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Abdominal adiposity is associated with high-density lipoprotein subclasses in Japanese schoolchildren

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ABSTRACT

Background: The large HDL subclass is considered to possess cardioprotective properties. The purpose of this study is to determine the relationship among abdominal adiposity, insulin resistance and HDL subclass profiles of Japanese schoolchildren.
Methods: The study subjects included 164 children (79 boys and 85 girls). We obtained waist to height ratio (WHtR), lipid profile, and HOMA-IR. The HDL subclass profile was analyzed by HPLC.
Results: Children of either sex with abdominal obesity (WHtR ≧ 0.5) had reduced concentrations of very large, large, and medium HDLC in conjunction with elevated triglyceride (TG) concentrations and HOMA-IR. WHtR was inversely related to the concentrations of very large (boys: $r = -0.5306$, $p < 0.0001$; girls: $r = -0.3483$, $p = 0.0011$), large ($r = -0.6168$, $p < 0.0001$; $r = -0.4387$, $p < 0.0001$), and medium ($r = -0.4170$, $p = 0.0001$; $r = -0.4116$, $p < 0.0001$) HDLC. The multiple regression analyses revealed that WHtR was an independent factor of the concentrations of very large, large, small, and very small HDLC in boys and the concentrations of large and medium HDLC in girls.
Conclusions: In Japanese schoolchildren, abdominal obesity is associated with atherogenic HDL subclass profile. Abdominal obesity may be an important target for the prevention and management of HDL subclass alteration, even in children who do not suffer from insulin resistance or hypertriglyceridemia.

1. Introduction

Many epidemiological studies have demonstrated that high-density lipoprotein cholesterol (HDLC) concentrations are strongly and inversely correlated with atherosclerotic cardiovascular disease [1]. In a cohort study of Japanese men, low HDLC concentrations were identified as a significant and independent risk factor for the occurrence of coronary artery disease [2]. Furthermore, even in adolescents, low HDLC concentrations are associated with an increased risk of high common carotid artery intima-media thickness in young adulthood [3]. Thus, HDLC concentration is an accepted predictor of future cardiovascular disease.

Obesity, especially abdominal obesity, is often accompanied by low HDLC concentrations [4]. In children, abdominal adiposity is also strongly associated with HDLC concentration [5,6]. In a longitudinal follow-up study, the change in visceral fat was significantly related to the changes in triglyceride (TG) and HDLC concentrations [7]. In addition, the reduction and long-term maintenance of visceral fat after weight loss intervention are associated with improvements in HDLC and TG [8]. Therefore, the HDLC concentration may be a target for the primary prevention of obesity-related atherosclerotic cardiovascular diseases.

HDL particles are heterogeneous in size, density, composition, and function. HDL plays a central role in reverse cholesterol transport for the removal of cholesterol from peripheral tissue and has other atheroprotective properties, such as anti-oxidative, anti-thrombotic, anti-apoptotic, and anti-infectious functions [1,9]. Several laboratory techniques, including ultracentrifugation, nuclear magnetic resonance spectroscopy, and electrophoresis, have been used to separate HDL particles. Electrophoresis can divide HDL particles into two major subclasses: pre-β and α. Pre-β HDLs play an important role in reverse cholesterol transport as the initial acceptors. Alpha HDLs, which are larger, cholesteryl-ester-rich particles, deliver cholesteryl-ester to the liver. Epidemiological studies have indicated that the large HDL subclass is linked to cardiovascular protection [10]. Therefore, HDL subclass analysis should be performed for a precise evaluation of the risks.

High-performance liquid chromatography (HPLC) is an alternative method for classifying lipoproteins by particle size [11]. Using this method, HDL is classified into five distinct subclasses: very large, large, medium, small, and very small. In a study of Japanese adults, visceral fat area, as well as body mass index (BMI), was inversely related to cholesterol in the large and medium HDL subclasses but not in the very large, small, and very small HDL subclasses [12].

