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Original Article

Plasma lipid profile and leptin concentration in super-obese children

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Abstract

Background Leptin induced weight loss is completely specific for adipose tissue loss, whereas food restriction result in both loss of adipose tissue and lean body mass in mammals. Most obese person has high endogenous leptin levels, indicating leptin resistance. There has been lack of data regarding plasma leptin level in Indonesian obese children.

Objective This study was aimed to investigate the plasma leptin level and lipid profile in super-obese children.

Methods This was a cross sectional study performed in Pediatric Out Patient Clinic Mangunkusumo Hospital and Private Women & Children Hospital in Eastern part of Jakarta. Super-obese is defined as children with BMI above 97 centiles CDC 2000 chart. Blood sample was obtained from all subjects, consisted of peripheral blood picture, lipid profiles and leptin level.

Results Seventy nine super-obese children were eligible with age ranged between 12 months and 180 months and mean of age was 84.9 months (SD 36.8). More than 60% subjects had high LDL cholesterol, while 19% had low HDL level. The lowest leptin blood level was 2.877 µg/dL, while the highest was 70.430 µg/dL (mean 23.990; SD 12.726). Forty five subjects, all boys, had increased plasma leptin level.

Conclusions In super-obese children, most of the subject experienced hyperlipidemia (LDL cholesterol) followed by hypertriglyceridemia. There was small number of low HDL cholesterol found. Super-obese girls had normal serum leptin level, in contrast, more than 60% super-obese boys had elevated serum leptin level. **[Paediatr Indones 2007;47:221-225]**.

Keywords: *children, obesity, leptin, lipid profile*

Management of obesity in children differs from that in adult, the prevention of weight gain is an important issue rather than focusing on weight loss. Lean body mass increase as children get older; thus keeping fat mass constant will help to normalized body weight. The best and the most effective way to treat children with obesity is to treat the family, and not the child alone, by encouraging to increase daily activity and healthy eating habits.[1]

The role of pharmacotherapy in children and adolescents is undefined but may be considered in extreme cases. There has been little or no efficacy of outcomes data on pharmacotherapy in children less than 18 years,[2] thus understanding the etiology is one of the childhood obesity management key success.[3]

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Leptin is a 167 kD amino acid peptide made exclusively in adipose tissue. Its absence produces the obese (ob/ob) mouse, which is characterized by obesity, hyperphagia, hyperglycemia, hyperinsulinemia and insulin resistance, hypothermia and infertility. Leptin corrects these defects. Leptin receptor is a member of the cytokine family of receptors with several splice variants. Leptin receptors are widely distributed, including in the brain and many peripheral tissues, suggesting that this peptide may provide a wide range of tissues information about fat stores. Genetic defect in leptin receptor produce diabetic (db/db) mouse, which is phenotypically identical with the ob/ob mouse when the genes are expressed on the same background strain and the obese falfa Zucker rat.[4-6]

The level of leptin is directly related to the quantity of body fat, suggesting that there is a signal to the brain and other tissues about the adequacy or inadequacy of fat store. The leptin that is secreted by fat cells appears to bind with one or more proteins in the circulation. The percentage of free leptin is higher in obese than in lean individuals. Indeed plasma leptin are closely correlated with body fat in both humans and rodents.[6-8]

Treatment with leptin reduced weight in all mammalian species tested, including rats, dogs, and monkey. In addition, the metabolic effects of leptin seem to be different qualitatively from those produced by food restriction. Leptin induced weight loss is completely specific for loss of adipose tissue, whereas food restriction resulted in both loss of adipose tissue and lean body mass in mammals. Although therapy with leptin is expected to be efficacious in few persons with leptin deficiency, it remains questioned whether leptin is safe and effective treatment for most obese person. Although most obese person have high endogenous leptin levels which indicates leptin resistance, it is unknown whether increased endogenous leptin levels indicate complete or relative resistance to exogenous leptin.[6,7,9]

Clinical trials in human are expected to answer this and similar clinical questions. A study by Farooqi and colleagues[10] reported that daily subcutaneous administration of leptin over 9 months to a leptin deficient patient may decrease body weight by 14.7 kg and greatly improve the patient metabolic profile. Congenital leptin deficient patients usually have normal weight at birth; however, beginning to gain weight excessively in early life, followed by marked hyperphagia and severe obesity. To our knowledge, there was no report of plasma leptin level in childhood obesity in this country. This study investigated the plasma leptin level in super-obese children in order to be able to elaborate the etiology of childhood obesity.

