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Original Article

The correlation between leptin and highly sensitive C-reactive protein levels in obese children aged 9-15 years

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Abstract

Background Obesity is a low level and chronic inflammatory condition predominantly affecting white adipose tissue, where macrophage infiltration is found. Leptin is one of many molecules relating obesity to cardiovascular disease. Leptin can increase cytokine production in macrophages and monocytes, and increase oxidative stress on endothelial cells. Pro-inflammatory cytokines, in turn, may trigger the release of C-reactive protein.

Objective To examine the correlation between leptin and hsCRP in obese children aged 9-15 years.

Methods This cross-sectional study was done in Manado from May to December 2009, on elementary and junior high school children. Subjects were obese children aged 9-15 years, with nutritional status determined by Body Mass Index and converted into z-score. Physical examination, blood pressure, and blood examinations for fasting blood sugar (FBS), lipid profile, leptin, and hsCRP were performed. Data were analyzed with appropriate statistical methods.

Results The mean leptin level in obese children was 34,009.2 pg/L (SD 18,224.79), higher than that of the control, 7,760.9 pg/L (SD 8,859.55) ($P < 0.0001$). The mean hsCRP level in obese children was 3.6 mg/L (SD 3.60), higher than that of the control, 0.7 mg/L (SD 1.32) ($P < 0.0001$). There was a significant positive correlation between leptin and hsCRP levels in obese children ($r = 0.355$, $P < 0.0001$).

Conclusions There is significant positive correlation between leptin and hsCRP levels in obese children aged 9-15 years. Increased leptin and hsCRP levels indicate a low degree of chronic inflammation. Thus, intervention is needed to decrease the body weight of obese children. **2011;51:47-51]**.

Keywords: *leptin, hs-CRP, obese, fasting blood sugar, body mass index*

Obesity is a low level and chronic inflammatory process that affects white adipose tissue (WAT), where macrophage infiltration is found. Macrophages release inflammatory mediators such as TNF–α, IL-1, and IL-6. These pro-inflammatory cytokines trigger the release of C-reactive protein. HsCRP is C-reactive protein measured with a high sensitivity assay. CRP is an acute phase reactant, produced by the liver under interleukin-6 control. CRP can increase endothelial dysfunction by causing energy and nitric oxide supply deprivation.[1]

Obese children have higher leptin levels, and leptin receptors are universally found in immune cells, endothelial cells, and in atherosclerotic plaques. Thus, leptin is thought to be a link between obesity and cardiovascular disease. Leptin can increase cytokine production in macrophages and monocytes, as well as increase oxidative stress in endothelial cells.[2] The objective of this study is to look for a correlation between leptin and hsCRP among obese children aged 9-15 years.

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Methods

This cross-sectional study was done on elementary and junior high school children in Manado City, North Sulawesi, from May to December 2009. Subjects were chosen by simple random sampling. We included obese children aged 9-15 years who were physically healthy in the 3 weeks prior to the study. We excluded children who suffered acute infection, hypertension, diabetes mellitus, cardiac problems, liver diseases, and those who used steroids or growth hormones. Informed consent was obtained from parents.

The need for a minimum sample size of 50 subjects was calculated using Sastroasmoro's formula.[3] Blood tests included fasting blood sugar (FBS), total cholesterol, triglyceride, low density lipoprotein (LDL), high density lipoprotein (HDL), leptin, and hsCRP levels. Obesity was determined using body mass index (BMI, weight in kilograms/height in meter^2) and converted to a *z*-score according to WHO standards for boys or girls. If a *z*-score exceeded 3-SD, the child was categorized as obese.

We used the chi square test for analyzing gender differences. We performed the t-test for age, blood pressure, fasting blood sugar, total cholesterol, LDL and HDL cholesterol, triglycerides, leptin levels, and hs-CRP level comparisons. We conducted Pearson's correlation coefficient test to determine the correlation between leptin and hs-CRP levels. Statistical analysis was done by using the 17th version SPSS software.

Results

Figure 1 shows the flow chart of subjects' enrollment. Ninety-three subjects were included in the obese group, and 93 were included in the normal weight group.

