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Chronic Low-grade Inflammation and Haematological, Circulatory, Metabolic, and Hepatic Abnormalities in Childhood Obesity

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ABSTRACT

Background: Little is known as to the associations between childhood obesity and chronic low-grade inflammation, circulatory, hepatic, metabolic and haematological abnormalities. Methods and Results: A total of 1,871 boys and 1,810 girls were measured anthropometric data, white blood cell (WBCC), platelet count, blood pressure, plasma concentrations of aspartate aminotransferase (AST), alanine aminotransferase (ALT), triglyceride (TG), and high-density (HDL) lipoprotein cholesterol,. The subjects were classified into three body mass index categories depending on the international standard definition for child overweight and obesity. WBCC, platelet counts, systolic blood pressure, serum levels of aminotransferases,TG and HDL-cholesterol were related with body composition in both boys and girls. Obese girls had high risks of having abnormal levels of WBCC, platelet count, systolic blood pressure (SBP), ALT, TG, HDL-cholesterol. Obese boys had high risks of having abnormal levels of WBCC, haemobobin concentration, platelet count, SBP, diastolic blood pressure, AST, ALT, TG, and HDL-cholesterol. Conclusions: Childhood obesity is related with chronic inflammation, hypercoagulability, as well as circulatory, metabolic, and hepatic abnormalities.

Keywords: Obesity; Metabolic Syndrome; Inflammation; Platelet; Children

1. INTRODUCTION

The prevalence of childhood obesity and metabolic syndrome are increasing in the western countries[1-5] as well as in Asia.[6-8] These conditions are known to be associated with hypertension,[10-12] abnormal lipid and glucose metabolism,[10] liver dysfunction,[13-16] chronic low-grade inflammation[17,18] and hypercoagulability[19-21] in the adult populations. However, little is known as to the association of obesity and these abnormalities in the paediatric populations.[22] Therefore, we aimed to investigate whether childhood obesity is related with these circulatory, metabolic and hepatic abnormalities, as well as with chronic low-grade inflammation.

2. METHODS

2.1. Study Subjects and Measurements

The subjects in the present study were all first-year junior high school students who had been admitted to Toyota municipal public junior high schools in the 2009 academic year. Their mean age is 12.5(SD = 0.3) years old in both boys and girls. We utilized the database of the results of the medical checkups performed by us and possessed by Toyota Municipal Board of Education. Information that could be used to identify individual subjects had been deleted before the Board of Education had provided us with the data.

At the medical check-up, experienced nurses measured the subject's body weight to the nearest 0.1 kg and height to the nearest 0.1 cm. Blood pressure was measured with an automatic oscillometric sphygmomanometer (BP-103iII, Colin, Nagoya, Japan) after the student had been resting on a chair for more than 5 minutes. A second measurement was performed 2 minutes later, and the lower of the two measurements was used in the analysis. After an overnight fast, blood samples (6ml) were drawn from the peripheral veins for the measurements of complete blood cell counts, plasma concentrations of aspartate aminotransferase (AST), alanine aminotransferase (ALT), triglyceride, high-density lipopro-

tein (HDL) cholesterol (Hitachi 917 Biochemical Analyzer, Tokyo, Japan). Valid measurements obtained from 1,871 boys and 1,810 girls were used in the analysis. The characteristics of the subjects are summarised in **Table 1**. The number of subjects included in the present study represented 95% of the peers in the 2009 academic year in Toyota city. Therefore, the subjects in the present study were considered to be valid and unbiased samples.

This study conformed with the Ethical Guidelines for Epidemiological Research of the Japanese Ministry of Education, Culture, Sports, Science and Technology, Ministry of Health, Labour and Welfare. We obtained permission to use and analyse these data from the municipal board of education on the condition with confidentiality of personal data.

2.2. Definitions of Overweight and Obesity, and Abnormal Values

The subjects were classified into three body mass index (BMI) categories depending on the international standard definition for childhood overweight and obesity[23]: nonobese defined by a BMI<21.56 kg/m^2 in boys and <22.14 kg/m^2 in girls, overweight defined by a BMI between 21.56 to 26.43 kg/m^2 in boys and 22.14 to 27.24 kg/m^2 in girls, and obese defined by a BMI ≥ 26.84 kg/m^2 in boys and ≥ 27.24 kg/m^2 in girls. A high systolic blood pressure was defined as a systolic blood pressure greater than or equal to the 95th percentile (≥132 mmHg in both boys and girls). A high diastolic blood pressure was defined as a diastolic blood pressure equal to or greater than 95th percentile (≥78 mmHg in boys and ≥79 mmHg in girls). High AST, high ALT, high TG, high white blood cell count (WBCC), high hemoglobin concentration(Hb), and high platelet count are defined by levels ≥ 95th percentile (AST: ≥ 33 IU/l in boys and ≥ 28 IU/l in girls; ALT ≥ 24 IU/l in boys and ≥ 18 IU/l in girls; TG: ≥ 188 mg/dl in boys and ≥ 190 mg/dl in girls; WBCC ≥ 8.3×10^3 in boys and ≥ 8.8×10^3 in girls; Hb ≥ 15.2 g/dl in boys and ≥ 14.6 g/dl in girls; platelet count 4.48×10^5 /mm^3 in boys and ≥ 3.49×10^5 /mm^3 in girls). Low HDL level was defined by a serum concentration ≤ 5th percentile, or ≤ 43 mg/dl in boys and ≤ 45 mg/dl in girls.

