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Original Article

Reference Values for The Triglyceride to High-Density Lipoprotein Cholesterol Ratio and Non-High-Density Lipoprotein Cholesterol in Korean Children and Adolescents: The Korean National Health and Nutrition Examination Surveys 2007-2013

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***Aim*: Cholesterol levels vary throughout childhood and adolescence. The aim of the present study was to evaluate and identify age- and gender-specific reference values for serum lipid concentrations including non-high-density lipoprotein cholesterol (non-HDL-C) and the triglyceride to HDL-C ratio (TG/HDL-C ratio) in apparently healthy Korean children and adolescents.**

***Methods*: A total of 6197 participants aged 10 to 19 years old from the 2007-2013 Korean National Health and Nutrition Examination Survey were analyzed. Serum lipid concentrations were evaluated according to age and gender.**

***Results*: The overall mean concentration of non-HDL-C was 105.5 ± 25.6 mg/dL, with a significant gender difference: 103.3 ± 26.1 mg/dL in boys and 107.9 ± 24.7 mg/dL in girls (p = 0.028). The median values of non-HDL-C concentrations in boys and girls, respectively, were 111 and 112 mg/dL in the 10-year-old age group, 95 and 103 mg/dL in the 15-year-old age group, and 109 and 103 mg/dL in the 19-year-old age group. The overall mean TG/HDL-C ratio was 1.74 ± 1.22, and there were no significant gender differences: 1.77 ± 1.25 in boys and 1.72 ± 1.22 in girls (p = 0.183). The median values of the TG/HDL-C ratio in boys and girls were 1.16 and 1.00 in the 10-year-olds, 1.54 and 0.95 in the 15-year-olds, and 1.74 and 0.84 in the 19-year-olds, respectively.**

***Conclusions*: Age- and gender-specific reference values for non-HDL-C and for the TG/HDL-C ratio in children and adolescents could provide valuable information for individualized interpretations of lipid profiles and interventions as well as for strategies to prevent and manage childhood and adolescent dyslipidemia.**

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Key words: Triglyceride to high-density lipoprotein cholesterol ratio, Non-high-density lipoprotein cholesterol, Dyslipidemia, Children, Adolescents

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Introduction

The morbidity and mortality because of atherosclerotic cardiovascular disease (CVD) has become the leading cause of death in Korea, accounting for approximately 25% of all deaths[1]; furthermore, the age of CVD onset now tends to be younger than in previous decades[2]. Atherosclerosis can begin in childhood, and its development has been related to cardiovascular risk factors, including dyslipidemia[3]. Early recognition of the risk factors and age-specific interventions are both important in preventing CVD in adulthood. However, the cholesterol levels of children and adolescents have attracted little interest.

Recently, non-conventional lipid profiles have been suggested to be predictors of cardiovascular events. These predictors include the concentrations of non-high-density lipoprotein cholesterol (non-HDL-C) and the triglyceride (TG) to HDL-C ratio (TG/

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HDL-C ratio). Non-HDL-C, defined as the total cholesterol minus the high-density lipoprotein cholesterol (HDL-C), includes all atherogenic cholesterols, such as low-density lipoprotein (LDL), lipoprotein (a), intermediate-density lipoprotein (IDL), and very-low-density lipoprotein (VLDL) remnants[4]. In the National Cholesterol Education Program-Adult Treatment Panel Ⅲ (NCEP-ATP Ⅲ), non-HDL-C concentrations have been restricted to being a secondary goal in patients with high triglyceride concentrations of ≥200 mg/dL, whereas low-density lipoprotein cholesterol (LDL-C) concentrations are used as a primary therapeutic target[5]. However, recent studies have demonstrated that non-HDL-C can be used as an accurate predictor of cardiovascular disease[6]. The TG/HDL-C ratio has been suggested as a measure to identify overweight individuals with insulin resistance[7, 8]. In recent studies, the TG/HDL-C ratio was found to be associated with cardiovascular mortality[9]. It is well established that cholesterol levels vary by nation and ethnicity[10]. Therefore, caution should be used in the application of reference values from other nations and ethnicities in the Korean population. However, there are scarce reports on the distribution of non-HDL-C and of the TG/HDL-C ratio in Korean children and adolescents.

In the present study, we aimed to evaluate and identify age- and gender-specific reference values for serum lipids, including total cholesterol (TC), HDL-C, TG, LDL-C, non-HDL-C and the TG/HDL-C ratio, in a apparently healthy population of Korean children and adolescents.

Methods

Subjects

Data from the Korean National Health and Nutrition Examination Survey (KNHANES) from 2007-2013 were used. The KNHANES, a cross-sectional, nationally representative and population-based surveillance system, has been conducted annually since 1998 to evaluate the health and nutritional status of the civilian, non-institutionalized population of the Republic of Korea[11]. The survey is conducted by the Division of Chronic Disease Surveillance at the Korean Centers for Disease Control and Prevention. This survey, a nationally representative study, uses a stratified, multistage probability sampling design to select household units. The participants complete questionnaires that include a health interview survey, a health behavior survey, and a nutrition survey. All participants also undergo a health examination survey that includes fasting glucose, fasting insulin and fasting lipid profiles.

