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Changes in Cardiovascular Risk Factors over a 24-Year Follow-Up Period: A Japanese Pediatric Cohort Study

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ABSTRACT

This study examined changes in body mass index (BMI), fasting blood sugar (FBS), total cholesterol (TC) and HDL-cholesterol (HDL-C) levels over a 24-year follow-up period in a pediatric cohort. An appropriate starting age for intervention to prevent cardiovascular diseases is still unclear. The subjects were 655 children, aged 10-12. A follow-up survey was conducted when the subjects reached ages 13-15, 16-18, and 35-45, respectively, and height, weight, and blood tests including FBS, TC and HDL-C were examined. Forty (6%) of these subjects participated. BMI at ages 35-45 were significantly higher than those at ages 10-12 ($p < 0.0001$), 13-15 ($p < 0.001$), and 16-18 ($p < 0.001$). TC levels at ages 35-45 were significantly higher than at ages 10-12 ($p < 0.0001$), 13-15 ($p < 0.0001$), and 16-18 ($p < 0.0001$). BMI at the end of the follow-up (ages 35-45) had a significant correlation with BMI at ages 13-15 ($R = 0.38$, $p = 0.041$) and 16-18 ($R = 0.41$, $p = 0.049$). TC and HDL-C values at the end of the follow-up had a significant correlation with those at ages 10-12 ($R = 0.55$, $p = 0.0004$; $R = 0.55$, $p = 0.016$), 13-15 ($R = 0.35$, $p = 0.045$; $R = 0.42$, $p = 0.015$), and 16-18 ($R = 0.47$, $p = 0.019$; $R = 0.44$, $p = 0.028$). These results may suggest that intervention for children in Japan with cardiovascular risk factors should be initiated in the early years of life.

Key words: *Asa Cohort Study, Cardiovascular risk factor, Follow-up study, BMI*

Epidemiological studies have demonstrated that the atherosclerotic process begins in childhood and that individual cardiovascular risk factors, such as obesity, hypertension, hyperglycemia, and dyslipidemia, tend to persist over time from childhood to adulthood[1,2]. For example, in the case of obesity, although Whitaker et al[15] reported that the risk of childhood obesity progressing to adult obesity rises markedly after the age of 10, there are no clear answers to questions such as when intervention should be initiated to prevent cardiovascular diseases. To answer these questions, it is necessary to understand the tracking tendency of cardiovascular risk factors. However, there are few reports on such factors, especially in Japanese children.

In the present study, therefore, we focused on the correlation in changes in body mass index (BMI), levels of fasting blood sugar (FBS), total cholesterol (TC) and HDL-cholesterol (HDL-C) over a 24-year follow-up period in a Japanese pediatric cohort.

MATERIALS AND METHODS

Study population

This study was conducted as part of a pediatric health promotion program--"Asa Cohort study"--initiated in 1978 in Asa, Hiroshima, Japan[7,8]. In addition to health checkups of elementary school students performed in accordance with the Japanese School Health Act (School Health and Safety Act, amended in 2008), Asa has a unique health-promotion program in place. Those who

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volunteered to take part in the program underwent blood and physical examinations.

The subjects were elementary school students aged 10-12 who agreed to participate in the study. A total of 1,407 students took part in the study's initial survey.

Examinations

A follow-up survey was conducted when the subjects reached ages 13-15 (junior high school), 16-18 (high school), and 35-45 (adults). At the time of the initial and follow-up surveys, the subjects underwent physical measurements including height and weight, and blood tests including FBS, TC and HDL-C. BMI was used as an index for obesity status. Only those who had reached the age of 35-45 by the end of the 24-year follow-up period, and who had taken part in the follow-up examinations, were included in the present study.

Statistical analysis

The ratio of the follow-up values compared to the base line data (ages 10-12), and data at ages 13-15 and 16-18, were examined for each test variable. A paired t-test and Spearman's correlation coefficient were used to evaluate any correlation between these values. Statistical analyses were made using JMP software (SAS Institute, Cary, NC, USA). $p < 0.05$ was settled as statistically significant.

Ethics

Informed consent was obtained from the subjects and their parents. This study was approved by the Ethics Committee of the Hiroshima Asa Medical Association.

RESULTS

Follow-up

The number of subjects who would reach the age of 35-45 by the end of the follow-up period was 655 (male/female: 301/354). Forty (6%) of these subjects participated in the examinations during the 24-year follow-up period. Relocation was the major reason that children were lost from follow-up. There were no statistical differences in baseline values between those available for follow-up and those lost from follow-up for factors including BMI, FBS, TC, and HDL-C (Table 1).

