〈Original Article〉

Association between serum triglyceride, HDL-cholesterol, and LDL-cholesterol levels in Japanese junior high school students

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Summary This study aimed to determine the association between the different types of serum lipids in Japanese junior high school students in the Nagano prefecture. Data from 4298 students were collected over 11 years (2005–2015). TG levels were slightly increased over this study period in boys and girls. There was an inverse relationship between TG and HDL-C concentrations, with a regression line and correlation coefficient of $y = -0.1015x + 70.665$ and $r = 0.3366$ for boys and $y = -0.0909x + 72.841$ and $r = 0.2876$ for girls. Correlation analysis showed that serum TG levels of boys and girls negatively correlated with HDL-C but not LDL-C. Lipid tests for 293 students with suspected lifestyle-related diseases (186 boys and 107 girls) were performed again four months later. The TG variation value versus LDL-C and HDL-C levels was $r = 0.3663$ and $r = 0.4131$, respectively, and negatively correlated for both, $y = -0.0633x + 0.1308$ and $y = -0.1172x + 1.4476$, respectively. This study showed that the decrease in the TG level contributed to improved HDL-C and LDL-C levels in junior high school students.

Key words: Triglyceride, HDL-cholesterol, LDL-cholesterol, junior high-school students

1. Introduction

Arteriosclerosis is a significant risk factor for the development of cardiovascular and cerebrovascular disease, and it begins in childhood[1-2]. Abnormalities in serum lipid metabolism are associated with the development of arteriosclerosis, and high levels of low-density lipoprotein cholesterol (LDL-C) and low levels of high-density lipoprotein cholesterol (HDL-C) are arteriosclerosis risk factors[3]. Serum triglyceride (TG) levels are reflected in the metabolism of subcutaneous and visceral fat, and a high TG level is also a risk factor[4]. Very low-density lipoproteins (VLDL) synthesized in the liver and chylomicrons formed as a result of dietary fat absorption are the main reservoirs of serum TG[5].

Serum lipid levels are affected by genetic factors; lifestyle factors such as dietary fat intake, physical activity, and smoking[6]; as well as factors associated with diabetes, renal disease, and fatty liver[7-9]. Although these diseases generally affect

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adults, they may begin in childhood and have been confirmed to promote arteriosclerosis[10]. Unhealthy levels of serum lipids can be modified via changes in lifestyle, including increased activity and a decreased dietary fat intake. Therefore, it is important to detect abnormalities in lipid metabolism via the measurement and evaluation of serum lipid levels of school-age children.

We conducted a study to examine the health of junior high school students in Nagano prefecture, Japan[11]. In this study, the lipid levels of junior high school students were examined over an 11-year period. Our previous study highlighted the association between adiposity and uric acid level in students[12]. This study herein aimed to determine the association between serum triglyceride, HDL-cholesterol, and LDL-cholesterol in students.

2. Subjects and methods

2.1. Subjects

Subjects were recruited from three junior high schools in Nagano prefecture in central Japan. Students and parents/guardians gave informed consent for participation. This study was approved by the Shinshu University School of Medicine ethics examination committee. One school was located in Matsumoto City (approximate population: 230,000 people, approximately 200 km northwest of Tokyo), the second school was located in a farming community (approximately 2000 people and 50 km from Matsumoto City), and the third school was in a suburban area (approximately 8000 people and 20 km from Matsumoto City). Data from 4298 students were collected over 11 years (2005–2015).

2.2. Serum lipid measurements

The blood drawing for health examinations was performed at each junior high school and tested at three clinical laboratory centers. All blood samples were collected into biochemical blood collection tubes from the antecubital vein, between 8 and 9 a.m., after 10 to 12 h of fasting. Serum lipids were measured using the standardization enzyme method based on JSCC compliant methods in biochemistry autoanalyzers, JCA-BM6070 (JEOL Ltd., Tokyo, Japan) and TBA200FR (Toshiba medical systems Co., Tochigi, Japan). The measurement reagents were those in the Deteminer L TC II test kit (Kyowa Medex Co., Ltd., Tokyo, Japan) for total cholesterol, Deteminer L TG II (Kyowa Medex Co., Ltd.) L-type TG M (Wako Pure Chemical Industries, Ltd., Osaka, Japan) for triglyceride, MetaboLead L HDL-C (Kyowa Medex Co., Ltd.) for HDL-cholesterol, and MetaboLead L LDL-C (Kyowa Medex Co., Ltd.) for LDL-cholesterol. All measurements followed detailed standard operating procedures that were general survey manual. The measurement precisions of the assay protocols were managed via internal quality controls in the clinical laboratories, and the external quality control survey provided by the Japan Medical Association.