A total of 6,213 subjects had measures for TC, HDL-C, and TG and were 10 to 19 years old in the 2007-2013 KNHANES. Participants who had type 1 or 2 diabetes mellitus (DM) or thyroid disease were excluded from this study. Additionally, we excluded subjects receiving current medication for hyperlipidemia. Current medication for hyperlipidemia was defined as the administration of a drug for more than 20 days each month. Because LDL-C was determined using Friedewald's equation (LDL-C = total cholesterol − HDL-C − TG/5), which cannot be used when the triglyceride concentration is ≥400 mg/dL[12], the participants with serum TG concentrations ≥400 mg/dL were also excluded. A final sample of 6,197 participants (3,260 males, 2,937 females) was available for analysis.

Anthropometric and Laboratory Measurements

The anthropometric data collected included height, weight, body mass index (BMI), waist circumference and blood pressure. BMI was determined by the weight in kilograms divided by the square of the height in meters (kg/m^2). Blood samples were obtained from all subjects after ≥8 h of fasting. The collected specimens were centrifuged, frozen at −70℃ and transported to a central laboratory (Seoul Medical Science Institute, Seoul, Korea before 2008 and NeoDIN Medical Institute, Seoul, Korea since 2008), where they were measured within 24 h. In 2007, the serum TC, HDL-C, and TG concentrations were measured enzymatically using ADIVIA1650 (Siemens/USA) with commercial reagents (Siemens/USA). After 2008, serum lipid concentrations, including total cholesterol (Pureauto S CHO-N; Daiichi, Tokyo, Japan), HDL-C (Cholestest N HDL; Daiichi), and triglycerides (Pureauto S TG-N; Daiichi), were analyzed by an enzymatic method using an automated analyzer (Hitachi Automatic Analyzer 7600, Hitachi). LDL-C concentrations were determined using Friedewald's formula. Non-HDL-C was calculated as: TC − HDL-C. Because the domestic laboratory which used to determine HDL-C changed in 2008, and the respective institutes used different analyzing methods and devices, some differences existed in the HDL-C results. Commutable frozen serum samples were prepared and sent to the Lipid Reference Laboratory at the Centers for Disease Control and Prevention in the USA. These data were compared with those from the two domestic laboratory institutes, and a conversion equation to adjust for the differences was formulated to obtain the true HDL-C value. The total coefficient of variation (CVs) for total cholesterol was 1.0%-2.8%. The total CV for HDL-C was 0.9%-3.2%, and the total CV for triglycerides was 0.9%-3.1%.

Table 1. Clinical characteristics of the study population (n=6197)

	Total	Boys	Girls	*P*
Number	6207	3260	2937	
Age (years)	14.1±2.8	14.0±2.7	14.2±2.8	0.011
Height (cm)	160.6±11.4	163.8±12.7	157.0±8.4	<0.001
Weight (kg)	53.7±13.9	56.9±15.5	50.0±10.8	<0.001
Waist circumference (cm)	69.3±9.7	71.3±10.5	67.0±8.2	<0.001
Body mass index (kg/m^2)	20.5	20.9±3.8	20.1±3.3	<0.001
Systolic blood pressure (mmHg)	106.0±10.5	108.3±10.9	103.5±9.4	<0.001
Diastolic blood pressure (mmHg)	66.3±9.3	66.9±9.9	65.6±8.5	<0.001

Definition

The presence of type 1 or 2 DM and thyroid disease and the current use of medications for hyperlipidemia were assessed using the responses to the questionnaire that the respective subjects had provided during the health interview. Dyslipidemia was defined by the following measures: 1) hyper-TC concentration (TC ≥200 mg/dL), hypo-HDL-C concentration (HDL-C <40 mg/dL), hyper-TG concentration (TG ≥130 mg/dL), hyper-LDL-C (LDL-C ≥130 mg/dL), and hyper-non-HDL-C (non-HDL-C ≥145 mg/dL)[5, 13].

Statistics

The data were analyzed using SPSS for Windows version 21 (IBM SPSS Inc., Chicago, IL, USA). The serum concentrations of TC, HDL-C, TG, LDL-C, and non-HDL-C and the TG/HDL-C ratio were analyzed according to age and gender for each age group and are presented as the mean±standard deviation (SD) and percentiles (5th, 10th, 25th, 50th, 75th, 90th, 95th). *P* values less than 0.05 were considered statistically significant. Data are reported as the mean± SD for the continuous variables.

Results

Clinical Characteristics of the Study Population

The clinical characteristics of the subjects are presented in **Table 1**. The boys had a significantly greater mean height (163.79 cm vs. 156.98 cm in girls, $p<0.001$), weight (56.92 kg vs. 50.02 kg, $p<0.001$) waist circumference (71.32 cm vs. 66.96 cm, $p<0.001$), BMI (20.89 kg/m^2 vs. 20.13 kg/m^2, $p<0.001$), systolic blood pressure (108.29 mmHg vs. 103.45 mmHg, $p<0.001$) and diastolic pressure (66.84 mmHg vs. 65.61 mmHg, $p<0.001$) than girls. The mean age was higher in the girls than in the boys (14.20 years old vs. 14.02 years old, respectively, $p=0.011$).

Age-specific Reference Values for Serum Lipid Concentrations According to Age and Gender

Table 2 shows the mean, standard deviation, median, and percentile values for the serum lipid levels according to age and gender.

TC Concentrations

The overall mean concentration of TC was 158.6±26.7 mg/dL, with a significant gender difference: 155.0±27.0 mg/dL in boys and 162.6±25.7 mg/dL in girls ($p<0.001$).