Table 2 shows values measured for each age group. BMI increased gradually as age increased. BMI at ages 35-45 was significantly higher than at ages 10-12 ($p < 0.0001$), 13-15 ($p < 0.001$), and 16-18 ($p < 0.001$), respectively. TC also increased gradually as age increased. TC at ages 35-45 was significantly higher than at ages 10-12 ($p < 0.0001$), 13-15 ($p < 0.0001$), and 16-18 ($p < 0.0001$), respectively. On the other hand, FBS and HDL-C showed no significant changes across the age groups.

Table 1. BMI, FBS, TC, and HDL-C in follow-up and control groups (mean ± standard deviation)

	Follow-up group (n=40)	Control group (n=615)	p value
BMI (kg/m^2)	17.4 ± 2.9	17.9 ± 2.8	0.275
FBS (mg/dl)	91.2 ± 7.3	92.4 ± 10.3	0.469
TC (mg/dl)	172.7 ± 31.7	178.7 ± 29.5	0.215
HDL-C (mg/dl)	61.5 ± 11.4	62.7 ± 15.6	0.633

BMI: body mass index, FBS: fasting blood sugar,
TC: total cholesterol, HDL-C: HDL-cholesterol

Correlation analysis

BMI at the end of the follow-up (ages 35-45) significantly correlated with BMI at ages 13-15 ($R = 0.38$, $p = 0.041$) and 16-18 ($R = 0.41$, $p =0.049$) (Fig. 1). BMI at ages 35-45, however, had no significant correlation with BMI at ages 10-12 ($R = 0.34$, $p = 0.15$).

TC and HDL-C levels at the end of the follow-up had a significant correlation with those at ages10-12 ($R = 0.55$, $p = 0.0004$; $R = 0.55$, $p = 0.016$), 13-15 ($R = 0.35$, $p = 0.045$; $R = 0.42$, $p = 0.015$), 16-18 ($R = 0.47$, $p = 0.019$; $R = 0.44$, $p = 0.028$), respectively (Fig. 2, 3).

The FBS level at the end of the follow-up was not significantly correlated with the levels observed at ages 10-12 ($R = 0.18$, $p = 0.28$), 13-15 ($R = 0.31$, $p = 0.077$) or 16-18 ($R = 0.18$, $p = 0.39$) (Fig. 4).

Table 2. Values measured at ages 10-12, 13-15, 16-18, and 35-45 (mean ± standard deviation)

	Ages			
	10-12	13-15	16-18	35-45
BMI (kg/m^2)	17.4 ± 2.9*	20.1 ± 3.0**	20.6 ± 2.0**	22.9 ± 3.4
FBS (mg/dl)	91.2 ± 7.3	94.4 ± 6.6	92.7 ± 14.2	94.5 ± 24.8
TC (mg/dl)	172.7 ± 31.7*	178.3 ± 28.4*	170.3 ± 21.8*	207.8 ± 35.3
HDL-C (mg/dl)	61.5 ± 11.4	60.5 ± 17.8	63.0 ± 12.9	61.7 ± 16.3

BMI: body mass index, FBS: fasting blood sugar, TC: total cholesterol,
HDL-C: HDL-cholesterol.

*$p < 0.0001$ compared with ages 35-45 by paired t-test
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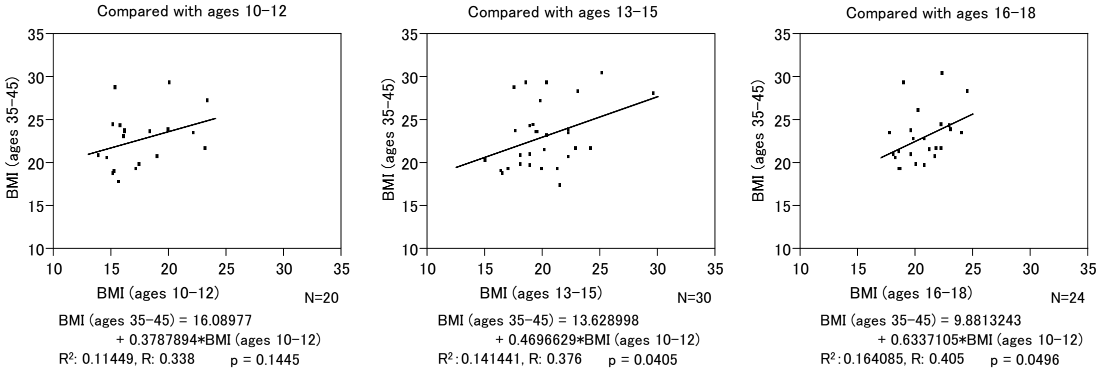

Fig. 1. Correlation of body mass index (BMI) between ages 35-45 and ages 10-12, 13-15, and 16-18.