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However, few studies have used this method to investigate HDL subclasses in children [13]. Furthermore, the relationship between adiposity and HDL subclass profile in Japanese children is not well studied [14,15]. In the present study, we analyzed HDL subclasses in Japanese schoolchildren using HPLC and investigated the association among abdominal adiposity, insulin resistance and cholesterol concentrations in each HDL subclass.

2. Materials and methods

The study subjects included 164 children (79 boys and 85 girls) aged 10.9 ± 1.6 years (mean ± SD; range = 9–13 years) who attended 1 of the 2 schools selected for this study and participated voluntarily in this study. All of the children were free from diseases other than dyslipidemia and obesity. Each child's standing height and weight were measured. Waist circumference was measured at the concentration of the umbilicus, and the waist-to-height ratio (WHtR) was calculated. Abdominal obesity is defined as WHtR ≧ 0.5 [6]. WHtR is accepted as a useful indicator in detecting central intra-abdominal obesity and related cardiometabolic risks among normal weight and overweight/obese children [5]. All of the blood samples were obtained from the cubital vein in the morning after an overnight fast. Total cholesterol (TC) and TG concentrations were measured by enzymatic methods. Serum lipoprotein analyses were performed by HPLC with gel permeation columns (LipoSEARCH; Skylight-Biotec, Inc., Akita, Japan), and the low-density lipoprotein cholesterol (LDLC), HDLC, and cholesterol concentrations in five HDL subclasses (very large, large, medium, small, and very small) were measured [11]. Plasma insulin and glucose concentrations were determined, and the homeostasis model of assessment ratio (HOMA-IR) was obtained using Matthews' formula as an index of insulin resistance [16].

Informed consent was obtained from each child and his or her parents. The study protocol was approved by the local ethics committee, which is composed of members of the school's health education committee. This committee also includes members of the local board of education and representatives from Nihon University Itabashi Hospital.

All of the data are expressed as the means ± SD. The group differences were assessed using ANOVA with Scheffe's post hoc tests. The sample size was assessed by power analysis and showed to be adequate for 4-subgroup analysis by ANOVA. Single and multiple regression analyses were used to assess the correlation between variables. A $p < 0.05$ was considered statistically significant. All of the statistical analyses were conducted using the JMP statistical package (v9.0; SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Characteristics of the subjects

Table 1 shows the clinical characteristics and serum lipid profile of the subjects. We found that 13 boys (16.5%) and 9 girls (10.6%) presented abdominal obesity. Compared to children without abdominal obesity, children with abdominal obesity exhibited higher TG and insulin concentrations and HOMA-IR as well as lower HDLC concentrations, regardless of the sex. LDLC and non-HDLC concentrations in boys with abdominal obesity were also higher than those in boys without abdominal obesity, and the difference in non-HDLC concentrations was statistically significant; however, no difference was observed in LDLC or non-HDLC concentrations in girls with and without abdominal obesity.

In children without abdominal obesity, girls showed higher non-HDLC and insulin concentrations than boys. In children with abdominal obesity, girls showed higher insulin concentration and HOMA-IR than boys.

3.2. HDL subclass profile measured using the HPLC method

Children with abdominal obesity had lower very large, large, and medium HDLC concentrations than those without abdominal obesity in both sexes (Table 1). In addition, small and very small HDLC concentrations in boys with abdominal obesity were higher than those in girls with abdominal obesity.

Table 1
Characteristics of the subjects.