Table 1 shows the characteristics of the obese and non-obese subjects. We observed a significant difference in systolic and diastolic blood pressures between the 2 groups, with P < 0.0001. In addition,

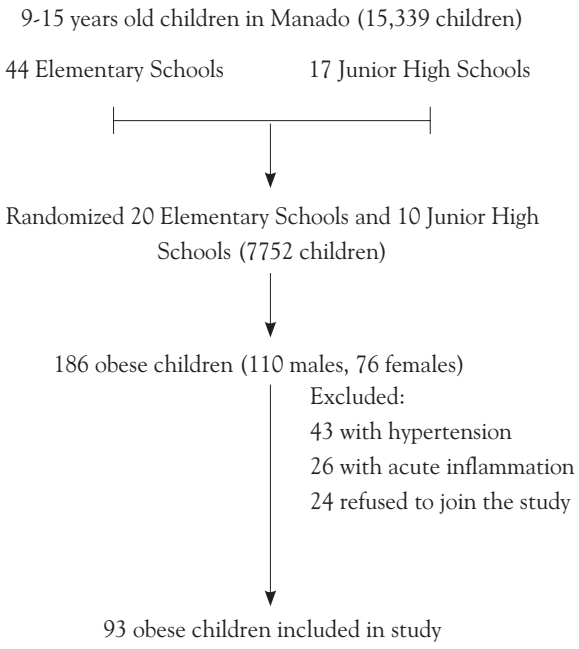

Figure 1. Flow chart of enrollment.

Table 1. Characteristics of subjects

Category	Group		
	Obese N=93	Non-Obese N=93	P value
Mean age (SD), years	12.1 (1.46)	12.3 (0.89)	0.294
Male, n	60	50	0.136
Mean systolic BP (SD), mmHg	115.4 (9.77)	107.5 (10.47)	< 0.0001
Mean diastolic BP (SD), mmHg	76.1 (7.39)	68.5 (9.31)	< 0.0001
Mean FBS (SD), mg/dL	88.9 (6.76)	87.0 (6.48)	0.061
Mean cholesterol (SD), mg/dL	169.9 (32.57)	159.6 (25.99)	0.018
Mean LDL (SD), mg/dL	121.0 (28.41)	106.3 (21.92)	< 0.0001
Mean HDL (SD), mg/dL	44.6 (8.93)	51.4 (9.86)	< 0.0001
Mean triglyceride (SD), mg/dL	119.8 (53.68)	87.8 (36.30)	< 0.0001

Table 2. Leptin and hsCRP results between groups

Category	Group		
	Obese N=93	Non-Obese N=93	P Value
Mean leptin (SD), pg/mL	34,009.2 (18,224.79)	7,760.9 (8,859.55)	< 0.0001
Mean hsCRP (SD), mg/L	3.6 (3.60)	0.7 (1.32)	< 0.0001

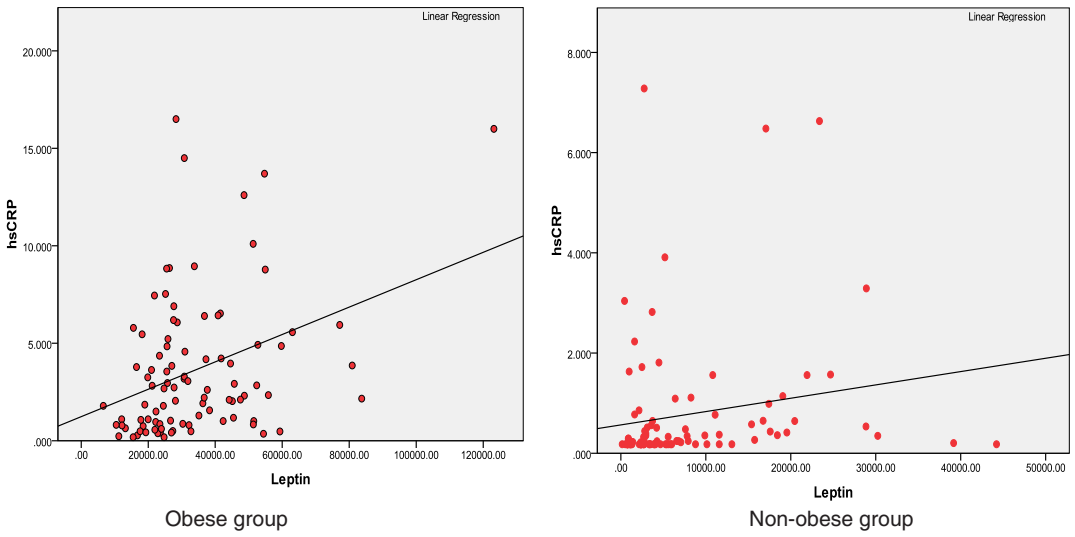

Figure 2. Correlation between leptin and hsCRP levels in each group.

there were significant differences in LDL, HDL, and triglyceride levels, with P < 0.0001 for all these conditions. However, there were no significant differences in age, gender, fasting blood sugar, and cholesterol levels.