3. Results

3.1. Baseline characteristics and serum lipid levels

We examined serum lipid levels of junior high school students over 11 years. This study population consisted of 4298 Japanese junior high school students, which included 2234 boys and 2064 girls. Baseline characteristics and serum lipid levels of all students are shown in Table 1. The mean ± standard deviation (SD) and 95% range according to gender are summarized.

3.2. Lipid levels of students over 11 years

We examined serum lipid levels of junior high school students over 11 years (Fig. 1). The TG level skewed to a lower level and changed to logarism value before analysis. After the conversion to normal distribution the median TG level in boys increased from 55.7 mg/dL (lower and upper limits; 22.4-139.0) in 2005-2007 to 59.3 mg/dL (21.9- 160.0) in 2014-2015. The median TG level in girls increased from 60.5 mg/dL (26.2-139.4) to 67.0 mg/dL (27.3-164.5). There was no significant difference in median LDL-C and HDL-C levels in both genders.

3.3 Correlations between serum TG, LDL-C and HDL-C levels

Table 1 Characteristics of Japanese junior high school students

tests	unit	Boys (n= 2234)		Girls (n=2064)	
		mean ± SD	2.5 ~ 97.5%	mean ± SD	2.5 ~ 97.5%
BH*	cm	161.0 ± 8.6	142.0 ~ 175.8	155.6 ± 5.6	144.6 ~ 166.5
BW*	Kg	50.3 ± 10.0	49.6 ~ 73.0	48.1 ± 7.7	35.0 ~ 65.2
AC*	cm	67.1 ± 7.5	66.0 ~ 86.7	67.3 ± 7.1	56.3 ~ 83.0
TC*		162.4 ± 24.4	119 ~ 215	173.2 ± 26.4	128 ~ 232
HDL-C*	mg/dL	63.0 ± 13.0	42 ~ 94	66.4 ± 13.0	44 ~ 94
LDL-C*	mg/dL	85.3 ± 20.3	50 ~ 127	93.1 ± 22.9	54 ~ 144
Triglyceride	mg/dL	69.8 ± 41.8	25 ~ 173	73.0 ± 39.8	30 ~ 167

*: BH: Body height, BW: Body weight, AC: Abdominal circumference, TC: Total cholesterol, LDL-C: LDL-cholesterol, HDL-C: HDL-cholesterol.

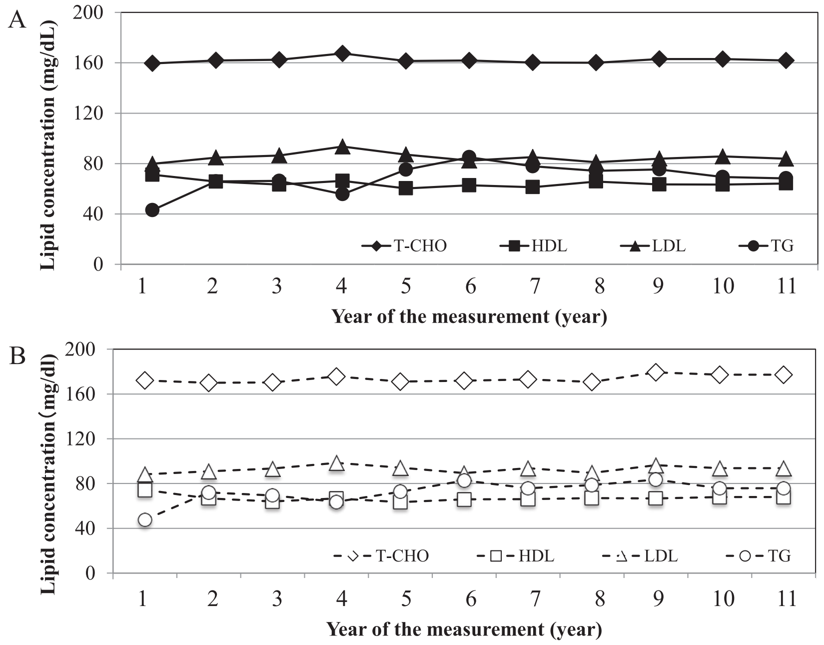

Fig. 1 Changes in serum lipid levels over 11 years in junior high school students.

