# Serum High-density Lipoprotein Cholesterol Level and Lifestyle Habits among Japanese Junior High School Students

Minoru HONGO<sup>1)\*</sup>, Hiroya HIDAKA<sup>2)</sup>, Shigeko SAKAGUCHI<sup>3)</sup>, Keisuke NAKANISHI<sup>3)</sup> Fumiko TERASAWA<sup>2)</sup>, Motoki ICHIKAWA<sup>4)</sup>, Naoko HIROTA<sup>5)</sup>, Goro TSURUTA<sup>6)</sup>

Naoki TANAKA<sup>7</sup>, Atsushi IZAWA<sup>8</sup>, Yoshikazu YAZAKI<sup>9</sup>, Uichi IKEDA<sup>8</sup>, Kenichi KOIKE<sup>6</sup> on behalf of the Investigators of the Study Project on Prevention of

Metabolic Syndrome among Children, Adolescents, and Young Adults in Shinshu

- 1) Department of Cardiovascular Medicine, Shinshu University School of Health Sciences
- 2) Department of Clinical Laboratory Medicine, Shinshu University School of Health Sciences
- 3) Department of Nursing, Shinshu University School of Health Sciences
- 4) Department of Pediatrics, Shinshu University School of Health Sciences
- 5) Faculty of Human Health Science, Matsumoto University
- 6) Department of Pediatrics, Shinshu University School of Medicine
- 7) Department of Gastroenterology, Shinshu University School of Medicine
- 8) Department of Cardiovascular Medicine, Shinshu University School of Medicine
- 9) Department of Cardiovascular Medicine, Saku General Hospital

**Aim**: We examined the relationship between serum high-density lipoprotein cholesterol (HDL-C) level and lifestyle habits among Japanese junior high school students.

**Methods**: Between April 2006 and March 2009, we conducted a cross-sectional study of 1064 Japanese junior high school students (570 boys and 494 girls, aged 12.1 to 15.0 years) who had annual school health examinations in Nagano Prefecture. They were divided into 4 groups according to HDL-C quartiles.

**Results** : There was a significant increase in the ratio of waist circumference to body height, percentage of being overweight, triglyceride, non-HDL-C, the ratio of low-density lipoprotein cholesterol to HDL-C, and uric acid in the lowest quartile of HDL-C compared with the highest quartile in both genders. Fasting plasma glucose was also significantly increased in the lowest quartile compared with the highest quartile in boys. With regard to lifestyle habits, the ratios of the students who were often commuting to and from school by car, did not like exercise, did not do sports outside of school, and watched television during meals were significantly higher in the lowest quartile of HDL-C compared with the highest quartile in both genders.

**Conclusions**: Serum HDL-C level was associated with reduced daily physical activity among junior high school students. This study may provide insights into the role of HDL-C in the school screening system for the development of more effective educational programs on the prevention of lifestyle-related diseases in the Japanese population of school children. *Shinshu Med J 61*: 205-215, 2013

(Received for publication January 8, 2013; accepted in revised form April 11, 2013)

Key words : high-density lipoprotein cholesterol, Japanese junior high school students, lifestyle habits

## I Introduction

A number of large-scale clinical trials have demonstrated an association between a high serum

Corresponding author: Minoru Hongo
 Department of Cardiovascular Medicine, Shinshu University School of Health Sciences, 3-1-1 Asahi,
 Matsumoto, Nagano 390-8621 Japan
 E-mail: hongo@shinshu-u.ac.jp

low-density lipoprotein cholesterol (LDL-C) level and the risk of coronary heart disease (CHD) in adults. Many epidemiological studies have revealed a consistent inverse association between high-density lipoprotein cholesterol (HDL-C) level and the risk of CHD events and prognosis, independent of LDL-C, in the general population of adults<sup>1)–5)</sup>. Furthermore, several autopsy studies, such as the Pathological Determinants of Atherosclerosis in Youth (PDAY) study<sup>6)7)</sup> and the Bogalusa Heart Study<sup>8)9)</sup>, have reported that the presence and extent of atherosclerotic lesions in the aorta and coronary arteries in young to middle-aged adults who had died of accidental causes are closely correlated with cardiovascular (CV) risk factors measured during life. In addition, investigations using carotid ultrasound in young and middle-aged adults have pointed out a positive relationship between childhood and adolescent CV disease risk and subclinical measures of atherosclerosis in adulthood<sup>10)11)</sup>. Based on these results, it is well established that the atherosclerotic process begins in childhood and progresses gradually through adolescence to young adulthood into middle age, and that high LDL-C and low HDL-C in childhood are associated with an increased risk of the development of atherosclerosis and future CV disease in adulthood<sup>12)-14)</sup>.

We have previously reported that the prevalence of young Japanese patients with CHD is increasing with a higher rate of onset during the summer months<sup>15)</sup>, and that childhood obesity and a lack of regular physical activity are the most important independent risk factors for CHD events<sup>16)</sup>. Our recent observations have also exhibited a strong association between serum uric acid level and cardiometabolic risk factors17) and between nonalcoholic fatty liver disease and obesity and lifestyle habits<sup>18)</sup> among Japanese junior high school students. Thus, it would be more effective to start to control the risk factors as early as possible in life. However, there have been only a few reports on the relationship between HDL-C and lifestyle habits among Japanese school children<sup>19)20)</sup>. The aim of the present study was to examine the relationship between serum HDL-C level and lifestyle habits in a sample of healthy Japanese junior high school students living in Nagano Prefecture.