The median TC level was approximately 160 mg/dL in 10- to 11-year-old boys and decreased to approximately 150 mg/dL in 12- to 18-year-old boys. The 95th percentile value was approximately 210 mg/dL in 10- to 12-year-old boys and approximately 200 mg/dL in 13- to 19-year-old boys. In girls, the median value of TC concentration was approximately 160 mg/dL in the 11- to 19-year-old age groups. The 95th percentile concentration was approximately 210 mg/dL in 12- to 19-year-old girls. The prevalence of a TC concentration >200 mg/dL was 5.6% in boys and 8.3% in girls.

HDL-C Concentrations

The overall mean concentration of HDL-C was 53.1±11.0 mg/dL with a significant gender difference: 51.7±10.8 mg/dL in boys and 54.6±10.6 mg/dL in girls ($p<0.001$).

In boys, the median concentration of HDL-C was approximately 55 mg/dL in the 10- to 11-year-old groups and decreased to approximately 50 mg/dL in the 12- to 19-year-old groups. The 5th percentile value of HDL-C was approximately 40 mg/dl in 10- to 19-year-old boys. In girls, the median concentration of HDL-C and the 5th percentile level of HDL-C was similar, approximately 55 mg/dL and 40 mg/dL, respectively, in the 10- to 19-year-old age groups. The prevalence of a HDL-C concentration <40 mg/dL was 12.0% in boys and 7.5% in girls.

Table 2. Means, standard deviations, medians and percentiles for serum lipid profiles, non-HDL-C and TG/HDL-C ratios by age and gender among Korean children and adolescents (n=6197)

Age	n	Mean	SD	Percentile							Age	n	Mean	SD	Percentile						
				5	10	25	50	75	90	95					5	10	25	50	75	90	95
Boys											Girls										
Total cholesterol (mg/dL)											Total cholesterol (mg/dL)										
10	354	167.9	24.4	134	139	151	165	181	202	213	10	315	167.6	26.0	129	135	148	166	184	200	219
11	376	163.7	25.8	125	133	145	163	183	197	208	11	332	161.9	23.7	126	131	145	161	178	192	202
12	401	157.7	29.1	116	126	139	154	172	193	207	12	311	161.1	24.8	124	132	146	160	177	196	209
13	375	151.6	25.0	113	123	135	149	166	183	197	13	327	161.1	25.3	124	131	146	160	173	196	208
14	388	148.2	25.3	108	117	131	147	163	178	190	14	343	161.9	25.2	122	128	144	163	177	195	207
15	332	147.6	26.6	106	115	129	145	166	180	194	15	279	159.1	11.2	123	128	142	157	173	194	207
16	290	150.6	28.1	109	118	133	146	165	186	197	16	278	161.0	26.0	122	129	143	158	177	196	207
17	293	148.7	24.7	113	121	129	146	166	182	192	17	290	161.9	26.7	126	132	142	158	178	199	212
18	260	153.7	27.3	115	123	135	151	169	190	202	18	228	164.6	27.0	124	134	146	162	178	202	217
19	191	159.8	24.7	118	130	143	159	176	190	199	19	234	165.1	26.4	125	133	147	164	181	197	206
Total	3260	155.0	27.0	115	123	137	153	171	190	202	Total	2937	162.6	25.7	124	132	145	161	178	196	209
High-density lipoprotein cholesterol (mg/dL)											High-density lipoprotein cholesterol (mg/dL)										
10	354	56.7	11.8	39	43	48	55	64	73	79	10	315	54.8	11.3	39	41	47	53	62	70	75
11	376	55.1	11.5	38	41	47	55	62	70	75	11	332	53.5	11.1	36	41	46	52	61	68	74
12	401	53.0	11.2	36	39	45	52	60	69	73	12	311	54.5	10.0	37	41	48	54	61	67	71
13	375	51.6	11.0	35	39	44	50	59	66	70	13	327	53.5	10.4	36	41	47	53	60	66	71
14	388	50.3	10.2	34	37	42	50	57	63	68	14	343	53.4	10.4	38	40	46	53	60	67	71
15	332	48.7	9.6	35	37	42	48	55	61	65	15	279	54.3	11.2	36	40	47	54	62	69	72
16	290	49.1	9.6	35	37	43	49	54	61	67	16	278	54.3	11.4	37	40	46	53	62	68	76
17	293	48.9	9.2	34	37	42	48	55	61	63	17	290	55.4	10.4	39	42	48	55	62	68	72
18	260	50.8	10.0	36	38	44	51	57	64	69	18	228	55.8	12.4	36	40	48	55	65	72	76
19	191	50.3	9.4	36	39	43	49	56	61	68	19	234	58.4	10.5	42	45	51	58	65	71	78
Total	3260	51.7	10.8	36	39	44	51	58	66	71	Total	2937	54.6	11.0	38	41	47	54	62	68	73
Triglyceride (mg/dL)											Triglyceride (mg/dL)										
10	354	76.7	42.6	31	37	47	65	97	125	168	10	315	89.4	43.9	35	44	59	80	112	146	164
11	376	81.5	51.1	30	36	48	67	96	148	195	11	332	95.1	50.2	38	44	59	83	119	160	192
12	401	81.6	48.3	33	37	50	70	95	140	184	12	311	93.3	45.4	42	47	65	84	110	147	180
13	375	86.3	51.0	33	38	52	73	105	151	197	13	327	87.4	44.5	38	45	58	78	103	132	183
14	388	79.3	43.4	32	38	48	67	97	142	165	14	343	89.0	46.1	38	46	57	77	108	149	189
15	332	83.6	44.9	36	41	55	73	99	142	176	15	279	84.5	47.7	36	44	54	74	103	140	166
16	290	86.7	46.1	36	41	56	78	106	146	178	16	278	79.8	40.4	36	41	54	71	94	130	159
17	293	87.5	47.9	38	42	55	75	103	153	189	17	290	78.0	38.4	33	40	51	69	95	126	158
18	260	86.5	47.0	38	43	54	74	105	143	168	18	228	79.2	36.0	39	43	55	71	94	127	158
19	191	99.0	51.6	42	51	65	87	113	169	207	19	234	80.1	46.3	33	39	51	69	92	130	176
Total	3260	84.1	48.3	34	39	52	72	101	144	180	Total	2937	86.3	45.0	37	44	56	76	104	140	171