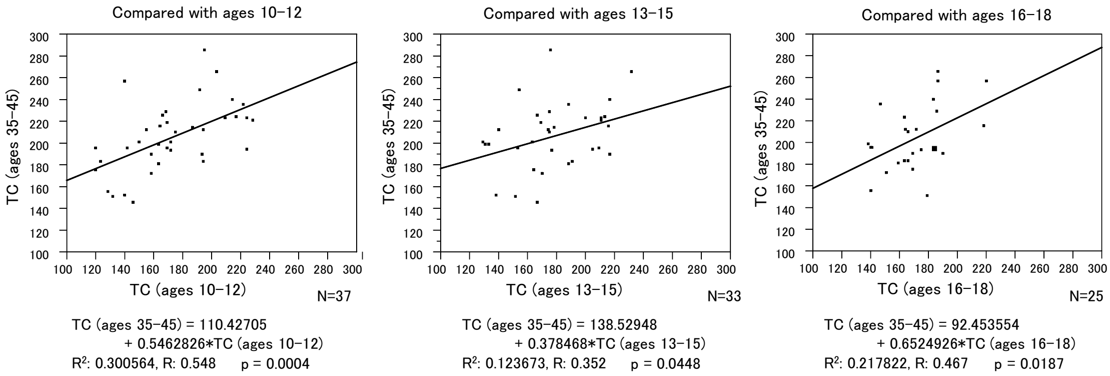

Fig. 2. Correlation of total cholesterol (TC) between ages 35-45 and ages 10-12, 13-15, and 16-18.

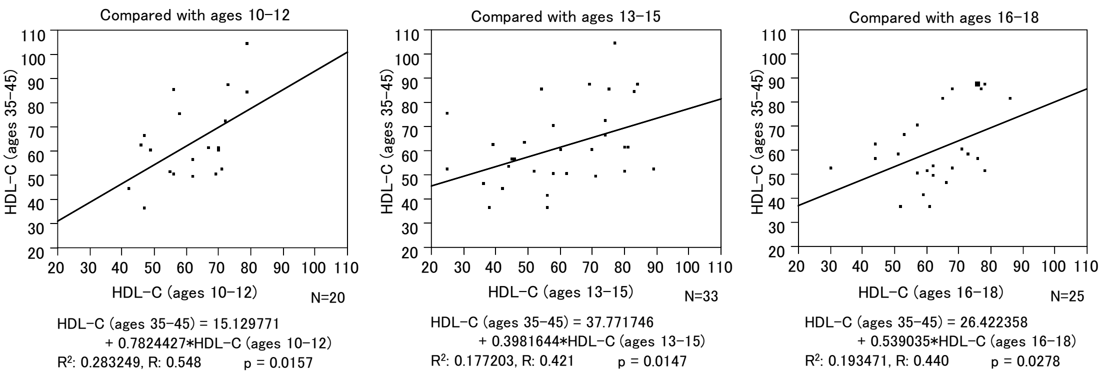

Fig. 3. Correlation of HDL-cholesterol (HDL-C) between ages 35-45 and ages 10-12, 13-15, and 16-18.

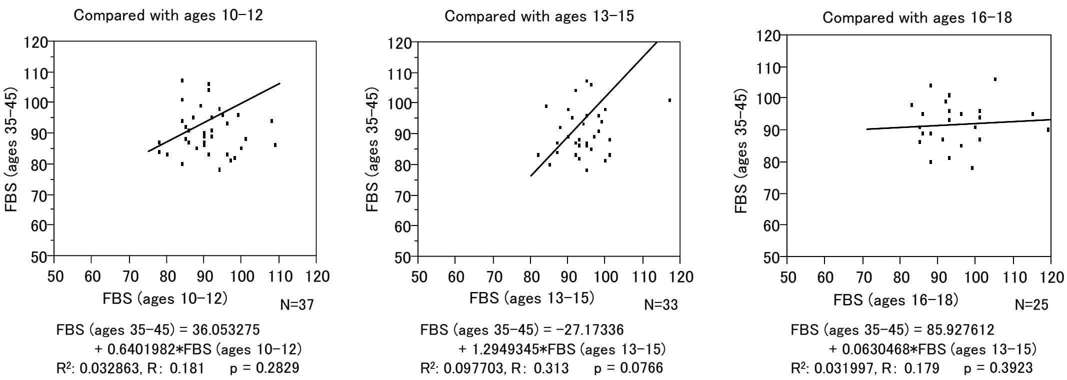

Fig. 4. Correlation of fasting blood sugar (FBS) between ages 35-45 and ages 10-12, 13-15, and 16-18.