# II Methods

#### A Study design

Between April 2006 and March 2009, we conducted a cross-sectional study of 1064 Japanese junior high school students (570 boys and 494 girls, aged 12. 1 to 15.0 years) who had annual school health examinations at 3 schools in the various regions (urban, rural, and mountain communities) of Nagano Prefecture. After written informed consent had been obtained from both the students and their parents, the students underwent measurements of resting systolic and diastolic blood pressure (SBP, DBP), and waist circumference (WC) as well as body height (BH) and weight, and provided overnight fasting venous blood samples. Each participant was then asked to complete a simple 12-item self-administered questionnaire addressing lifestyle factors, such as dietary patterns and habits and physical activity, as well as the co-existence of cardiometabolic risk factors, including dyslipidemia, impaired glucose tolerance, and hypertension. The study protocol was approved by the Medical Ethics Committee of Shinshu University School of Medicine (Nos. 1598, 1711, and 1712).

#### **B** Measurements

WC was measured at the level of the umbilicus using a measuring tape, and then the ratio of WC to BH (WC/BH ratio) was derived. Percentage of being overweight (POW) was calculated from an age-height-related standard of weight for healthy Japanese children. The POW was defined as percentage of weight difference from the standard weight. BP was determined after a 10-min rest in the sitting position using a mercury-gravity sphygmomanometer. All laboratory analyses of the blood samples, including serum concentrations of total cholesterol (TC), triglyceride (TG), and uric acid (SUA), fasting plasma glucose (FPG), and hemoglobin (Hb) A1c, were performed using standard methods. Serum HDL-C level was measured by the direct method in 3 laboratories, in which the accuracy was strictly managed and standardized among the laboratories. Serum LDL-C was calculated using Friedewald's equation, except for serum TG level > 400 mg/dL, and non-HDL-C level was calculated by subtracting the HDL-C from the TC concentration. The LDL-C/HDL-C ratio was then derived. Measurement of lipids and FPG was carried out in the participants who had fasted 12 hours or more. The value of HbA<sub>1c</sub> was described according to the criteria of the National Glycohemoglobin Standardization Program<sup>21)</sup>. All participants had no chronic diseases and were receiving no medication in the present study.

#### C Definition of cardiometabolic risk factors

Abdominal obesity was defined as a WC  $\geq$  80 cm and/or WC/BH ratio  $\geq 0.5^{22}$ . Hypertriglyceridemia was determined by serum concentration of TG  $\geq$  120 mg/dL<sup>22</sup>). Low HDL-C was identified by serum HDL-C  $< 40 \text{ mg/dL}^{23}$  and increased fasting glucose was defined as FPG  $\geq 100 \text{ mg/dL}^{22}$ . In addition, we adopted the criteria of hypertension in Japanese junior high school students at a medical check-up recommended by the Japanese Society of Hypertension, in which hypertension was defined as  $SBP \ge 140 \text{ mmHg and/or } DBP \ge 85 \text{ mmHg in boys}$ and SBP  $\geq$  135 mmHg and/or DBP  $\geq$  80 mmHg in girls<sup>24)</sup>. Metabolic syndrome in the pediatric setting was identified by the presence of abdominal obesity in association with at least 2 of the 3 conditions, such as hypertriglyceridemia and/or low HDL-C, high BP which was defined as SBP  $\geq 125 \text{ mmHg}$ and/or DBP  $\geq$  70 mmHg, and elevated FPG levels according to the criteria proposed by a Task Force financed by the Ministry of Health, Welfare, and Labor Science Research Grants in Japan<sup>22)</sup>.

## **D** Statistical analysis

Continuous variables with normal distribution were expressed as mean  $\pm$  SD and those with nonnormal distribution, such as TG, were presented as the median. The difference of categorical variables, including lifestyle habits, was examined with the chisquare test or Fisher's exact test. The significance of continuous variables, such as age, WC, WC/BH ratio, POW, SBP, DBP, HDL-C, TG, LDL-C, non HDL-C, LDL-C/HDL-C ratio, FPG, HbA1c, and SUA, between groups was analyzed by using an unpaired t-test or an analysis of variance for repeated measures and Newmann-Keuls post hoc test. All analyses were performed with the SPSS software Version 12.0 for Windows (SPSS, Chicago, IL, USA) and a p value of < 0.05 was considered statistically significant.

## III Results

The data were analyzed among boys and girls separately, and gender-specific quartiles of HDL-C levels were used because they were observed to approximate a normal distribution, as shown in **Fig. 1**. HDL-C levels were classified into the following 4 categories: (1)  $\leq 55 \text{ mg/dL}$  (mean 49 mg/dL), (2) 56 to 63 mg/dL (mean 60 mg/dL), (3) 64 to 73 mg/dL (mean 68 mg/dL), and (4)  $\geq 74 \text{ mg/dL}$  (mean 81



Fig. 1 Distribution of serum high-density lipoprotein cholesterol concentration in boys and girls