TG Concentrations

The overall mean concentration of TG was 85.0±46.2 mg/dL, with no significant gender difference: 84.1±48.3 mg/dL in boys and 86.3±45.0 mg/dL in girls (p=0.057).

In boys, the median value of TG concentration increased gradually from 65 mg/dL in the 10-year-old age group to approximately 75 mg/dL in the 18-year-old age group. Overall, the 95th percentile concentration was approximately 185 mg/dL in the 10- to

(Cont Table 2)

Age	n	Mean	SD	Percentile							Age	n	Mean	SD	Percentile						
				5	10	25	50	75	90	95					5	10	25	50	75	90	95
Boys											Girls										
Low-density lipoprotein cholesterol (mg/dL)											Low-density lipoprotein cholesterol (mg/dL)										
10	354	95.9	21.8	64	71	81	95	109	126	135	10	315	94.9	22.3	59	67	78	94	111	123	134
11	376	92.2	22.3	58	65	75	91	107	122	130	11	332	89.5	21.0	54	64	77	89	101	117	127
12	401	88.5	25.2	55	61	73	85	100	119	131	12	311	89.0	21.9	55	63	74	88	101	118	130
13	375	82.7	20.9	52	57	70	80	94	111	120	13	327	90.1	22.8	59	65	77	86	102	117	133
14	388	82.1	22.8	48	56	66	80	96	109	119	14	343	90.6	22.0	58	64	76	89	103	119	130
15	332	82.1	22.2	49	55	66	80	96	112	119	15	279	87.9	22.2	56	64	72	86	100	118	128
16	290	84.1	25.1	47	57	68	82	96	113	129	16	278	90.7	22.8	58	62	74	90	105	122	132
17	293	82.3	22.8	48	55	67	80	98	112	121	17	290	90.9	23.3	59	65	74	88	102	125	139
18	260	85.6	23.3	50	59	69	84	99	116	127	18	228	93.0	23.1	62	66	77	90	107	122	138
19	191	89.6	21.6	54	63	76	89	103	116	125	19	234	90.6	22.8	58	64	76	88	105	117	127
Total	3260	86.5	23.4	52	59	71	84	100	116	126	Total	2937	90.7	22.4	58	64	75	89	104	120	131
Non-high-density lipoprotein cholesterol (mg/dL)											Non-high-density lipoprotein cholesterol (mg/dL)										
10	354	111.3	23.4	78	84	95	111	124	144	156	10	315	112.8	23.7	76	85	94	112	129	143	153
11	376	108.5	24.8	73	77	90	106	125	143	151	11	332	108.5	23.7	71	79	94	107	121	140	149
12	401	104.8	27.7	67	76	88	99	119	139	156	12	311	107.7	23.7	70	78	91	106	121	141	156
13	375	100.0	24.7	64	71	84	97	113	131	143	13	327	107.6	24.5	72	81	92	104	122	138	154
14	388	98.0	25.4	61	69	81	96	113	128	140	14	343	108.4	23.3	74	80	91	107	123	139	154
15	332	98.8	25.1	62	68	80	96	116	129	143	15	279	104.8	25.6	68	77	87	101	118	139	152
16	290	101.5	28.1	63	69	82	98	114	135	154	16	278	106.7	25.8	69	77	89	104	121	140	155
17	293	99.8	25.7	63	68	82	99	116	134	146	17	290	106.5	25.7	71	78	88	102	120	143	158
18	260	102.9	27.1	65	72	83	101	119	136	150	18	228	108.8	25.8	73	79	91	105	124	143	154
19	191	109.4	25.4	70	78	93	109	126	145	151	19	234	106.6	26.1	71	77	89	103	122	137	155
Total	3260	103.3	26.1	66	73	85	101	119	136	150	Total	2937	107.9	24.7	72	79	91	105	122	140	153
Triglyceride to high-density lipoprotein cholesterol ratio											Triglyceride to high-density lipoprotein cholesterol ratio										
10	354	1.48	1.05	0.45	0.55	0.79	1.16	1.83	2.75	3.74	10	315	1.78	1.21	0.59	0.73	1.00	1.45	2.22	3.09	4.06
11	376	1.63	1.29	0.51	0.60	0.83	1.21	1.88	3.35	4.20	11	332	1.96	1.38	0.55	0.71	1.06	1.63	2.49	3.55	4.63
12	401	1.69	1.23	0.52	0.62	0.89	1.29	2.06	3.20	4.45	12	311	1.85	1.19	0.66	0.80	1.13	1.59	2.24	3.06	4.00
13	375	1.83	1.36	0.53	0.65	0.95	1.44	2.29	3.37	4.55	13	327	1.76	1.16	0.66	0.76	1.00	1.47	2.10	2.91	4.18
14	388	1.70	1.15	0.59	0.69	0.93	1.35	2.06	3.17	4.11	14	343	1.81	1.24	0.65	0.78	1.00	1.46	2.20	3.16	4.16
15	332	1.83	1.21	0.68	0.80	1.01	1.54	2.24	3.16	4.19	15	279	1.72	1.45	0.63	0.69	0.95	1.34	1.98	2.91	3.92
16	290	1.86	1.13	0.61	0.77	1.05	1.60	2.39	3.27	3.81	16	278	1.61	1.12	0.57	0.68	0.92	1.31	1.87	2.79	4.11
17	293	1.92	1.30	0.68	0.79	1.07	1.55	2.29	3.71	4.40	17	290	1.53	1.03	0.58	0.65	0.84	1.25	1.86	2.71	3.66
18	260	1.83	1.19	0.64	0.78	0.98	1.51	2.27	3.16	4.18	18	228	1.56	0.98	0.56	0.67	0.91	1.26	1.86	2.73	3.79
19	191	2.10	1.32	0.75	0.90	1.19	1.74	2.49	4.02	4.97	19	234	1.47	1.10	0.53	0.63	0.84	1.17	1.63	2.54	3.83
Total	3260	1.77	1.25	0.57	0.68	0.94	1.44	2.17	3.25	4.20	Total	2937	1.72	1.22	0.60	0.71	0.97	1.40	2.04	3.04	4.04

