body mass index

but this was not difference between prepubertal girls and prepubertal boys. There was no difference in BMI of girls and boys (29.1 ± 6.5 , 29.4 ± 3.5 , respectively)

The concentrations of leptin significantly

correlated with BMI as shown in Fig. 1 ($r=0.461$, $p=0.003$). Leptin levels positively correlated with BMI in obese girls ($r=0.594$, $p=0.006$) (Fig. 2) but not in obese boys.

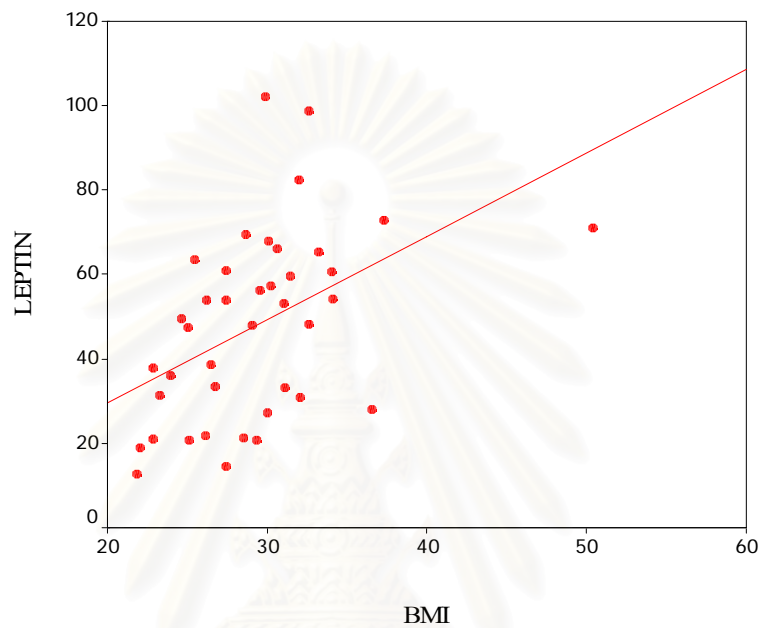


Figure 1. Correlation between leptin levels and BMI in obese children.

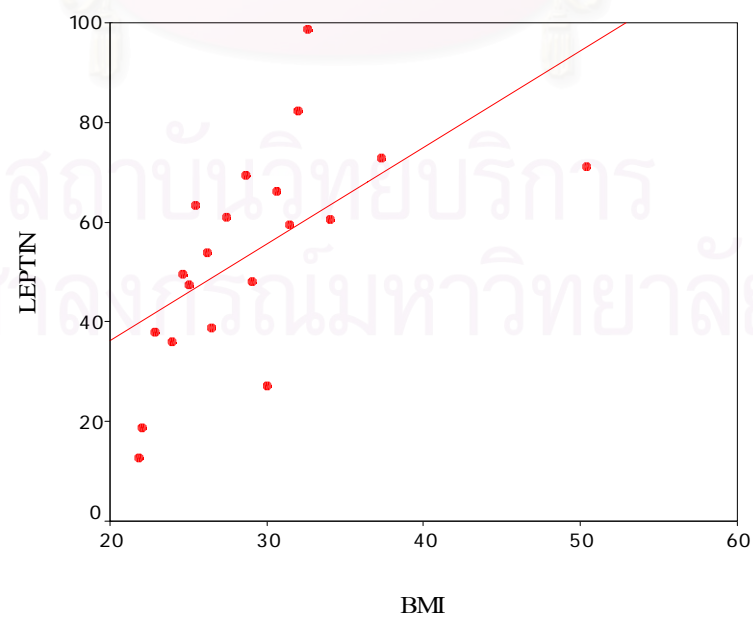


Figure 2. Correlation between leptin levels and BMI in pubertal obese girls.