Methods

Subjects were super-obese children who attended public and private children hospital in Central and East Jakarta from February to Augusts 2004. Samples were calculated using estimation of proportion, and further 78 subjects are needed for the total samples. Parental consent was obtained and this study protocol was approved by the Ethics Committee of the Medical School University of Indonesia. Obesity was determined using Body Mass Index (BMI) of CDC 2000 chart; subjects were classified as super-obese if BMI above 97 centiles. Blood sample consisted of lipid profiles, i.e., total cholesterol, HDL & LDL cholesterol, and triglyceride. Plasma leptin was measured using The Quantikine^{R} human Leptin Immunoassay, designed by R&D Systems, USA. The Quantikine is a 3.5 hour solid phase ELISA to measure soluble human Leptin in cell culture, serum, and plasma.[11]

Results

Seventy nine super-obese children were eligible in this study. The majority of parent's subjects were from high economic level, only few were from middle society. Subjects were ranged between 12 months and 180 months of age with mean of age was 84.9 months (SD 36.8). Of 79 subjects, 53 subjects were boys. Serum total cholesterol ranged between 88 mg/dL and 261 mg/dL, with mean 167.6 mg/dL (SD 32.0). Serum HDL cholesterol ranged between 28 mg/dL and 80 mg/dL, with mean 49.6 mg/dL (SD 11.3), while serum LDL cholesterol ranged between 40 mg/dL and 184 mg/dL, with mean 110.9 mg/dL (SD 28.4). Serum triglyceride level ranged between 15 mg/dL and 428 mg/dL, with mean 110.4 mg/dL (SD 67.5). None of the subjects had high HDL cholesterol and low triglyceride level. **Table 1** shows the distribution of subject's blood lipid abnormality.

Plasma leptin was collected in the morning after subjects fasting for 12 hours. Due to technical

Table 1. Lipid profile abnormality according to cholesterol fraction

Lipid profile	Normal	Low	High
Total cholesterol	74	2	3
HDL cholesterol	64	15	0
LDL cholesterol	29	0	50
Triglyceride	65	0	14

problems, only in 72 subjects plasma leptin were available. The lowest leptin blood level was 2.877 µg/dL, while the highest was 70.430 µg/dL (mean 23.990; SD 12.726). **Table 2** shows characteristic of subject's plasma leptin.

Table 2. Characteristic of subject's plasma leptin.

Leptin characteristic	Boys	Girls
Plasma leptin level (ug/dL)		
Minimum	2.877	7.971
Maximum	70.430	46.560
Normal level	3	24
Increased level	45	0

Normal level: Boys: 2.205 – 11.149 µg/dL; Girls: 3.877 – 77.273 µg/dL

Out of 79 subjects, 45 subjects had increased plasma leptin level and surprisingly all of them were boys. All of 27 girls had normal plasma leptin level.

In order to investigate the relation between plasma leptin level and age, we divided age into 3 groups and performed chi-square test. The result was statistically no difference as shown in **Table 3**.

Table 3. Plasma leptin level according to age groups

Age group	Leptin level	
	Normal	High
0 - 59 months	12	10
60 – 119 months	9	23
120 – 180 months	6	12
$X^2 = 4.06$	df = 2	P= 0.13

Discussion

As many studies has been shown, obese child particularly with severe/super-obese very often followed by co-morbidity such as anemia, diabetes mellitus type 2, hypertension, hypercholesterolemia, non alcoholic steatohepatitis and others. In this study, some of those co-morbidity appeared, although not in very common frequency (data not shown).