SD; standard deviation

19-year-old age groups. In girls, the median TG concentration decreased gradually from 80 mg/dL in the 10-year-old age group to approximately 70 mg/dL in the 19-year-old age group. Overall, the 95th percentile TG was approximately 170 mg/dL in girls of all ages. The prevalence of a TG concentration ≥130 mg/dL was 13.3% in boys and 12.9% in girls.

LDL-C Concentrations

The overall mean concentration of LDL-C was

88.5 ± 23.0 mg/dL, with a significant gender difference: 86.5 ± 23.4 mg/dL in boys and 90.7 ± 22.4 mg/dL in girls ($p < 0.001$).

In boys, the median concentration of LDL-C was approximately 90 mg/dL in the 10- to 11-year-old age groups and approximately 85 mg/dL in the 12- to 19-year-old age groups. The 95th percentile LDL-C concentration was approximately 130 mg/dL in 10- to 12-year-olds and decreased to approximately 125 mg/dL in 13- to 19-year-olds. In girls, the median value of LDL-C concentration was relatively consistent at approximately 90 mg/dl. The 95th percentile LDL-C concentration was approximately 130 mg/dL in 10- to 19-year-old girls. The prevalence of a LDL-C concentration ≥ 130 mg/dL was 4.2% in boys and 5.5% in girls.

Non-HDL-C Concentration

The overall mean concentration of non-HDL-C was 105.5 ± 25.6 mg/dL, and there was a significant gender difference: 103.3 ± 26.1 mg/dL in boys and 107.9 ± 24.7 mg/dL in girls ($p = 0.028$).

In boys, the median value of non-HDL-C concentrations was approximately 110 mg/dL in the 10- to 11-year-old age groups and approximately 100 mg/dL in the 12- to 17-year-old age groups. Finally, the median value of non-HDL-C concentrations was approximately 110 mg/dL in the 18- to 19-year-olds. The 95th percentile non-HDL-C concentration was approximately 150 mg/dL in the 10- to 19-year-old age groups (**Fig. 1-A**). The curve of the non-HDL-C was U-shaped in boys. In girls, the median non-HDL-C concentration was approximately 110 mg/dL in the 10- to 11-year-old age groups and approximately 105 mg/dL in the 12- to 19-year-old age groups. The 95th percentile concentration of non-HDL-C was relatively consistent, at an approximate level of 150 mg/dL (**Fig. 1-B**). The prevalence of a non-HDL-C concentration ≥ 145 mg/dL was 6.5% in boys and 7.8% in girls.

TG/HDL-C Ratio

The overall mean TG/HDL-C ratio was 1.74 ± 1.22, and there was no significant gender difference: 1.77 ± 1.25 in boys and 1.72 ± 1.22 in girls ($p = 0.183$).

In boys, the median TG/HDL-C ratio increased gradually from 1.16 in the 10-year-olds to 1.75 in the 19-year-olds. Although the 95th percentile values of the TG/HDL-C ratio varied, they showed an increasing tendency overall (**Fig. 2-A**). In girls, the median TG/HDL-C ratio decreased gradually from 1.46 in the 10-year-old age group to 1.17 in the 19-year-old age group. The 95th percentile TG/HDL-C ratio decreased gradually from 4.61 in 10-year-old girls to 3.83 in 19-year-old girls (**Fig. 2-B**).