2.3. Statistics

A probability value of $p<0.05$ was considered to be statistically significant. Mean values were compared using Student's *t*-test. All statistical analyses were performed with the Japanese edition of SPSS version 15.0 (Tokyo, Japan).

3. RESULTS

Mean values of the measurements as classified by body composition are listed in **Table 1.** The odds ratios of having abnormal measurements are listed in **Table 2**.

3.1. Blood Pressure

In both boys and girls, systolic blood pressure was related with body composition. Also, the risk of having abnormally high systolic blood pressure was greater in

Table 1. Mean values of the measurements as classified by body composition.

	girls				boys			
	obese	overweight	normal	p	obese	overweight	normal	p
	n = 20	n = 177	n = 1613		n = 39	n = 189	n = 1643	
Height (cm)	154.1 (5.8)	152.6 (5.7)	151.0 (6.0)	<0.001	157.4 (5.6)	154.7 (7.7)	150.6 (7.8)	<0.001
Weight (kg)	71.1 (8.1)	56.9 (5.7)	41.1 (6.1)	<0.001	72.7 (10.4)	56.2 (6.4)	40.1 (6.7)	<0.001
BMI (kg/m^2)	29.9 (2.4)	24.0 (1.5)	18.0 (1.9)	<0.001	29.3 (3.4)	23.4 (1.3)	17.6 (1.8)	<0.001
SBP (mmHg)	122 (14)	117 (11)	113 (11)	<0.001	124 (9)	119 (11)	114 (12)	<0.001
DBP (mmHg)	66 (9)	64 (9)	64 (9)	0.34	67 (9)	63 (9)	62 (9)	0.013
AST (IU/l)	19 (9)	18 (6)	20 (5)	0.001	30 (25)	23 (6)	23 (6)	<0.001
ALT (IU/l)	17 (9)	12 (10)	11 (4)	<0.001	39 (58)	19 (11)	13 (5)	<0.001
TG (mg/dl)	141 (70)	101 (69)	86 (51)	<0.001	139 (73)	110 (74)	77 (47)	<0.001
HDL-cholesterol (mg/dl)	49 (9)	56 (12)	65 (13)	<0.001	51 (10)	55 (12)	65 (13)	<0.001
WBCC (×10^3/μl)	8.1 (1.8)	7.1 (1.3)	6.2 (1.4)	<0.001	7.5 (1.8)	6.5 (1.4)	5.8 (1.2)	<0.001
Hb (g/dl)	13.6 (0.8)	13.4 (0.8)	13.4 (0.8)	0.71	14.4 (1.0)	13.9 (0.7)	13.7 (0.8)	<0.001
Platelet (×10^5/μl)	3.1 (0.6)	2.8 (0.5)	2.6 (0.5)	<0.001	3.1 (0.6)	2.8 (0.5)	2.6 (0.5)	<0.001

Data are mean (SD) values. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TG, triglyceride; HDL, high-density lipoprotein; WBCC, white blood cell count; Hb, haemoglobin.

Table 2. The odds ratio of having abnormal circulatory, hepatic, metabolic and haematological abnormalities in obese and overweight children.