## Hongo·Hidaka·Sakaguchi et al.

	Boys	Girls	p value
Number of subjects	570	494	
Age (yrs)	$13.2 \pm 0.6$	$13.1 \pm 0.6$	0.063
WC (cm)	$68.0 \pm 7.9$	$67.5 \pm 6.8$	0.301
WC/BH ratio	$0.42 \pm 0.04$	$0.43 \pm 0.04$	< 0.001
POW (%)	$1.0 \pm 14.3$	$0.4 \pm 13.9$	0.495
Systolic BP (mmHg)	$113\pm12$	$108\!\pm\!11$	< 0.001
Diastolic BP (mmHg)	$63\pm10$	$63\pm9$	0.971
TG (mg/dL)	63	67	< 0.001
(95% CI)	(38-122)	(36 - 110)	
LDL-C (mg/dL)	$88\pm20$	$94\!\pm\!24$	< 0.001
HDL-C (mg/dL)	$65\pm13$	$66\pm13$	0.153
non-HDL-C (mg/dL)	$100\!\pm\!12$	$108\pm13$	< 0.001
LDL-C/HDL-C ratio	$1.36 \pm 0.42$	$1.42 \pm 0.47$	0.008
FPG (mg/dL)	$88\pm8$	$87\pm7$	0.217
Hemoglobin A <sub>1c</sub> (%)	$5.4\pm0.3$	$5.3 \pm 0.3$	0.076
SUA (mg/dL)	$5.7 \pm 1.1$	$4.5 \pm 0.8$	< 0.001

Table 1	Baseline	Characteristics
---------	----------	-----------------

Data are presented as numbers or mean $\pm$ SD or medians.

WC, waist circumference; BH, body height; POW, percentage of being overweight; BP, blood pressure; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; FPG, fasting plasma glucose; SUA, serum uric acid.

mg/dL) for boys and (1)  $\leq$  56 mg/dL (mean 51 mg/dL), (2) 57 to 64 mg/dL (mean 60 mg/dL), (3) 65 to 74 mg/dL (mean 69 mg/dL), and (4)  $\geq$  75 mg/dL (mean 82 mg/dL) for girls.

Metabolic syndrome was found in only 5 (0.5 %)of the students (4 boys and 1 girl). The highest number of the students was located at a HDL-C level between 60 mg/dL and 65 mg/dL in both genders, and only 11 (1.0 %) (8 boys and 3 girls) of the students showed low HDL-C (Fig. 1). SBP and SUA were significantly higher and WC/BH ratio, TG, LDL-C, non-HDL-C, and LDL-C/HDL-C ratio were lower in boys than in girls (Table 1). POW, HDL-C, FPG, and HbA1c did not differ between genders (Table 1). The lowest 5th percentile of HDL-C level was 40.0 mg/dL for boys and 40.3 mg/dL for girls. There was no significant difference in HDL-C level among students from the 3 different areas. In boys, TG and LDL-C/HDL-C ratio showed a graded decrease according to HDL-C quartiles. There was a significant increase in WC, WC/BH ratio, POW, non-HDL-C, FPG, and SUA in the lowest quartile of HDL-C compared with the highest quartile (**Table 2**). The prevalence of abdominal obesity, hypertriglyceridemia, and increased FPG was significantly greater in the lowest quartile of HDL-C compared with the highest quartile (**Table 3**). In girls, there was a graded decrease in LDL-C/ HDL-C ratio and a significant increase in WC, WC/ BH ratio, POW, TG, non-HDL-C, and SUA in the lowest quartile of HDL-C compared with the highest quartile (**Table 2**). The prevalence of abdominal obesity and hypertriglyceridemia was significantly increased in the lowest quartile of HDL-C compared with the highest quartile (**Table 3**). No significant difference was found in the prevalence of hypertension or high LDL-C among quartiles of HDL-C in both genders (**Table 3**).

According to HDL-C quartiles, there was a graded increase in the ratio of students who were doing sports outside of school in both genders and a graded decrease in the ratio of students who were often commuting to and from school by car in girls (**Table 4**). The ratios of the students who were often commuting to and from school by car, did not like exercise, and watched television (TV) during meals