Studies have shown association between obesity and cardiovascular disease risk factors (high blood pressure, high cholesterol level and blood glucose level). Lipid profile results in this study is similar compare to previous study, where as boys had a higher lipid concentration than girls. To explain this finding, dietary analysis and life style record is needed. Several study has shown that changes in life style or dietary pattern or both has been correlated with increase body weight, blood pressure and lipid concentration among teenage school children.[12,13] Study in Milan showed that obese school children had higher lipid and lipoprotein concentration than non obese children. Compare with non obese children, obese boys had higher triglyceride and obese girls had higher total cholesterol, triglyceride, and LDL cholesterol. The small number of higher total cholesterol level in this study might be due to ethnic origin, and cultural difference which have impact on food consumption.[14]

In human, a highly significant correlation between body fat content and serum leptin concentration has been observed. In general obese human have high leptin levels.[15] The relationship of leptin to other form of obesity can be inferred by measurement of plasma leptin level. An increase in plasma level suggests that obesity is the result of leptin resistance. A low or normal plasma concentration of leptin in the context of obesity suggests a possible defect in the synthesis and /or secretion of leptin. In this study most of the subject had high level of leptin, suggesting that this phenomena is associated with insensitivity to leptin.[16]

The limitation in this study is that serum leptin was taken early in the morning after overnight fast. As have been shown in previous study, serum leptin levels decrease rapidly during the early morning, thus assessment of leptin in this time may be potentially confounded by spontaneous variations. It is suggested that to minimize the confounding effect from diurnal rhythms, the sampling should be taken within 30 minute between 10.00 and 16.00. However, ideal time of blood sampling was difficult to achieve because it's very hard to do 12 hours fasting for the subject particularly those with very young age.[17-19]

Other limitation of this study was that we did not measure sexual hormones which have been known to influence plasma leptin level.

Fasting serum leptin level is higher in women than in men regardless of fat mass. Thus, to explain

why all the girl subjects in our study had normal leptin level, where as most of boys subject had high leptin level is not so easy. The mechanism of this sexual dimorphism are unknown, however leptin may have a reproductive function. Serum leptin concentration may also be increase by overfeeding, adiposity and exogenous glucocorticoid, where as cold exposure, fasting, androgens and cathecolamines may have suppressive effect.[15,19,20]

More than 60% of the subjects with high plasma leptin level found in this study should aware us about the risk of arterial disease. Although leptin predominantly involved in the hypothalamic control of body weight, leptin receptor are widely distributed on endothelial cells, on other arterial wall subpopulations and on atheroschlerotic lesions. An action via these receptors may stimulate smooth muscle cell proliferation and migrations, where as prolonged treatment with leptin has been shown to increase vascular cells calcification. Leptin has also been shown to induced oxidative stress in endothelial cells, which could contribute to vascular pathology.[12,13,16]

Study of plasma leptin has shown that the level increases with age during childhood and adolescence as levels of soluble leptin receptor decline in both sexes. There are gender-specific and age-dependent gender-specific differences in serum leptin and soluble leptin receptor concentration during development. Although the developmental pattern of serum leptin and soluble leptin receptor did not differ substantially in boys and girls to the onset of puberty, the mean level of serum soluble leptin receptor in young male subjects were significantly higher than those in young female subjects. [6,7,16,20,21]

The findings of leptin concentration related to age in this study were similar with other study which stated that serum leptin concentration did not change with age in either sex.[21]

In conclusion, our study showed that in super-obese children most of the subject experience hyperlipidemia (LDL cholesterol) followed by hypertriglyceridemia. Low HDL cholesterol level was also found although not in a big number. Super-obese girls have normal serum leptin level, in contrast more than sixty percent super-obese boys have elevated serum leptin level.

Further investigation whether or not subjects with normal serum leptin have leptin deficiency and subjects with elevated serum leptin have leptin resistance is needed.

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