		Girls						Boys					
		obese		overweight		normal		obese		overweight		normal	
High SBP	prevalence	35.0%		8.5%		4.9%		20.5%		8.5%		5.0%	
	OR (95% CI)	10.3	(4.1-26.5)	1.8	(0.99-3.2)	1		4.4	(2.0-10.0)	1.6	(0.9-2.8)	1	
High DBP	prevalence	5.0%		6.9%		5.0%		12.8%		7.9%		4.6%	
	OR (95% CI)	1.1	(0.6-2.1)	0.83	(0.1-6.3)	1		3.0	(1.1-8.0)	1.8	(1.0-3.2)	1	
High AST	prevalence	10.0%		4.0%		5.0%		20.5%		5.3%		4.8%	
	OR (95% CI)	1.9	(0.4-8.4)	0.7	(0.3-1.6)	1		5.1	(2.3-11.5)	1.1	(0.6-2.2)	1	
High ALT	prevalence	40.0%		9.0%		4.1%		46.2%		20.6%		2.5%	
	OR (95% CI)	15.6	(6.2-39.5)	2.3	(1.3-4.1)	1		33.4	(16.6-67.5)	10.1	(6.3-16.2)	1	
High TG	prevalence	20.0%		7.9%		4.6%		17.9%		14.3%		3.6%	
	OR (95% CI)	5.2	(1.7-15.9)	1.8	(0.9-3.2)	1		5.9	(2.5-13.8)	4.5	(2.8-7.3)	1	
Low HDL	prevalence	55.0%		15.3%		4.9%		25.6%		15.9%		4.1%	
	OR (95% CI)	16.8	(6.7-41.7)	3.7	(2.3-5.9)	1		7.5	(3.4-16.6)	5.0	(3.2-8.0)	1	
High WBCC	prevalence	35.0%		10.7%		4.6%		25.6%		10.1%		4.3%	
	OR (95% CI)	11.5	(4.5-29.8)	2.6	(1.5-4.4)	1		7.7	(3.6-16.5)	2.5	(1.5-4.3)	1	
High Hb	prevalence	10.0%		6.8%		5.0%		25.6%		6.3%		4.7%	
	OR (95% CI)	1.7	(0.4-7.3)	1.1	(0.6-2.0)	1		7.0	(3.3-14.9)	1.4	(0.7-2.6)	1	
High platelet count	prevalence	40.0%		7.9%		4.6%		17.9%		8.9%		4.3%	
	OR (95% CI)	13.9	(5.5-34.9)	1.8	(1.1-3.2)	1		5.0	(2.1-11.7)	2.3	(1.3-3.9)	1	

OR, odds ratio, CI, confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TG, triglyceride; HDL, high-density lipoprotein; WBCC, white blood cell count; Hb, haemoglobin.

obese boys and girls. Diastolic blood pressure was related with body composition only in boys, not in girls. The risk of having abnormally high diastolic blood pressure was found in overweight and obese boys, but not in girls.

3.2. Aminotransferases

In both boys and girls, aminotransfereses (AST and ALT) were related with body composition. The odds ratio for having abnormally high serum AST was greater in obese boys. The odds ratio for having abnormally high serum ALT was greater in both obese and overweight boys and girls.

3.3. Serum Lipid Levels

Serum TG level was related with body composition in both boys and girls. The odds ratio for having abnormally high TG level was greater in obese girls and in obese and overweight boys. Serum HDL level was associated with body composition in both boys and girls. The odds ratios for having abnormally low HDL level were greater in obese and overweight boys and girls.

3.4. Blood Cell Counts

WBCC was related with body composition in both boys and girls. The risk for having abnormally high WBCC was observed in both obese and overweight boys and girls. Hb was related with body composition in boys, but not in girls. The risk of having abnormally high Hb levels was found in obese boys. Platelet count was related with body composition in both bys and girls. The risk of having abnormally high platelet counts was found in both obese and overweight boys and girls.

4. DISCUSSION

The most striking finding of the present study is that childhood obesity is related with WBCC, a marker of chronic inflammation, as well as with platelet count, possible marker of hypercoagulability. Also, the present study has revealed that childhood obesity is related with circulatory, metabolic, and hepatic abnormalities.

Obesity and metabolic syndrome are known to be related with chronic inflammation not only in adults[17-21] but also in children.[22] WBCC is a marker of chronic inflammation[24] and is known to correlate with the amount of body fat in adults.[25] To our knowledge, this study is the first one that has revealed the association between childhood obesity and increased WBCC. This finding confirms the relation of chronic inflammation with childhood obesity.[22] Childhood obesity may be

more dangerous than adult obesity, as the patients with childhood obesity have longer history of having chronic inflammation than adulthood obesity patients, which can cause early development of cardiovascular diseases.

The present study is also the first one that has shown the relation of childhood obesity with increased platelet counts, a well-known risk factor for fatal coronary heart disease in adult population.[26] Taniguchi et al. showed a relationship between platelet count and insulin resistance in non-obese adult Japanese type 2 diabetic patients.[27] Thus, increased platelet count may be related with impaired insulin sensitivity in obese children. The mechanisms for the increase in platelet counts are unknown. But, it seems interesting that insulin is thought to reduce platelet sensitivity to aggregating agents such as adenosine diphosphate.[28]

The present study shows that body composition is closely related with systolic blood pressure and that obese boys and girls have high risks of having abnormally high systolic blood pressure. These findings confirm the findings of previous studies that childhood and adolescent obesity is related with hyperkinetic circulation.[7,29] The close and early association of systolic hypertension with adiposity suggests the role of impaired autonomic function in the pathogenesis of adiposity-associated hypertension.

The present study has some limitations. We did not measure blood glucose or insulin activity. Also, the data of waist circumference is lacking. These measurements are essential for the diagnosis of metabolic syndrome. Therefore, addition of these data may provide us further knowledge as to the understanding of childhood obesity or metabolic syndrome and their associations with haematological, hepatic and circulatory disorders, which awaits further investigations.

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