## HDL-C and lifestyle habits

	Quartiles of HDL-C					
	Q1	Q2	Q3	Q4		
Boys (n=570)						
Range of HDL-C (mg/dL)	$\leq 55$	56-63	64-73	$\geq 74$		
Number of subjects	143	149	137	141		
Age (yrs)	$13.3 \pm 0.7$	$13.3 \pm 0.7$	$13.2 \pm 0.7$	$13.2 \pm 0.6$		
WC (cm)	$70.4 \pm 10.1^{**}$	$66.7 \pm 7.5$	$66.6 \pm 6.4$	$67.1 \pm 8.5$		
WC/BH ratio	$0.43 \pm 0.06*$	$0.42 \pm 0.03$	$0.42 \pm 0.03$	$0.42 \pm 0.05$		
POW (%)	$6.0 \pm 18.4^{***}$	$0.5 \pm 13.2^{**}$	$-1.1 \pm 13.0$	$-1.3 \pm 10.8$		
Systolic BP (mmHg)	$113\!\pm\!12$	$113\!\pm\!12$	$114\!\pm\!11$	$114\!\pm\!13$		
Diastolic BP (mmHg)	$64\pm9$	$63\pm10$	$63\pm10$	$64\!\pm\!11$		
TG (mg/dL)	82***	74***	57*	51		
(95% CI)	(54-122)	(51-112)	(46-91)	(38-73)		
LDL-C (mg/dL)	$87\!\pm\!19$	$89\pm22$	$88\!\pm\!19$	$89\!\pm\!20$		
non-HDL-C (mg/dL)	$102\!\pm\!20^*$	$103 \pm 23*$	$98\pm20$	$97\pm21$		
LDL-C/HDL-C ratio	$1.77 \pm 0.37^{***}$	$1.49 \pm 0.36^{***}$	$1.29 \pm 0.29^{**}$	$1.10 \!\pm\! 0.27$		
FPG (mg/dL)	$91 \pm 7^{***}$	$88\pm8$	$88\pm7$	$86\pm8$		
Hemoglobin A <sub>1c</sub> (%)	$5.4\pm 0.3$	$5.4\!\pm\!0.4$	$5.4 \pm 0.3$	$5.4 \pm 0.3$		
SUA (mg/dL)	$5.9 \pm 1.2^{**}$	$5.4 \pm 1.1$	$5.5 \pm 1.1$	$5.5 \pm 1.2$		
Girls ( n=494)						
Range of HDL-C (mg/dL)	$\leq 56$	57-64	65-74	$\geq 75$		
Number of subjects	125	125	120	124		
Age (yrs)	$13.2 \pm 0.7$	$13.1 \pm 0.7$	$13.2 \pm 0.7$	$13.1 \pm 0.6$		
WC (cm)	$69.0 \pm 7.4^{***}$	$67.5 \pm 6.1^*$	$67.7 \pm 6.8*$	$65.7 \pm 6.3$		
WC/BH ratio	$0.44 \pm 0.04^{**}$	$0.43 \pm 0.04*$	$0.43 \pm 0.04*$	$0.42 \pm 0.04$		
POW (%)	$3.0\pm14.9^{***}$	$1.6 \pm 12.0$	$1.8 \pm 16.1$	$-3.3 \pm 11.9$		
Systolic BP (mmHg)	$108\!\pm\!10$	$109\!\pm\!10$	$109\!\pm\!11$	$108\!\pm\!11$		
Diastolic BP (mmHg)	$62\pm8$	$62\pm8$	$62\pm11$	$63\!\pm\!10$		
TG (mg/dL)	76*	66	64	48		
(95% CI)	(53 - 110)	(41-97)	(40-93)	(35-79)		
LDL-C (mg/dL)	$95\pm27$	$91\!\pm\!27$	$92\!\pm\!29$	$93\!\pm\!28$		
non-HDL-C (mg/dL)	$112 \pm 23*$	$107\!\pm\!25$	$106\!\pm\!27$	$107\!\pm\!26$		
LDL-C/HDL-C ratio	$1.86 \pm 0.46^{***}$	$1.52 \pm 0.41^{**}$	$1.34 \pm 0.39^{**}$	$1.13 \pm 0.31$		
FPG (mg/dL)	$87\pm7$	$87\pm 6$	$87\pm7$	$87\pm7$		
Hemoglobin A <sub>1c</sub> (%)	$5.4 \pm 0.4$	$5.4\!\pm\!0.3$	$5.3 \pm 0.4$	$5.3 \pm 0.3$		
SUA (mg/dL)	$4.7 \pm 0.9^*$	$4.5 \pm 0.8$	$4.5 \pm 0.8$	$4.3 \pm 0.8$		

Table 2 Gender-specific Baseline Characteristics According to HDL-C Quartiles

\*p<0.05, \*\*p<0.01, and \*\*\*p<0.001 vs Q4. Data are presented as numbers or mean $\pm$ SD or medians. Abbreviations as in Table 1.

were significantly higher in the lowest quartile of HDL-C compared with the highest quartile in both genders (**Table 4**). In the lowest quartile of HDL-C, the prevalence of students who were often commuting to and from school by car was significantly higher, and of those who liked exercise was lower, in girls than in boys (**Table 4**).

# **Ⅳ** Discussion

The results of the present study in a school-based sample of Japanese junior high school students demonstrated that serum HDL-C level was associated with reduced daily physical activity. This study may provide insights into the role of HDL-C level in the school screening system for the development of more effective educational programs on

# Hongo·Hidaka·Sakaguchi et al.

	Quartiles of HDL-C				
	Q1	Q2	Q3	Q4	
Boys					
Abdominal obesity	16.9***	6.5	5.8	6.4	
Hypertension	1.5	0	0	0	
Hypertriglyceridemia	11.8**	9.4**	0.7	0	
High LDL-C	0.7	2.2	1.3	0.7	
Increased FPG	13.1*	5.4	2.9	2.9	
Girls					
Abdominal obesity	14.7*	6.5	6.8	4.0	
Hypertension	0.9	0.8	2.2	0	
Hypertriglyceridemia	12.1**	8.9*	5.2	2.4	
High LDL-C	1.7	3.2	4.5	4.8	
Increased FPG	4.3	3.2	3.0	3.7	

Table 3	Prevalence of	Cardiometabolic	Risk Fac	ctors According	; to	HDL-C	Quartiles
---------	---------------	-----------------	----------	-----------------	------	-------	-----------

The numbers indicate prevalence of each variable (percentages).

p < 0.05 vs Q4, p < 0.01 vs Q4, and p < 0.01 vs Q4.

Abbreviations as in Table 2.