Discussion

In the present study, we identified the reference values of fasting serum lipid profiles including non-HDL-C and TG/HDL-C ratios in Korean children and adolescents from a nationally representative survey. We evaluated the distributions of non-HDL-C and of TG/HDL-C ratios in Korean children and adolescents aged 10 to 19 years. The overall means of the non-HDL-C and of the TG/HDL-C ratio in boys were 103.3 ± 26.1 mg/dL and 1.77 ± 1.25, respectively, and 107.9 ± 24.7 mg/dL and 1.22 ± 0.60 in girls, respectively.

In pediatric fields, measuring non-HDL-C has a distinct advantage because it does not require fasting. The Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents recommends the use of non-fasting non-HDL-C concentrations as a screening method for dyslipidemia. Several lines of evidence have supported non-HDL-C as a good predictor of CVD risk. In the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study, adolescents and adults aged 15 to 34 years with high non-HDL-C concentrations were at a significantly high risk for histological progression from fatty streaks to advanced atherosclerotic lesions[14]. In the Bogalusa Heart Study, non-HDL-C levels were as good as or better than other lipoprotein measurements, including LDL-C level, for identifying subclinical atherosclerosis among young subjects aged 24 to 48 years[15]. A study of US children and adolescents aged 12 to 19 years demonstrated that non-HDL-C was significantly associated with metabolic syndrome, which is significantly associated with CVD in adulthood[16]. In a US study of non-HDL-C, youth with non-HDL-C concentrations ≥ 120 mg/dL and ≥ 145 mg/dL were at borderline high and high risk of metabolic syndrome, respectively. Therefore, in the Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents, a non-HDL-C concentration < 120 mg/dL, between 120 and 144 mg/dL and ≥ 145 mg/dL are defined as acceptable, borderline high and high, respectively[13]. Recently, a study of Japanese children and adolescents aged 9 to 16 years presented reference values for non-fasting non-HDL-C[17]. In that population, a non-HDL-C concentration ≥ 122 mg/dL in boys and ≥ 125 mg/dL in girls were considered borderline high risk (highest 75th percentile), whereas a non-HDL-C concentration of ≥ 152 mg/dL in boys and ≥ 159 mg/dL in girls indicated high risk (highest 95th percentile). Another Japanese study reported that

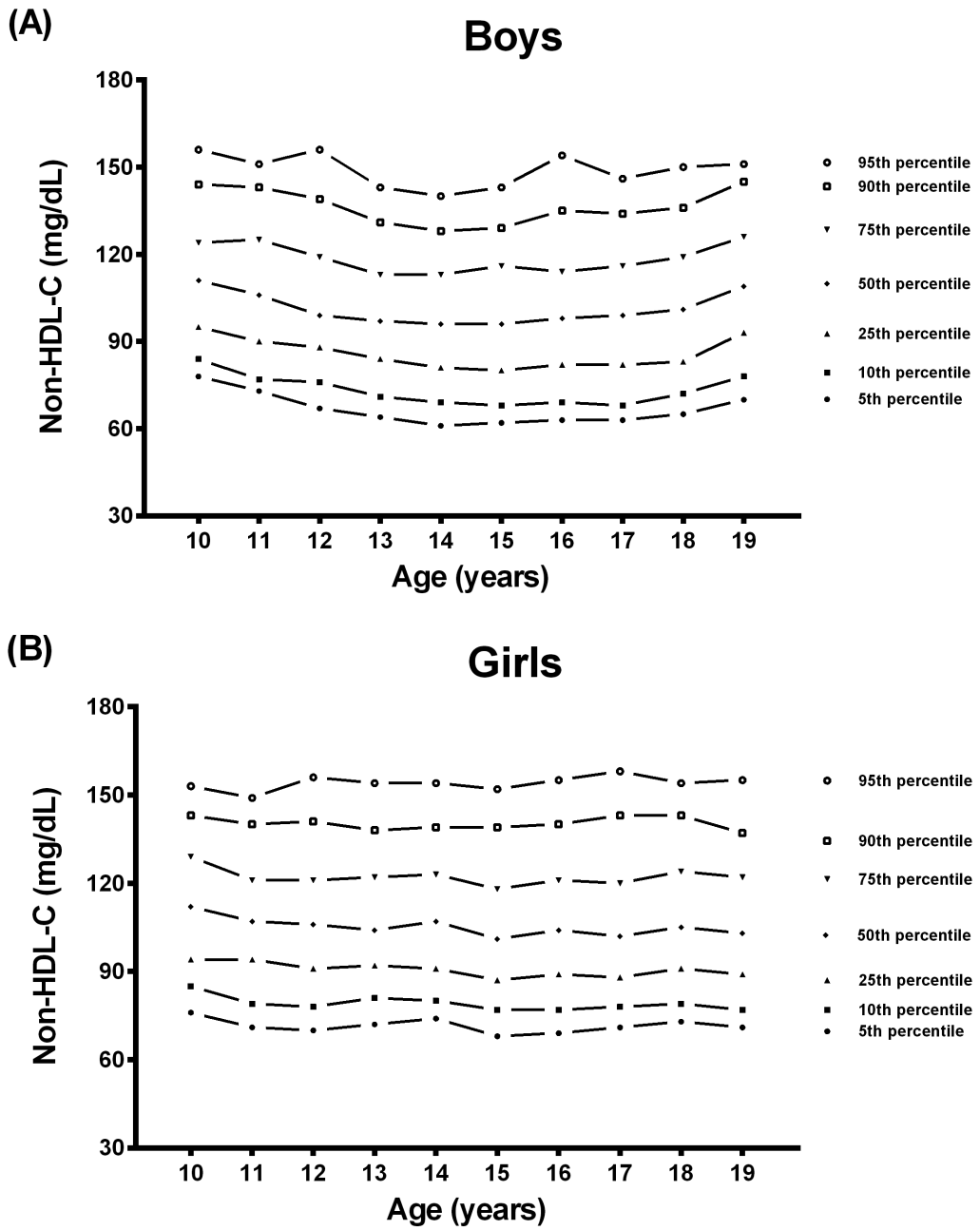


Fig. 1. Reference percentile curves for non-HDL-C according to age in Korean boys (A) and girls (B) (n = 6,197)