	Boys n = 79		Girls n = 85		p value
	Without abdominal obesity n = 66	With abdominal obesity n = 13	Without abdominal obesity n = 76	With abdominal obesity n = 9	
Age (year)	11.0 ± 1.6	10.8 ± 1.6	10.8 ± 1.6	11.7 ± 1.0	NS
Height (cm)	146.1 ± 12.9	146.5 ± 12.5	142.3 ± 10.8	150.5 ± 6.9	NS
Body weight (kg)	37.3 ± 9.7[c,f]	52.1 ± 14.8[c,e]	35.6 ± 9.3[d,e]	59.6 ± 9.5[d,f]	<0.0001
Waist circumference (cm)	60.0 ± 6.0[c,f]	82.3 ± 9.4[c,e]	59.8 ± 6.5[d,e]	80.1 ± 3.5[d,f]	<0.0001
Body mass index	17.1 ± 1.9[c,f]	23.9 ± 3.6[c,e]	17.3 ± 2.5[d,e]	26.1 ± 2.2[d,f]	<0.0001
Waist/height ratio	0.41 ± 0.03[c,f]	0.56 ± 0.04[c,e]	0.42 ± 0.03[d,e]	0.53 ± 0.02[d,f]	<0.0001
Total cholesterol (mg/dl)	168.5 ± 21.1	173.8 ± 28.3	176.9 ± 22.0	162.6 ± 24.8	NS
LDLC (mg/dl)	90.9 ± 17.2	105.2 ± 25.6	99.7 ± 20.1	96.0 ± 22.1	0.0210
HDLC (mg/dl)	69.2 ± 12.6[c,f]	53.5 ± 9.6[c,e]	66.9 ± 11.3[d,e]	49.8 ± 8.5[d,f]	<0.0001
Triglyceride (mg/dl)	42.0 ± 17.4[c,f]	75.7 ± 27.1[c,e]	51.5 ± 2.9[d,e]	83.8 ± 8.3[d,f]	<0.0001
Non-HDL cholesterol (mg/dl)	99.3 ± 18.1[b,c]	120.3 ± 26.1[c]	110.0 ± 20.7[b]	112.8 ± 27.1	0.0010
Fasting glucose (mg/dl)	88.7 ± 4.9	91.7 ± 5.0	87.5 ± 6.2	89.9 ± 5.1	NS
Insulin (μU/ml)	6.1 ± 2.9[b,c,f]	12.1 ± 6.4[a,c]	8.4 ± 4.8[b,d]	18.5 ± 7.5[a,d,f]	<0.0001
HOMA-IR	1.3 ± 0.7[c,f]	2.8 ± 1.6[a,c,e]	1.8 ± 1.1[d,e]	4.1 ± 1.9[a,d,f]	<0.0001
Very large HDLC (mg/dl)	4.6 ± 1.9[c,f]	2.3 ± 0.7[c,e]	4.3 ± 1.7[d,e]	2.6 ± 0.9[d,f]	<0.0001
Large HDLC (mg/dl)	20.4 ± 6.7[c,f]	9.7 ± 3.4[c,e]	19.0 ± 6.1[d,e]	10.8 ± 4.0[d,f]	<0.0001
Medium HDLC (mg/dl)	22.6 ± 3.6[c,f]	19.0 ± 3.1[c,e]	22.1 ± 3.2[d,e]	17.5 ± 3.0[d,f]	<0.0001
Small HDLC (mg/dl)	12.0 ± 1.9	13.2 ± 1.8[a]	12.0 ± 1.4	11.0 ± 1.1[a]	0.0170
Very small HDLC (mg/dl)	5.9 ± 1.0	6.4 ± 1.1[a]	6.0 ± 0.7	5.3 ± 0.6[a]	0.0207

ANOVA with Scheffe's post hoc test.
[a] Boys with abdominal obesity vs. girls with abdominal obesity; $p < 0.05$.
[b] Boys without abdominal obesity vs. girls without abdominal obesity; $p < 0.05$.
[c] Boys with abdominal obesity vs. boys without abdominal obesity; $p < 0.05$.
[d] Girls with abdominal obesity vs. girls without abdominal obesity; $p < 0.05$.
[e] Boys with abdominal obesity vs. girls without abdominal obesity; $p < 0.05$.
[f] Boys without abdominal obesity vs. girls with abdominal obesity; $p < 0.05$.