Table 4	HDL-C	Level	and	Lifestyle	Habits

	Quartiles of HDL-C				
	Q1	Q2	Q3	Q4	
Boys (n=570)					
Skipping breakfast ( $\geq 2$ times/week)	24 (16.8)	17 (11.4)	18 (13.1)	17 (12.1)	
Eating quickly	66 (46.2)	64 (43.0)	59 (43.1)	60 (42.6)	
Drinking more than half of the broth with noodles	74 (51.7)	76 (51.0)	67 (48.9)	67 (47.5)	
Consuming sweetened drinks every day	61 (42.7)	61 (40.9)	55 (40.1)	54 (38.3)	
Eating a midnight snack ( $\geq 3$ times/week)	57 (39.9)	53 (35.6)	45 (32.8)	44 (31.2)	
Watching television during meals	128 (89.5)***	115 (77.2)	103 (75.2)	102 (72.3)	
Eating cakes/sweet rolls ( $\geq$ 3 times/week)	50 (35.0)	50 (33.6)	43 (31.4)	40 (28.4)	
Eating convenience store lunches ( $\geq$ once/week)	31 (21.7)	25 (16.8)	22 (16.1)	21 (14.9)	
Often commuting to and from school by car	65 (45.5)***	31 (20.8)**	18 (13.1)	14 (9.9)	
Playing computer games (≥1 h/day)	109 (76.2)	101 (67.8)	96 (70.1)	94 (66.7)	
Liking exercise	70 (49.0)***	113 (75.8)*	109 (79.6)	126 (89.4)	
Doing sports outside of school	4 (2.7)***	29 (19.5)***	43 (31.4)**	75 (53.2)	
Girls (n=494)					
Skipping breakfast ( $\geq 2$ times/week)	17 (13.6)	16 (12.8)	13 (10.8)	13 (10.5)	
Eating quickly	51 (40.8)	51 (40.8)	47 (39.2)	49 (39.5)	
Drinking more than half of the broth with noodles	44 (35.2)	42 (33.6)	36 (30.0)	37 (29.8)	
Consuming sweetened drinks every day	33 (26.4)	30 (24.0)	26 (21.7)	29 (23.4)	
Eating a midnight snack ( $\geq 3$ times/week)	39 (31.2)	38 (30.4)	37 (30.8)	35 (28.2)	
Watching television during meals	107 (85.6)*	99 (79.2)	98 (81.7)	92 (74.2)	
Eating cakes/sweet rolls ( $\geq$ 3 times/week)	35 (28.0)	35 (28.0)	31 (25.8)	27 (21.8)	
Eating convenience store lunches ( $\geq$ once/week)	16 (12.8)	13 (10.4)	15 (12.5)	10 (8.1)	
Often commuting to and from school by car	73 (58.4)***, ‡	59 (47.2)***	24 (20.0)**	11 (8.9)	
Playing computer games (≥1 h/day)	33 (26.4)	27 (21.6)	26 (21.7)	25 (20.2)	
Liking exercise	24 (19.2)***, §	63 (50.4)*	67 (55.8)	77 (62.1)	
Doing sports outside of school	2 (1.6)***	12 (9.6)***	21 (17.5)**	39 (31.5)	

\*p<0.05, \*\*p<0.01, and \*\*\*p<0.001 vs Q4.  $\ddagger p<0.01$  and p<0.001 vs Q1 in boys. Data are expressed as numbers (percentages).

prevention of lifestyle-related diseases in the Japanese population of school children.

## A HDL-C and CV disease risk

HDL-C possesses not only reverse cholesterol transport function but also several beneficial biological properties, including direct endothelial protection, anti-oxidation of LDL, and anti-thrombotic, anti-inflammatory, and anti-apoptotic effects, all of which may contribute to protect against atherosclerosis<sup>25)</sup>. Since the Framingham Heart Study<sup>26)</sup>, a number of epidemiological studies have revealed a consistent negative association of HDL-C level with CV disease risk in adults in Western countries<sup>1)2)</sup>. The incidence of CHD<sup>3)</sup> and all-cause mortality<sup>4)</sup> has also been inversely related to HDL-C in the adult Japanese general population<sup>27)</sup>. A recent cohort study with 12 years of follow-up in the male Japanese population has identified lower HDL-C as an independent risk factor for CHD<sup>5)</sup>.

In the Japanese population of school children, there was an increase in the prevalence of TC level from 1960 to 1996 in the nation-wide school health program conducted by the Ministry of Education, which was in parallel with an increase in obesity during the same period<sup>28)</sup>. However, a recent study on population-based annual screening of fifth-grade elementary school children in a regional district from 1993 to 2008 observed no significant change in TC, non-HDL-C, or HDL-C among school children<sup>29)</sup>. Okada et al. proposed new criteria of normal serum lipid levels among Japanese school children aged 9 to 16 years who were enrolled from 19 prefectures and received screening and care programs for prevention of lifestyle-related diseases from 1993 to 1999, in which the level below the 5th percentile of HDL-C was defined to be low and the cut-off value was determined as  $40 \text{ mg/dL}^{23}$ . In the present study, the prevalence of HDL-C < 40 mg/dL was only 1.0 %, but the value of the lowest 5th percentile of HDL-C was consistent with the finding by Okada et al<sup>23)</sup>. The finding that students in the lowest quartile of HDL-C showed increased prevalence of abdominal obesity, hypertriglyceridemia, and increased FPG compared with the highest quartile was not surprising because HDL-C and other cardiometabolic risk factors are the components of metabolic syndrome<sup>22)</sup>.

