

The Levels of Serum Low-Density Lipoprotein Cholesterol Using Direct Measurement in Healthy Japanese School Children

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Abstract This study aimed to investigate the levels of serum low-density lipoprotein cholesterol (LDLC) using direct measurement in healthy Japanese school children. The subjects were 621 children (325 boys and 296 girls) aged 9 to 10 in the 4th grade, and 688 children (334 boys and 354 girls) aged 12 to 13 in the 7th grade. The levels of serum LDLC and high-density lipoprotein cholesterol were measured by direct determination (Cholestest LDL and Cholestest NHDL; Daiichi Pure Chemicals Co., Ltd., Tokyo, Japan). In boys in the 4th grade, the mean, the 75th, the 90th and the 95th percentiles of LDLC levels (mg/dl) were 91.6, 104, 124 and 134, respectively. In girls in the 4th grade, they were 92.8, 108, 122 and 130. In boys in the 7th grade, they were 83.4, 96, 113 and 123. In girls in the 7th grade, they were 93.0, 106, 126 and 137. Serum LDLC levels in boys in the 7th grade were lower than those of other groups. The direct measurement of serum LDLC level is useful for evaluation of dyslipidemia in healthy school children, because the method is applicable to non-fasting serum.

Key words: children, low-density lipoprotein cholesterol, lipids

Introduction

Serum low-density lipoprotein cholesterol (LDLC) level is one of the most important risk factors of coronary heart disease, and also in childhood, hypercholesterolemia is closely related with atherosclerotic change (1, 2). Only through

examinations can we discover the children with dyslipidemia. Therefore Japanese school children should have an examination of their serum lipids and the children with dyslipidemia should be counseled on how to improve their lifestyle.

Coronary heart disease has a closer correlation with serum LDLC levels than serum total cholesterol levels. Formerly, the Friedewald formula (3) has been used to evaluate serum LDLC level, and fasting serum triglyceride level is needed for this formula. It is difficult to evaluate the serum LDLC levels of school children and outpatients using the Friedewald formula, because they are usually in a non-fasting state.

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Recently some assays for direct determination of serum LDLC level have been developed. Cholestest LDL (Daiichi Pure Chemicals Co., Ltd., Tokyo, Japan) is a kit which can directly measure the serum LDLC by a new homogeneous method based on innovative detergent technology. LDLC level measured by this kit shows a close correlation with that obtained by an ultra-centrifugation method (4). Direct measurement of the serum LDLC level can be used for the non-fasting serum samples (5).

In a previous report (6), the serum LDLC level was calculated using the Friedewald formula in Japanese children, and it was stated that the LDLC cut-off values were 110 mg/dl for the borderline range and 140 mg/dl for the high range.

The levels of serum LDLC using a direct method in healthy Japanese school children have not been reported. The aim of this study was to measure the serum LDLC and high-density lipoprotein cholesterol (HDL) using a direct method in healthy Japanese school children, and to compare the values determined here with those of previous values determined by the Friedewald formula in Japanese children.

Subjects

The study subjects consisted of 621 children (325 boys and 296 girls) aged 9 to 10 in the 4th grade, and 688 children (334 boys and 354 girls) aged 12 to 13 in the 7th grade. All subjects received medical check-ups under the program entitled "The Prevention of Cardio-and Cerebrovascular Diseases in Childhood" during 1997–2002. The Department of Pediatrics, Niigata University School of Medicine and the School Health Division of the local governments in Niigata Prefecture undertake this program each year. In this program, anthropometric data and blood tests were taken for all subjects. None had diabetes, endocrine disorders, hereditary diseases, systemic diseases and systemic inflammatory diseases. All were non-smokers without regular medication.

Data Collection, Assays and Analysis

All blood samples were obtained from the antecubital vein of the subjects and were centrifuged at 3000 rpm for 10 min. The serum was frozen and stored at -20°C until analysis. Serum LDLC levels and HDL levels were measured by direct methods (Cholestest LDL and Cholestest HDL; Daiichi Pure Chemicals Co., Ltd., Tokyo, Japan) (4, 5). Serum LDLC and HDL levels were expressed by age group in boys and girls. All statistical analyses were performed using the Stat View program for Windows (version 5.0; Abacus Concepts, Berkeley, USA). The unpaired t-test was used to compare values of the two groups. Data are expressed as the means and standard deviations and values of $p < 0.05$ were considered as statistically significant.

Results

Table 1 lists the means, standard deviations and percentiles of serum LDLC and HDL levels by age group in boys and girls. The 75th percentile of serum LDLC levels was 104–108 mg/dl and the 95th percentile of serum LDLC levels was 130–137 mg/dl in the 4th grade and girls in the 7th grade. The 75th percentile of serum LDLC levels was 96 mg/dl and the 95th percentile of serum LDLC levels was 123 mg/dl in boys in the 7th grade. The fifth percentile of serum HDL levels was 40–43 mg/dl in all groups.