Serum lipid levels were measured each year from 2005 to 2015. Panel A: boys, Panel B: girls. Diamonds: total cholesterol, squares: HDL-cholesterol, triangles: LDL-cholesterol, and circles: triglyceride.

We examined correlations between serum TG levels, LDL-C, and HDL-C levels. The TG versus HDL-C analysis showed correlation coefficients of r = 0.3366 and r = 0.2876 for boys and girls, respectively (Fig. 2-A). There was a weak, inverse relationship between serum TG and HDL-C levels (y = −0.1015x + 70.665 for boys and y = −0.0909x + 72.841 for girls). The TG versus LDL-C analysis showed correlation coefficients of r = 0.0295 and r = 0.0729 for boys and girls, respectively (Fig. 2-B). Regression analysis showed y = 0.0141x + 84.596 for boys and y = 0.0424x + 90.053 for girls. Serum TG levels were inversely related to HDL-C, but not LDL-C, in boys and girls.

3.4. Changes in lipid levels

Lipid tests for the 293 students with suspected lifestyle-related diseases (186 boys and 107 girls) were performed again four months later. The results indicated that TG levels decreased over 10 mg/dL in 59% of these students, and increased over 10 mg/dL in 18% of students. Analysis of the changes in TG variation values versus LDL-C and HDL-C levels revealed r = 0.3663 (TG variation value versus

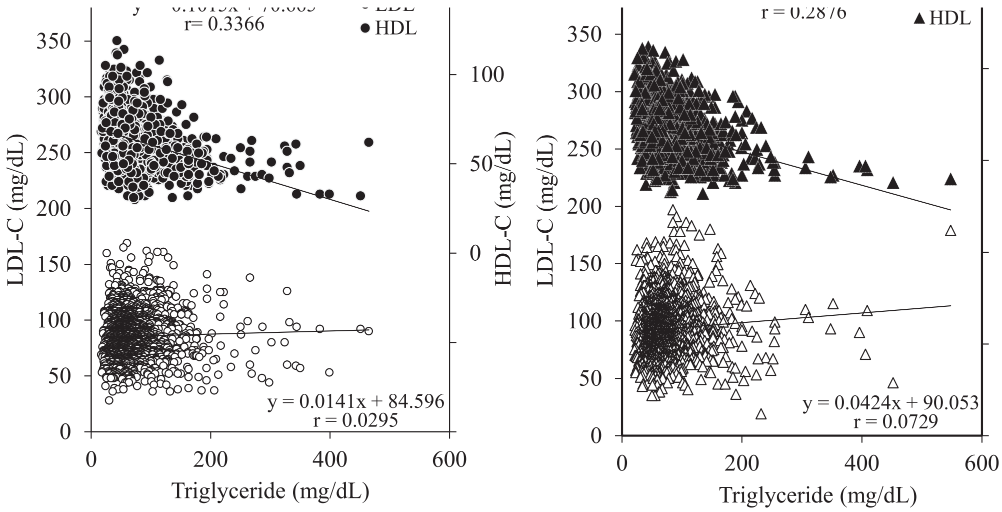

Fig. 2 Correlations between triglyceride levels and HDL-cholesterol (HDL-C) and LDL-cholesterol (LDL-C) levels.

Correlation analysis was performed between TG levels, HDL-C, and LDL-C levels. Panel A: boys, Panel B: girls, Closed circles and triangles: HDL-C versus TG, open circles and triangles: LDL-C versus TG.