obese boys with MetS have elevated non-HDL-C levels and may have a higher risk for the development of atherosclerosis[18]. In their study, the mean non-HDL-C level in obese boys was 139.0 mg/dl and that in boys with abdominal obesity, pre-MetS (abdominal obesity plus one component of MetS), and MetS were 112.9, 135.4, and 149.0 mg/dl, respectively. However, there have been no available data for non-HDL-C in Korea. In the present study, a non-HDL-C of ≥ 111 mg/dL in boys and ≥ 112 mg/dL in girls was the highest 75th percentile, and a non-HDL-C ≥ 156 mg/dL in boys and ≥ 158 mg/dL in girls was the highest 95th percentile. The prevalence of a non-HDL-C concentration ≥ 145 mg/dL was 6.5% in boys and 7.8% in girls. Our results will help clinicians interpret lipid profiles in Korea. Further studies are needed to identify the optimal cutoff points for non-HDL-C concentrations in Korean children and adolescents.

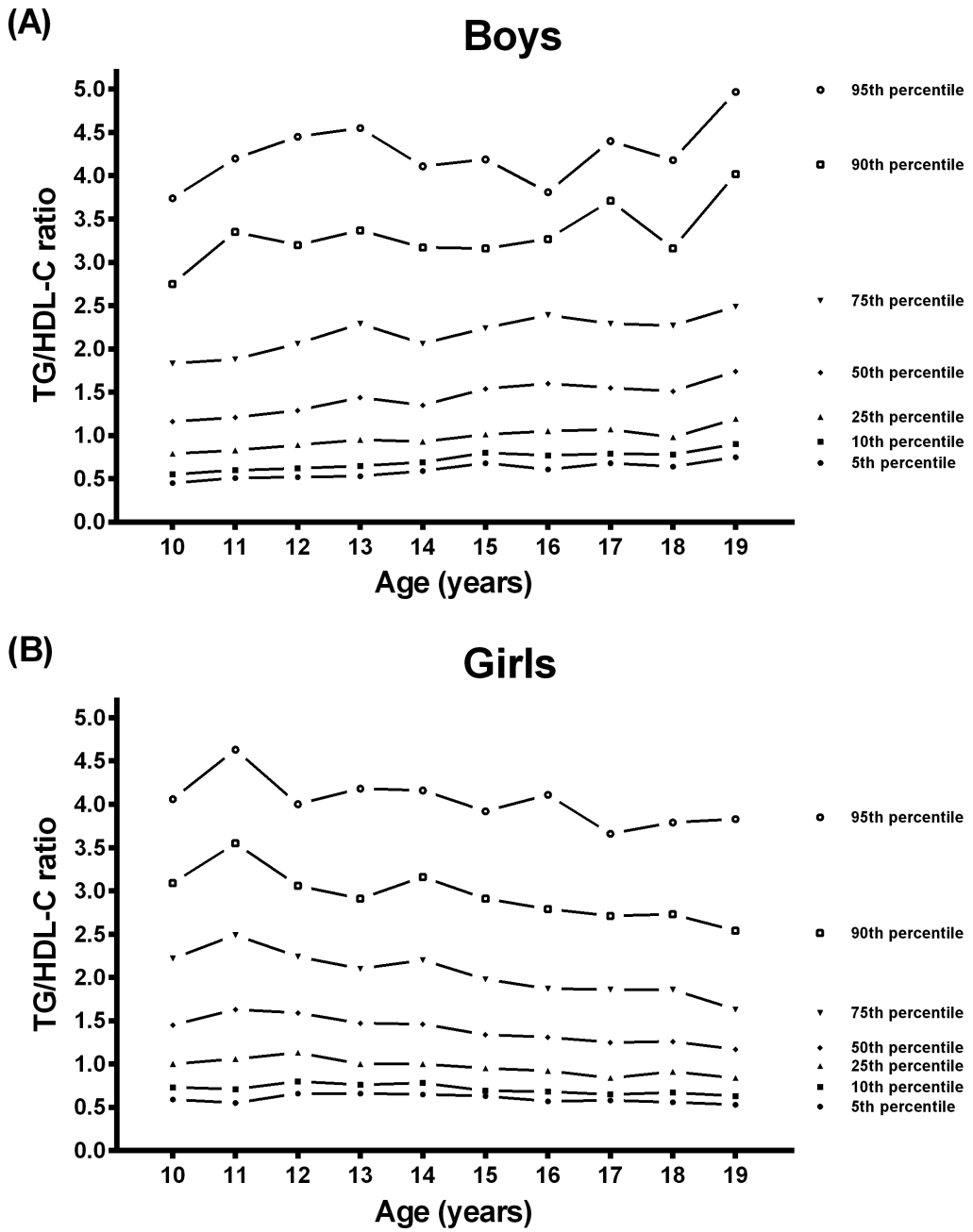


Fig. 2. Reference percentile curves for the TG/HDL-C ratio according to age in Korean boys (A) and girls (B) (n=6,197)