DISCUSSION

In the present study, we demonstrated that TC and HDL-C levels in adulthood have moderate correlations with those in childhood and adolescence, and that BMIs in adulthood and adolescence are moderately correlated. These results may suggest that health education should be provided during childhood, and that intervention in Japanese children with cardiovascular risk factors should be initiated early on in life.

There are several reports in pediatric cohort studies from western countries on changes in cardiovascular risk factors. For example, the Bogalusa Heart Study[1)] showed that the correlation coefficients over 12 years were 0.42-0.66 for TC and 0.29-0.43 for HDL-C; and over 15 years they were 0.43-0.74 for BMI, 0.35-0.69 for TC, 0.17-0.61 for HDL-C, 0.38-0.43 for systolic BP, and 0.21-0.29 for diastolic BP. The Young Finns Study[11)] reported that correlation coefficients over 6 years were 0.65-0.73 for TC and 0.66-0.76 for HDL-C; and over 12 years, they were 0.48-0.58 for TC and 0.53-0.58 for HDL-C. Laskarzewski et al[9)] reported that the correlation coefficients over 4 years were 0.68 for TC and 0.53 for HDL-C. On the other hand, only one pediatric cohort study on this issue was conducted in Japan. The study by Tan et al[14)] demonstrated that correlation coefficients over 4 years were 0.62 for TC, and 0.66 for HDL-C. In our study, correlation coefficients over 24 years were 0.55 for both TC and HDL-C. Although the observation period in our study was longer compared with previous studies, the values were similar to those in previous reports. TC and HDL-C levels in adulthood may be moderately associated with those in childhood. These findings suggest that health education on the prevention of dyslipidemia should be conducted during childhood, and that intervention should be initiated in these early years of life to prevent cardiovascular diseases.

It is generally believed that obese children will become obese adults, with reports demonstrating that the greater the age at which a child becomes obese, the greater the link to adult obesity[3,5,10)]. It has been reported that the risk of child obesity progressing to adult obesity increases significantly after the age of 10[9)]. Our data support the idea that obese children will go on to become obese adults. BMI at ages 35-45 was correlated with BMI at ages 13-15. In Finland, an intervention study was conducted in which the intake of lipids was restricted, beginning at 7 months after birth. Results of this study demonstrated a significant difference in the incidence of obesity between the control and intervention groups after the age of 8 [4,12)]. Such findings suggest that health education and intervention to prevent obesity should be initiated in childhood. Indeed, a Japanese study[6)] has shown that dyslipidemia is reversed in children who recover from obesity.

It has been reported that the frequency of obesity gradually increases from ages 10-14, reaching a peak during junior high school and then decreasing during the high school period[13)]. However, we did not find such a tendency. BMI increased gradually as age increased. Earlier reports of decreasing BMI during the high school period were published before 2000. The trend might have changed since that time. To confirm this, a cohort study with a large number of subjects should be conducted.

One of the limitations of the current study is a reduced follow-up rate. Since Asa is a suburban area, many subjects have relocated during the 24-year follow-up period. In addition to this, we focused on changes in cardiovascular risk factors between childhood and the age of 35-45, and subjects whose age was below 35 during the follow-up were not enrolled in the present study. Therefore, only a limited number of subjects were included.

The second limitation is that we evaluated subjects from only one area in Japan. However, anthropometric and blood examination values in the present study were similar to the mean values obtained from nationwide statistics on the Japanese population.

In conclusion, we demonstrated that TC and HDL-C levels in adulthood have moderate correlations with those in childhood and adolescence, and that BMI in adulthood and adolescence are moderately correlated. The results of this Asa Cohort Study may suggest the importance of programs aimed at reducing cardiovascular risk factors in Japanese children. Further studies are needed to clarify what intervention methods would be useful in preventing cardiovascular risk factors in Japanese school children.

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REFERENCES

1. **Berenson, G.S., Srinivasan, S.R., Bao, W., Newman, W.P., 3rd, Tracy, R.E. and Wattigney, W.A.** 1998. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study. N. Engl. J. Med.