## **B** HDL-C and lifestyle habits

It is generally recognized that increased physical activity, cessation of smoking, weight loss, moderate alcohol intake, a diet rich in omega-3 polyunsaturated fatty acids, and a diet low in carbohydrates are strategies for HDL-C elevation and that drugs that raise the HDL-C level as the principal pharmacodynamic effect do not exist<sup>30)</sup>. In addition, a frequent Japanese-style diet, which is characterized by adequate total calories, increased intake of fish and plant foods, and decreased intake of carbohydrates and animal fat, has been shown to cause an elevation of HDL-C level<sup>31)</sup>. A previous study in the Japanese population of fourth-grade elementary school children demonstrated that compared with normal-fat group, high-fat children were less physically active and consumed a larger amount of food, which was associated with decreased HDL-C level<sup>19)</sup>. In contrast, a recent observation revealed no change in HDL-C level after dietary treatment combined with exercise treatment in obese Japanese children aged 10.1 years old despite marked improvement of visceral fat and other cardiometabolic risk factors, such as TG, TC, and uric acid, and liver dysfunction<sup>20)</sup>. The discrepancies in the results might be due to the differences in the study design, including the subjects and intensity and duration of exercise. In the present study, the ratios of the students who were often commuting to and from school by car, did not like exercise, did not do sports outside of school, and watched TV during meals were significantly higher in the lowest quartile of HDL-C level compared with the highest quartile in both genders. It was of particular interest that in the lowest quartile of HDL-C level, the prevalence of students who were often commuting to and from school by car was significantly higher, and of those who liked exercise was lower, in girls than in boys, despite an almost identical mean HDL-C level. In contrast, no significant relationship of other dietary patterns or habits to HDL-C level was found among the school children. These findings were in accordance with a recent observation by Yoshinaga, et al. that lifestyle conditions, such as participation in school-based extracurricular physical activities and TV-watching time, were inversely correlated with HDL-C level in Japanese healthy adolescent high school students aged 15 to 18 years<sup>32)</sup>, suggesting that a lower HDL-C level is associated with reduced daily physical activity among school children. Aerobic exercise has been reported to elevate HDL-C level by 5-10 %. Although its precise mechanism is unclear, increased activity of muscle lipoprotein lipase has been suggested as one of the possible contributing factors<sup>33)</sup>.

## **C** Limitations and Implications

There were several limitations in the present study. First, because this is a cross-sectional study, it remains unknown whether children with lower HDL-C level may show changes in lipid profiles following lifestyle modifications or develop future CV disease if they did not do so. To establish the exact prognostic significance of HDL-C in the development of CV events among children, further longer follow-up studies are required. Second, the questionnaire was very simple and contained only 12 items concerning lifestyle patterns. Furthermore, the association between HDL-C and lifestyle habits was not adjusted for confounding factors, such as the magnitude of physical activity, in the present study; such factors might influence the relationship, resulting in overestimation or underestimation in the results. Therefore, a more detailed analysis after adjustment by using multivariate analysis or stratified analysis is necessary for precise assessment. Third, it has been reported that lower HDL-C levels are accompanied by several conditions other than reduced daily physical activity in children, such as exposure to environmental tobacco smoke<sup>34)</sup> and maternal smoking in pregnancy<sup>35)</sup>. In addition, several investigators have observed that children born small who are associated with postnatal rapid weight gain have increased LDL-C, LDL-C/HDL-C ratio, and insulin resistance and decreased HDL-C compared with control subjects and that the unfavorable lipid profiles might track through adolescence<sup>36)-38</sup>. Thus, attention should be focused on not only physical activity but also the relationship between the lipid profiles and the birth weight as well as the catch-up increase in weight early in life. Fourth, although central adiposity as measured by WC has been associated with cardiometabolic risk factors as well as fasting insulin level, independent of body mass index39,40, and measurement of WC and POW is easily performed in children, whether WC and POW or HDL-C level measurement might be better for identifying children at more risk metabolically and predicting future CV disease remains to be elucidated. Finally, it would be expected that the prevalence of obesity and other cardiometabolic risk factors substantially varies in the different regions of Japan. Thus, a nation-wide prospective survey is required to verify the present findings of an association of lower HDL-C level with lifestyle habits in the entire Japanese population of school children.

It is important to recognize predictors of risk of future atherosclerotic CV diseases for early detection and more effective preventive measures in individual children and adolescents. The results of the present study indicate that HDL-C level is associated with daily physical activity among school children. First of all, it is important to offer educational opportunities that show the relationship between lifestyle pattern, such as reduced daily physical activity, and unfavorable lipid profiles among junior high school students, particularly in girls, because there was a significant difference in the prevalence of students who were often commuting to and from school by car and who liked exercise between both genders in the lowest quartile of HDL-C level. Children and adolescents with lower HDL-C level can be considered as a special target group for implementation of a family-based repeated lifestyle intervention, especially increased daily physical activity.

## V Acknowledgments

This study was supported by grants from the Ministry of Welfare and Labor in Japan 2009–2013 (Nos. 21500650 and 24500813), the Special Research Fund of the Vice-chancellor of Shinshu University 2010–2013, the Japanase Society of Child Health 2009, and the Advanced Preventive Medical Center, Shinshu University Hospital 2009–2013. We thank

all other members of the Study Project on Prevention of Metabolic Syndrome among Children, Adolescents, and Young Adults in Shinshu for their valuable suggestions and assistance.