The TG/HDL-C ratio, a recently introduced lipid profile measure, may be a better predictor of small, dense low-density lipoprotein (LDL)[19], an atherogenic lipoprotein particle that strongly predicts coronary heart disease and has been related to an increased risk of CVD[20]. An elevated TG/HDL-C ratio has been associated with coronary artery disease in adults who underwent cardiac catheterization[21]. TG/HDL-C was found to be an independent predictor of carotid intima-media thickness progression, which is an independent risk factor for CVD in adults[22]. In a study of US adolescents and adults aged 10 to 26 years, the TG/HDL-C ratio was found to be an independent predictor of arterial stiffness in adolescents and young adults[23]. In addition, a large Italian study showed that the TG/HDL-C ratio can be a simple and effective tool to identify children and adolescents with atherogenic dyslipidemia and cardio-metabolic risk[24]. In

that Italian study, individuals with a TG/HDL-C ratio ≥ 2.2 were at high risk of preclinical signs of organ damage. Another study in the US demonstrated that white children and adolescents with a TG/HDL-C ratio ≥ 2.27 were at a high risk of insulin resistance[25]. Insulin resistance is a main mechanism involved in metabolic syndrome, which is a significant risk factor for CVD. Thus individuals with a TG/HDL-C ratio ≥ 2.27 can be considered at risk for CVD. However, in a study by Ostfeld *et al*.[21], adults with a TG/HDL-C ratio ≥ 3.5 were significantly associated with CAD. Furthermore, in a study on US adolescents and young adults by Urbina *et al*.[23], individuals with a TG/HDL-C ratio ≥ 2.7 were at high risk (the highest tertile). There is thus controversy over the cutoff point for cardiovascular risk. There have been few studies on the distribution of the TG/HDL-C ratio in healthy children and adolescents. In this study, the overall mean TG/HDL-C ratio was 1.77 in boys and 1.72 in girls. The highest 75th percentile was 2.39 in boys and 2.49 in girls, and the highest 95th percentile was 4.55 in boys and 4.63 in girls. The highest 75th percentile of the TG/HDL-C ratio in both genders was within the values of 2.2 to 2.7, which were the values associated with a high risk of CVD in children adolescents in this study.

In our study, the trends in TG/HDL-C ratio regarding age differed between boys and girls. The TG/HDL-C ratio tended to increase with age in boys, whereas the trend in TG/HDL-C ratio was decreasing with age in girls. Serum lipids are affected by age, gender, ethnicity, nutritional state, pubertal stage, physical activity, and hormonal status including menstrual cycle for women[26-29]. Although the study populations in a study by Skinner *et al*.[26] did not fast, the curves of TG regarding age had a slightly increasing trend after the age of 10 in boys but a decreasing trend in girls. On the other hand, the HDL-C curve for age showed a decreasing trend in boys, whereas the HDL-C curve for age showed an increasing trend in girls. A Japanese study found a decreasing trend in HDL-C with age in boys and an increasing trend in HDL-C with age in girls[17]. Moreover, a previous Korean study showed that the HDL-C concentrations had an increasing trend with age in girls but a decreasing trend in boys[30]. The TG levels regarding age had an increasing trend in boys and a decreasing trend in girls[30]. Those results showed a similar pattern in TG and HDL-C concentrations as the present study. Although the direct TG/HDL-C ratio was not estimated in that study, we can postulate that the TG/HDL-C ratio for age would have a similar pattern as the one in our study throughout childhood and adolescence.

The results of this study confirmed previous findings that the distribution of serum lipids vary with age and gender[26, 31, 32]. This can be related to physiologic changes that indicate hormonal influences and lead to lipid variations. However, current guidelines for lipids and treatment based on fixed cutoff values do not reflect a normal distribution of age and gender. Evaluating lipid profiles against age- and gender-specific curves could be helpful in managing lipid problems in children and adolescents. It is expected that these curves could play a role in preventing over- and under-treatment. From the individual's perspective, proper management of lipids within age- and gender-specific reference values can help delay future cardiovascular events[33]. From a national perspective, these curves could play a significant role in planning national strategies for the prevention and control of cholesterol in children and adolescents.

There were several limitations to this study. The results were based on cross-sectional data; therefore, we cannot track whether each child followed the pattern of the curves. We were unable to evaluate the associations between the distribution of serum lipids and pubertal stage. There were no available data from previous studies to compare with the present study, and we cannot evaluate the trends in serum lipid concentrations. Further studies are needed to evaluate trends in the distribution of serum lipids with an increased sample size.

Conclusion

This study on the distribution of serum lipid concentrations in Korea demonstrated age- and gender-specific reference values of serum lipid profiles including non-HDL-C and TG/HDL-C ratios in children and adolescents based on a nationally representative survey. These results provide not only more information for individualized interpretation of lipid profiles and interventions but also valuable information for planning strategies to prevent and manage childhood and adolescent dyslipidemia.

Acknowledgement

None.

Conflicts of Interest

The authors declare no conflicts of interest.

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