Discussion

The concentration of leptin reflects the amount of adipose tissue especially of subcutaneous fat.⁽⁵⁾ In young girls, subcutaneous accumulation of body fat seems to be related, in an almost parallel way, to increased concentration of leptin during puberty. The results of our study were similar to previous studies which showed that the concentration of leptin increased with age in girls but not in boys.^(6,7) Inadequate nutrition retards growth and delays sexual maturation but high nutrition may advance growth and sexual maturation. Therefore the onset of puberty may be triggered when a critical percentage of fat is attained. The ob/ob mouse can obtain sexual development after exogenous administration of leptin.⁽⁸⁾ In addition, leptin could accelerate the onset of puberty in young female mice.⁽⁹⁾ In this study, an elevated concentration of leptin was demonstrated in pubertal obese girls but not in pubertal obese boys. This suggested that the mechanism of GnRH secretion by pituitary gland might be sex-difference. In girl, leptin may act as a hormone which informs the brain about the readiness of the body for reproductive function. However, the actual mechanism remains unknown. Serum leptin and serum testosterone levels may show in an opposite direction as a study in rats showing leptin inhibits the secretion of testosterone from testes.⁽¹⁰⁾ Hypogonadal men with suppressed concentrations of testosterone exhibit elevated leptin levels⁽¹¹⁾ In conclusion, leptin levels had a positive correlation with obesity and this may initiate the onset of puberty in obese girls with unexplained mechanism.

References

1. Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman JM. Positional cloning of the mouse obese gene and its human homologue. *Nature* 1994 Dec 1;372(6505):425-32
2. Levin N, Nelson C, Gurney A, Vandlen R, de Sauvage F. Decreased food intake does not completely account for adiposity reduction after ob protein infusion. *Proc Natl Acad Sci U S A* 1996 Feb 20;93(4):1726-30
3. Considine RV, Sinha MK, Heiman ML, Kriauciunas A, Stephens TW, Nyce MR, Ohannesian JP, Marco CC, McKee LJ, Bauer TL, et al. Serum immunoreactive-leptin concentrations in normal-weight and obese humans. *N Engl J Med* 1996 Feb 1; 334(5):292-5
4. Hassink SG, Sheslow DV, de Lancey E, Opentanova I, Considine RV, Caro JF. Serum leptin in children with obesity: relationship to gender and development. *Pediatrics* 1996 Aug;98 (2 Pt 1):201-3
5. Lahlou N, Landais P, De Boissieu D, Bougneres PF. Circulating leptin in normal children and during the dynamic phase of juvenile obesity: relation to body fatness, energy metabolism, caloric intake, and sexual dimorphism. *Diabetes* 1997 Jun;46(6):989-93
6. Garcia-Mayor RV, Andrade MA, Rios M, Lage M, Dieguez C, Casanueva FF. Serum leptin levels in normal children: relationship to age, gender, body mass index, pituitary-gonadal hormones, and pubertal stage. *J Clin Endocrinol Metab* 1997 Sep;82(9):2849-55
7. Blum WF, Englaro P, Hanitsch S, Juul A, Hertel NT, Muller J, Skakkebaek NE, Heiman ML, Birkett M, Attanasio AM, et al. Plasma leptin levels in healthy children and adolescents:

- dependence on body mass index, body fat mass, gender, pubertal stage, and testosterone. *J Clin Endocrinol Metab* 1997 Sep;82(9):2904-10
8. Barash IA, Cheung CC, Weigle DS, Ren H, Kabigting EB, Kuijper JL, Clifton DK, Steiner RA. Leptin is a metabolic signal to the reproductive system. *Endocrinology* 1996 Jul;137(7):3144 -7
9. Ahima RS, Dushay J, Flier SN, Prabakaran D, Flier JS. Leptin accelerates the onset of puberty in normal female mice. *J Clin Invest.* 1997 Feb 1;99(3):391-5
10. Stock SM, Sande EM, Bremme KA. Leptin levels vary significantly during the menstrual cycle, pregnancy, and in vitro fertilization treatment: possible relation to estradiol. *Fertil Steril* 1999 Oct;72(4):657-62
11. Jockenhovel F, Blum WF, Vogel E, Englaro P, Muller-Wieland D, Reinwein D, Rascher W, Krone W. Testosterone substitution normalizes elevated serum leptin levels in hypogonadal men. *J Clin Endocrinol Metab* 1997 Aug;82(8):2510-3