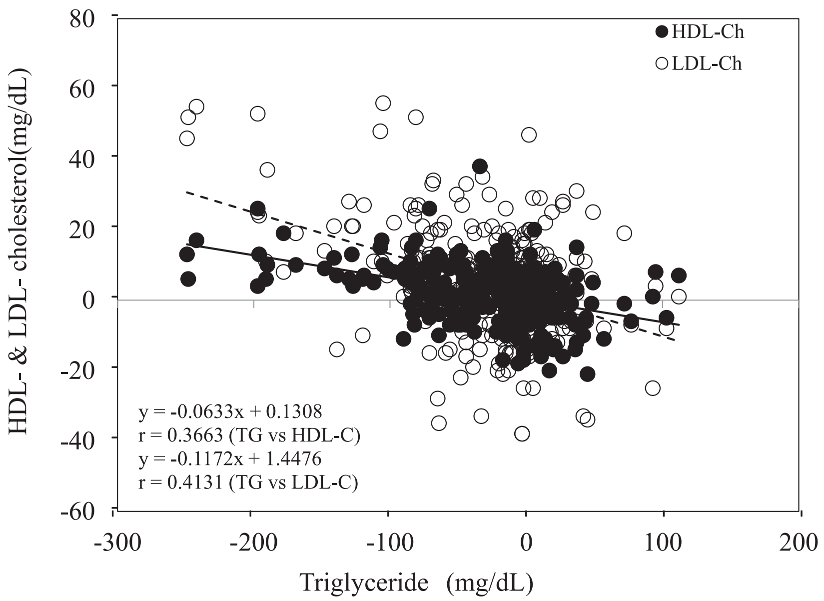

Fig. 3 Correlations between triglyceride variation and HDL-cholesterol (HDL-C) and LDL-cholesterol (LDL-C) levels.

Correlation analysis was performed between TG variation and HDL-C and LDL-C levels. Panel A: boys and Panel B: girls, Closed circles and triangles: HDL-C versus TG, open circles and triangles: LDL-C versus TG.

HDL-C level) and r = 0.4131 (TG variation value versus LDL-C level), and there were inverse relationships for both LDL-C and HDL-C, y = −0.0633x + 0.1308 and y = −0.1172x + 1.4476, respectively.

4. Discussion

In the present study, the lipid levels in Japanese junior high school students were examined over an 11-year period. The decrease in TG levels contributed to improved HDL-C and LDL-C levels. The average TG levels of boys and girls slightly increased during our investigation. In addition, serum TG levels negatively correlated with HDL-C levels. A high TG level presumably contributed to decreased HDL-C levels. Although LDL-C-levels did not necessarily correlate with TG levels, the decrease in TG levels was associated with decreased LDL-C levels. Serum cholesterol levels are primarily regulated by genetic factors, while TG is strongly related to diet[13]. The LDL-C level may be strongly affected by genetic factors as compared with that of HDL.

Serum triglycerides are derived from two major sources: liver-synthesized VLDL and diet-derived chylomicrons[14]. Liver VLDL production is dependent on triglyceride supply, and VLDL biosynthesis is promoted by overeating, alcohol polyposis, diabetes, and obesity. Previously, we reported that junior high students with high uric acid levels showed significant differences in obesity, high-blood pressure, and lipid abnormalities compared with junior high students with low levels of uric acid[12]. Behavioral modification of lifestyles, such as dieting or changing eating habits, was thought to improve TG levels.

The lipid abnormalities included high levels of LDL-C and TG and low levels of HDL-C but not TC. In addition, we reported that a low level of HDL-C was associated with significantly elevated TG. Recent studies showed that a higher TG/HDL-C ratio was associated with an increasingly atherogenic lipid phenotype and was an independent risk factor for CKD in adults[14, 15]. Marco et al. reported that the TG/HDL ratio could be useful in children to identify obese, young patients as a risk factor for IGT[16]. The decrease in TG may significantly contribute to an improved TG/HDL-C ratio with increasing HDL levels.

Serum LDL-C levels increased with the decrease in TG levels in students, but serum LDL-C levels did not correlate with TG levels in junior high school students. Serum LDL-C levels in adults correlate with TG levels in IIb type hyperlipidemia[17]. The LDL-C levels of boys and girls may be affected by other factors, such as genetic factors, unlike the TG level that is strongly dependent on diet. Plasma cholesterol levels are affected by dietary intake, biosynthesis, tissue LDL uptake, and bile acid catabolism in the liver. The LDL receptor plays a major role in LDL metabolism[18]. Familial hypercholesterolemia (FH) is a disease of receptor dysfunction with an autosomal dominant inheritance pattern[19]. The estimated prevalence of the FH heterozygote is not in high frequency, which is approximately 1 in 200 people, although homozygosity is approximately 1 in 1 million people[20]. The high LDL-C levels in students without hypertriglyceridemia, hypertension, and diabetes may have been due to genetic factors, such as heterozygous FH.

Lipid abnormalities in children are associated with hyperuricemia, hyperglycemia, and hypertension, and high levels of serum TG are linked to a variety of cardiovascular diseases[21]. Healthy serum TG levels are required for good lipid metabolism in children. As eating habits are formed in childhood, programs aimed at improving lipid metabolism should commence at this time. In addition, secondary hyperlipidemia should be suspected in students in whom improvements in lifestyle do not positively affect lipid metabolism. In summary, we demonstrated that decreasing serum TG levels were important for lipid metabolism improvement in junior high school students.

Conflicts of interest

All authors must declare any conflicts of interest.

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