# VI Conflicts of Interest

The authors declare no potential conflicts of interest.

#### References

- Gordon DJ, Probstfield JL, Garrison RJ, Neaton JD, Castelli WP, Knoke JD, Jacobs DR Jr, Bangdiwala S, Tyroler HA: High-density lipoprotein cholesterol and cardiovascular disease: Four prospective American studies. Circulation 79: 8-15, 1989
- 2) Weverling-Rijnsburger AWE, Jonkers IJAM, van Exel E, Gussekloo J, Westendorp RGJ: High-density vs lowdensity lipoprotein cholesterol as the risk factor for coronary artery disease and stroke in old age. Arch Intern Med 163: 1549-1554, 2003
- 3) Kitamura A, Iso H, Naito Y, Iida M, Konishi M, Folsom AR, Sato S, Kiyama M, Shimamoto T, Komachi Y : Highdensity lipoprotein cholesterol and premature coronary heart disease in urban Japanese men. Circulation 89 : 2533– 2539, 1994
- 4) Okamura T, Hayakawa T, Kadowaki T, Kita Y, Okayama A, Ueshima H, the NIPPON DATA90 Research Group: The inverse relationship between serum high-density lipoprotein cholesterol level and all-cause mortality in a 9.6-year follow-up study in the Japanese general population. Atherosclerosis 184: 143-150, 2006
- 5) Satoh H, Tomita K, Fujii S, Kishi R, Tsutsui H: Lower high-density lipoprotein cholesterol is a significant and independent risk for coronary artery disease in Japanese men. J Atheroscler Thromb 16: 792-798, 2009
- 6) McGill HC Jr, McMahan CA, Malcolm GT, Oalmann MC, Strong JP: Effects of serum lipoproteins and smoking on atherosclerosis in young men and women: Pathobiological determinants of atherosclerosis in youth. Arterioscler Thromb Vasc Biol 17: 95-106, 1997
- 7) McGill HC Jr, McMahan CA, Zieske AW, Malcolm GT, Tracy RE, Strong JP, for the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group : Effects of nonlipid risk factors on atherosclerosis in youth with a favorable lipoprotein profile. Circulation 103 : 1546–1550, 2001
- 8) Newman WP III, Freedman DS, Voors AW, Gard PD, Srinivasan SR, Cresanta JL, Williamson GD, Webber LS, Berenson GS: Relation of serum lipoprotein levels and systolic blood pressure to early atherosclerosis: The Bogalusa Heart Study. N Engl J Med 314: 138-144, 1986
- 9) Berenson GS, Srinivasan SR, Bao W, Newman WP III, Tracy RE, Wattigney WA, for the Bogalusa Heart Study: Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. N Engl J Med 338: 1650-1656, 1998
- 10) Davis PH, Dawson JD, Riley WA, Lauer RM: Carotid intimal-medial thickness is related to cardiovascular risk factors measured from childhood through middle age: The Muscatine Study. Circulation 104: 2815-2819, 2001
- Raitakari OT, Juonala M, Kähönen M, Taittonen L, Laitnen T, Mäki-Torkko N, Järvisalo MJ, Uhari M, Jokinen E, Rönnemaa T, Åkerblom HK, Viikari JSA : Cardiovascular risk factors in childhood and carotid intima-media thickness in adulthood : The Cardiovascular Risk in Young Finns Study. JAMA 290 : 2277-2283, 2003
- 12) McGill HC Jr, McMahan CA, Gidding SS: Preventing heart disease in the 21st century: Implications of the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Study. Circulation 117: 1216-1227, 2008