In boys, serum LDLC levels in the 4th grade were significantly higher than those in the 7th grade ($p < 0.0001$). In the 7th grade, serum LDLC levels in boys were significantly lower than those in girls ($p < 0.0001$). In boys, serum HDL levels in the 4th grade were significantly higher than those in the 7th grade ($p < 0.01$). In girls, serum HDL levels in the 4th grade were significantly lower than those in the 7th grade ($p < 0.05$). In the 4th grade, serum HDL levels in boys were significantly higher than those in girls ($p < 0.01$).

Table 1 The levels of serum low-density lipoprotein cholesterol and high-density lipoprotein cholesterol levels using direct measurement (mg/dl)

A school yr	Age (yr)	No.	Low-density lipoprotein cholesterol (mg/dl)			High-density lipoprotein cholesterol (mg/dl)					
			Mean \pm SD	Percentiles			Mean \pm SD	Percentiles			
				75	90	95		25	10	5	
Boys	The 4th grade	9~10	325	91.6 \pm 24.4*	104	124	134	65.0 \pm 14.2 [‡] ^β	55	46	43
	The 7th grade	12~13	334	83.4 \pm 21.5 [§]	96	113	123	61.9 \pm 12.5	53	46	43
Girls	The 4th grade	9~10	296	92.8 \pm 22.8	108	122	130	61.4 \pm 13.0 [¶]	52	44	40
	The 7th grade	12~13	354	93.0 \pm 24.3	106	126	137	63.5 \pm 12.1	56	48	43

*: p < 0.0001 vs boys in the 7th grade. ‡: p < 0.01 vs boys in the 7th grade. §: p < 0.0001 vs girls in the 7th grade. ¶: p < 0.05 vs girls in the 7th grade. β: p < 0.01 vs girls in the 4th grade.

Table 2 Serum low-density lipoprotein cholesterol levels (mg/dl) by the Friedewald formula and serum high-density lipoprotein cholesterol levels (mg/dl) in Japanese children (Okada *et al.* *Pediatr Int* 2002; 44)

Age (yr)	Low-density lipoprotein cholesterol (mg/dl)					High-density lipoprotein cholesterol (mg/dl)					
	No.	Percentiles				No.	Percentiles				
		50	75	90	95		50	25	10	5	
Boys	10	2627	96.2	113.2	132.0	143.1	3491	62	54	47	43
	13	3209	88.8	101.8	118.5	130.7	2617	61	53	46	42
Girls	10	2233	97.4	114.9	132.9	141.7	3125	61	53	46	42
	13	3127	92.5	108.8	125.9	135.9	2563	63	55	48	45

Discussion

Serum LDLC levels in boys in the 7th grade tended to be lower than those of other groups. This trend of lower levels of serum LDLC in adolescent boys was also observed in a previous nationwide report of Japanese children (6).

Table 2 shows the percentiles of serum LDLC and HDLC levels by each age group in boys and girls from the nationwide study according to Okada *et al.* (6). HDLC levels in our study are similar to their data. Compared to the fasting serum LDLC levels calculated using the Friedewald formula by Okada *et al.*, the non-fasting serum LDLC levels in our study tended to be lower in both the 4th grade children and 7th grade boys. The discrepancy of serum LDLC levels might be caused by the lower

number of samples in our study or by the limited geographical area where our study was undertaken. Matthias *et al.* reported an evaluation of the analytical and clinical performance of two homogeneous LDLC assays (direct determination of serum LDLC level) and the Friedewald formula, and those assays correlated highly with the ultracentrifugation-dextran sulfate-Mg²⁺ method (4, 5). On the other hand, in a few previous reports (7, 8) direct LDLC assays demonstrated limited utility in children. The discrepancy of serum LDLC levels might also be due to a difference of method to determine serum LDLC level in each study. A further examination about the direct determination of serum LDLC level in Japanese children is necessary.

The measurement of triglyceride levels in the

fasting state is important for evaluating dyslipidemia, but it is difficult to obtain fasting serum samples in healthy children in a school-based study. The direct measurement of serum LDLC level is applicable to non-fasting serum and is useful for the school-based study. The National Cholesterol Education Program Working Group on Lipoprotein Measurement recommended direct methods for determination of LDLC because of the limitations of the Friedewald formula (9). The direct measurement of serum LDLC level is a reliable and practicable method, and it will be useful for the evaluation of dyslipidemia in healthy school children.

Conclusion

We measured the levels of serum LDLC and HDLC using direct methods in healthy Japanese school children. The levels of serum LDLC varied depending on age and sex, and those in boys in the 7th grade were lower than those in other groups. The direct measurement of serum LDLC level is useful for the evaluation of dyslipidemia in healthy school children, because the method is applicable to non-fasting serum.

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