338: 1650-1656.

2. **Berenson, G.S., Wattigney, W.A., Bao, W., Srinivasan, S.R. and Radhakrishnamurthy, B.** 1995. Rationale to study the early natural history of heart disease: the Bogalusa Heart Study. Am. J. Med. Sci. **310 Suppl 1:** S22-28.
3. **Gunnell, D.J., Frankel, S.J., Nanchahal, K., Peters, T.J. and Davey Smith, G.** 1998. Childhood obesity and adult cardiovascular mortality: a 57-y follow-up study based on the Boyd Orr cohort. Am. J. Clin. Nutr. **67:** 1111-1118.
4. **Hakanen, M., Lagström, H., Kaitosaari, T., Niinikoski, H., Näntö-Salonen, K., Jokinen, E., Sillanmäki, L., Viikari, J., Rönnemaa, T. and Simell, O.** 2006. Development of overweight in an atherosclerosis prevention trial starting in early childhood. The STRIP study. Int. J. Obes. (Lond). **30:** 618-626.
5. **Juonala, M., Magnussen, C.G., Berenson, G.S., Venn, A., Burns, T.L., Sabin, M.A., Srinivasan, S.R., Daniels, S.R., Davis, P.H., Chen, W., Sun, C., Cheung, M., Viikari, J.S., Dwyer, T. and Raitakari, O.T.** 2011. Childhood adiposity, adult adiposity, and cardiovascular risk factors. N. Engl. J. Med. **365:** 1876-1885.
6. **Kouda, K., Fujita, Y., Nakamura, H., Takeuchi, H. and Iki, M.** 2011. Effect of recovery from obesity on cardiovascular risk factors among Japanese schoolchildren: the Iwata population-based follow-up study. J. Epidemiol. **21:** 370-375.
7. **Kuwabara, M. and Shohoji, T.** 1987. Contact between school health and community medicine –Prediction and early detection of juvenile diseases associated with aging. p.113-128. *In* E.K. Harris and T. Yasaka (eds.), Maintaining a Healthy State within the Individual. Elsevier Science Publishers, BV.
8. **Kuwabara, M., Shohoji, T. and Sumiya, T.** 1992. School health care for detecting early juvenile diseases associated with aging. Health Systems-the challenge of change. p.422-425. *In* M.K. Chytil, G. Duru, W. Eimeren and C.D. Flagle (eds.), 5th International Conference on System Science in Health Care. Omnipress Publishing, Prague.
9. **Laskarzewski, P., Morrison, J.A., deGroot, I., Kelly, K.A., Mellies, M.J., Khoury, P. and Glueck, C.J.** 1979. Lipid and lipoprotein tracking in 108 children over a four-year period. Pediatrics **64:** 584-591.
10. **Nishimura, R., Sano, H., Matsudaira, T., Morimoto, A., Miyashita, Y., Shirasawa, T., Kokaze, A. and Tajima, N.** 2009. Changes in body mass index, leptin and adiponectin in Japanese children during a three-year follow-up period: a population-based cohort study. Cardiovasc Diabetol. **8:** 30.
11. **Porkka, K.V. and Viikari, J.S.** 1994. Should children or young adults be screened for serum lipid levels to prevent adult coronary heart disease? Experience from the Cardiovascular Risk in Young Finns study. J. Intern. Med. **236:** 115-123.
12. **Rask-Nissilä, L., Jokinen, E., Terho, P., Tammi, A., Lapinleimu, H., Rönnemaa, T., Viikari, J., Seppänen, R., Korhonen, T., Tuominen, J., Välimäki, I. and Simell, O.** 2000. Neurological development of 5-year-old children receiving a low-saturated fat, low-cholesterol diet since infancy: A randomized controlled trial. JAMA. **284:** 993-1000.
13. **Sugimori, H., Yoshida, K., Miyakawa, M., Izuno, T., Takahashi, E. and Nanri, S.** 1999. Temporal course of the development of obesity in Japanese school children: a cohort study based on the Keio Study. J. Pediatr. **134:** 749-754.
14. **Tan, F., Okamoto, M., Suyama, A. and Miyamoto, T.** 2000. Tracking of cardiovascular risk factors and a cohort study on hyperlipidemia in rural school-children in Japan. J. Epidemiol. **10:** 255-261.
15. **Whitaker, R.C., Wright, J.A., Pepe, M.S., Seidel, K.D. and Dietz, W.H.** 1997. Predicting obesity in young adulthood from childhood and parental obesity. N. Engl. J. Med. **337:** 869-873.