Table 2 shows significant differences in leptin and hsCRP levels between the 2 groups, with P < 0.0001 for both molecules.

Figure 2 shows the results of Pearson's test on the correlation of leptin and hs-CRP levels from both groups. In obese children, there was a significant positive correlation (r = 0.355 and P < 0.0001) between leptin and hsCRP levels. In non-obese children, there was also a significant positive correlation (r = 0.178 and P= 0.044) between leptin and hs-CRP levels.

Discussion

Of the 93 obese subjects from elementary and junior high schools in Manado, 60 (65%) were boys and 33 (35%) were girls. This gender composition is consistent with the study from Wolff et al,[4] where obese subjects aged 5-15 years consisted of 60% boys and 40% girls. Likewise, Ikezaki et al[5] found that from 105 obese children surveyed, 61% were boys and 39% were girls. Steinbeck et al[6] said that girls increase in body fat from age 4 years, thus girls have more body fat than boys, however, this difference decreases during the adolescent period. Lederman et al[7] shows that there is no significant difference in the risk of obesity between boys and girls. (Comment: Authors are contradicting themselves. Should we Remove?)

We chose subjects aged 9-15 years because previous studies on super obese boys aged 5-9 years, showed no correlation between leptin, adiponectin, TNF-α, and CRP levels and insulin resistance. A possible explanation is that adipocyte cells underwent hyperplasia but not hypertrophy in super obese 5-9 year-olds. Therefore, the low level of chronic inflammation was not yet present.[8] Furthermore, Punthakee et al[9] found that elevated hsCRP and decreased adiponectin levels represent the start of chronic inflammation, often by the age of 9 years.

We observed significant differences in mean systolic and diastolic blood pressures between the obese and normal weight groups. Schiel et al[10] and Barath et al[11] found that systolic and diastolic blood pressures are higher in obese children. Fox et al[12] reported a positive correlation between blood pressure and body mass index.

We found a significantly higher mean leptin level in obese children than that of normal weight children, consistent with studi es from Vallet et al,[13] and Diamont et al.[14] The elevation of serum leptin can be caused by increased fat deposition and leptin resistance. During puberty, leptin levels increase in

girls, but decrease in boys in parallel with body fat changes during puberty. Leptin levels were observed to have a positive correlation with body mass index.[13,15]

We observed a positive correlation between leptin and hsCRP levels. Both of these pro-inflammatory agents tend to increase in obese children. Our findings are consistent with a study from Li et al.[21] In obese children with a positive calorie balance, energy is stored in the form of adipocyte hypertrophy, followed by adipocyte hyperplasia. These hypertrophic, dysfunctional adipocytes can cause an elevation of free fatty acids in blood, thus increasing fatty acid oxidation in muscle. Inhibited glucose uptake by muscles can cause hyperglycemia.[22]

In our study, the mean hsCRP level in obese children was 3.6 mg/L (3.60), while that of non-obese children was 0.7 mg/L (1.32). Kapiotis et al[16] and Wu et al[17] found that hsCRP levels increased in direct proportion to body mass index in obese children. Yoshida et al[18] reported that elevated hsCRP levels in obese, Japanese children were an atherosclerotic, coronary heart disease risk factor. Oliveira et al[19] found that hsCRP levels in young adults were closely related to components of metabolic syndrome. In addition, Mattson et al[20] found that high hsCRP levels in obese children were a predictive factor for metabolic syndrome upon reaching adulthood.

Because this study was cross-sectional, we do not know the duration of chronic inflammation in the obese children. We also do not know the lifestyle habits of the subjects, such as food intake and physical activity. Nor did we examine genetics, pubertal status, or inflammatory status.

In conclusion, there was a positive correlation between leptin and hsCRP levels in obese children aged 9-15 years. Leptin and hsCRP are indicators of low degree of chronic inflammation. Therefore, intervention is needed to decrease the body weight of obese children through nutritional education and increased physical activity.

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