## Hongo·Hidaka·Sakaguchi et al.

- Daniels SR, Greer FR, the Committee on Nutrition: Lipid screening and cardiovascular health in childhood. Pediatrics 122: 198-208, 2008
- 14) Steinberger J, Daniels SR, Eckel RH, Hayman L, Lustig RH, McCrindle B, Mietus-Snyder ML: Progress and challenges in metabolic syndrome in children and adolescents. Circulation 119: 628-647, 2009
- 15) Azegami M, Hongo M, Yazaki Y, Yanagisawa S, Yamazaki A, Imamura H: Seasonal diffrence in onset of coronary heart disease in young Japanese patients: A comparison with older patients. Circ J 69: 1176-1179, 2005
- 16) Azegami M, Hongo M, Yanagisawa S, Yamazaki A, Sakaguchi K, Yazaki Y, Imamura H: Characteristics of metabolic and lifestyle risk factors in young Japanese patients with coronary heart disease: A comparison with older patients. Int Heart J 47: 343-350, 2006
- 17) Hongo M, Hidaka H, Sakaguchi S, Nakanishi K, Ichikawa M, Hirota N, Tanaka N, Tsuruta G, Yazaki Y, Kinoshita O, Ikeda U, Koike, K, on behalf of the Investigators of Study Project on Prevention of Metabolic Syndrome among Children, Adolescents, and Young Adults in Shinshu: Association between serum uric acid levels and cardiometabolic risk factors among Japanese junior high school students. Circ J 74: 1570-1577, 2010
- 18) Tsuruta G, Tanaka N, Hongo M, Komatsu M, Horiuchi A, Hamamoto K, Iguchi C, Nakayama Y, Umemura T, Ichijo T, Matsumoto A, Yoshizawa K, Aoyama T, Tanaka E: Nonalcoholic fatty liver disease in Japanese junior high school students: Its prevalence and relationship to lifestyle habits. J Gastroenterol 45: 666-672, 2010
- 19) Washino K, Takada H, Nagashima M, Iwata H: Significance of the atherosclerogenic index and body fat in children as markers for future, potential coronary heart disease. Pediatr Int 41: 260-265, 1999
- 20) Togashi K, Masuda H, Iguchi K : Effect of diet and exercise treatment for obese Japanese children on abdominal fat distribution. Res Sports Med 18 : 62–70, 2010
- 21) Kashiwagi A, Kasuga M, Araki E, Oka Y, Hanafusa T, Ito H, Tominaga M, Oikawa S, Noda M, Kawamura T, Sanke T, Namba M, Hashiramoto M, Sasahara T, Nishio Y, Kuwa K, Ueki K, Takei I, Umemoto M, Murakami M, Yamakado M, Yatomi Y, Hatsumi Ohashi H, Committee on the Standardization of Diabetes Mellitus-Related Laboratory Testing of Japan Diabetes Society : International clinical harmonization of glycated hemoglobin in Japan : From Japan Diabetes Society to National Glycohemoglobin Standardization Program values. Diabetol Int 3: 8-10, 2012
- Ozeki T, Satake E: Diagnostic criteria for metabolic syndrome and visceral adiposity in children. Adiposcience
  4: 359-364, 2007 (in Japanese)
- 23) Okada T, Murata M, Yamauchi K, Harada K: New criteria of normal serum lipid levels in Japanese children: the nationwide survey. Pediatr Int 44: 596-601, 2002
- 24) The Japanese Society of Hypertension : Guidelines for the management of hypertension JSH2009. pp 83-86, 2009 (in Japanese)
- 25) Natarajan P, Ray KK, Cannon CP: High-density lipoprotein and coronary heart disease. J Am Coll Cardiol 55: 1283-1299, 2010
- 26) Gordon DJ, Castelli WP, Hjortland MC, Kannel WB, Dawber TR : High density lipoprotein as a protective factor against coronary heart disease : The Framingham Study. Am J Med 62 : 707-714, 1977
- 27) Iso H: Changes in coronary heart disease risk among Japanese. Circulation 118: 2725-2729, 2008
- 28) Murata M: Secular trends in growth and changes in eating patterns of Japanese children. Am J Clin Nutr 72 (suppl): 1379S-1383S, 2000
- 29) Kouda K, Nakamura H, Nishio N, Fujita Y, Takeuchi H, Iki M : Trends in body mass index, blood pressure, and serum lipids in Japanese children : Iwata population-based annual screening (1993-2008). J Epidemiol 20 : 212-218, 2010
- 30) Can AS, Uysal C, Palaoĝlu KE: Short term effects of a low-carbohydrate diet in overweight and obese subjects with low HDL-C levels. BMC Endocr Disord 10: 18, 2010

# HDL-C and lifestyle habits

- 31) Hata Y, Nakajima K: Life-style and serum lipids and lipoproteins. J Atheroscler Thromb 7: 177-197, 2000
- 32) Yoshinaga M, Hatake S, Tachikawa T, Shinomiya M, Miyazaki A, Takahashi H: Impact of lifestyles of adolescents and their parents on cardiovascular risk factors in adolescents. J Atheroscler Thromb 18: 981-990, 2011
- 33) Thompson PD: What do muscles have to do with lipoproteins? Circulation 81: 1428-1430, 1990
- 34) Hirata K, Yamano Y, Suzuki H, Miyagawa S, Nakadate T : Passive smoking is associated with lower serum HDL-C levels in school children. Pediatr Int 52 : 252–256, 2010
- 35) Ayer JG, Belousova E, Harmer JA, David C, Marks GB, Celermajer DSC: Maternal cigarette smoking is associated with reduced high-density lipoprotein cholesterol in healthy 8-year-old children. Eur Heart J 32: 2446-2453, 2011
- 36) Fabricus-Bjerre S, Jensen RB, Faerch K, Larsen T, Molgaard C, Michaelsen KM, Vaag A, Greisen G : Impact of birth weight and early infant weight gain on insulin resistance and associated cardiovascular risk factors in adolescence. PLos One 6 : e20595, 2011
- 37) Efstathiou SP, Skeva II, Zorbala E, Georgiou E, Mountokalakis TD: Metabolic syndrome in adolescence: Can it be predicted from natal and parental profile? The Prediction of Metabolic Syndrome in Adolescence (PREMA) Study. Circulation 125: 902-910, 2012
- 38) Nadeau KJ, Maahs DM, Daniels SR, Eckel RH: Childhood obesity and cardiovascular disease: links and prevention strategies. Nat Rev Cardiol 8: 513-525, 2011
- 39) Maffeis C, Pietrobelli A, Grezzani A, Provera S, Tatò L: Waist circumference and cardiovascular risk factors in prepubertal children. Obes Res 9: 179-187, 2001
- 40) Lee S, Bacha F, Gungor N, Arslanian SA: Waist circumference is an independent predictor of insulin resistance in black and white youths. J Pediatr 148: 188-194, 2006

(2013. 1. 8 received; 2013. 4. 11 accepted)