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Association between the triglyceride to
high-density lipoprotein cholesterol
ratio and insulin resistance in Korean
adolescents: A nationwide
population-based study

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population-based study

Directed by Professor Duk-Chul Lee

The Master's Thesis
submitted to the Department of Medicine,
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in partial fulfillment of the requirements for the degree
of Master of Medical Science

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This certifies that the Master's Thesis of
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ABSTRACT

Association between the triglyceride to high-density lipoprotein cholesterol ratio and insulin resistance in Korean adolescents: A nationwide population-based study

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Purpose: Studies have suggested the triglyceride (TG) to high-density lipoprotein cholesterol (HDL-C) ratio (TG/HDL-C) as a surrogate marker of insulin resistance. However, few studies have examined the association between TG/HDL-C and insulin resistance in general adolescent population. This study examined the association between TG/HDL-C and insulin resistance in a nationally representative sample of Korean adolescents.

Materials and Methods: A total of 2,649 participants aged 12-18 years were selected from the Korean National Health and Nutrition Examination Survey performed during 2007-2010. Insulin resistance was defined as a homeostasis model assessment of insulin resistance (HOMA-IR) values greater than the 80th percentile. The odds ratio (OR) and 95% confidence intervals (CIs) for insulin resistance were calculated using multiple logistic regression analysis across sex-specific TG/HDL-C quartiles.

Results: The mean values of most cardiometabolic variables increased proportionally with TG/HDL-C quartiles. The mean values of age-adjusted HOMA-IR were progressively increased for the higher quartiles of TG/HDL-C

for boys and girls. Compared to individuals in the lowest TG/HDL-C quartile, the odds ratio for insulin resistance for individuals in the highest quartile was 2.90 in boys and 2.34 in girls after adjusting for age, systolic blood pressure, physical activity, residential area, body mass index z-score, and waist circumference.

Conclusion: A higher TG/HDL-C was positively associated with a higher risk of insulin resistance in Korean adolescents. This study suggests that TG/HDL-C could be a convenient marker for identifying Korean adolescents with insulin resistance.

Key words: the triglyceride to high-density lipoprotein cholesterol ratio, insulin resistance, HOMA-IR, adolescents

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I. INTRODUCTION

Insulin resistance, which is characterized by a subnormal glucose response to insulin, is thought to be an underlying cause of numerous medical disorders¹. Individuals with insulin resistance are more susceptible to cardiovascular disease,² cerebrovascular disease,³ type 2 diabetes mellitus,⁴ neurodegenerative disease,⁵ infectious disease⁶ and certain cancers⁷. Although these diseases are all leading causes of mortality in adults, insulin resistance is also observed in prepubertal children and early adolescents, and can continue into adulthood⁸⁻¹⁰. As the prevalence of childhood obesity has reached alarming levels and become epidemic during the past few decades, public health concern about children and adolescents with insulin resistance has increased.¹¹⁻¹³ Therefore, early identification of insulin resistance in children and adolescents is important from a public health perspective.

While the homeostasis model assessment of insulin resistance (HOMA-IR) is

potentially important, it is not routinely available in standard clinical practice. Thus, a simple, global, and more accessible marker of insulin resistance could help detect individuals who are in the initial stages of insulin resistance. Individuals in the early stages of insulin-resistance have elevated levels of triglyceride (TG) and decreased levels of high-density lipoprotein cholesterol (HDL-C).¹⁴

More recently, the ratio of TG to HDL-C (TG/HDL-C) has become a more widely used measurement of insulin resistance. Previous epidemiological studies in adult populations have reported that a high TG/HDL-C has a positive correlation with HOMA-IR and is an independent predictor of cardiometabolic events.¹⁵⁻¹⁸ Moreover, several studies suggested TG/HDL-C as a marker of cardiovascular risk and insulin resistance in children and adolescents.¹⁹⁻²³ However, most of these studies either focused on obese children and adolescents, or used a small participant population, not the general pediatric population. In addition, a recent study could not find that TG/HDL-C is a useful predictor of insulin resistance.²⁴ Therefore, we examined the association between the TG/HDL-C and insulin resistance in a nationally representative sample of Korean adolescents, after adjusting for confounding factors including body mass index (BMI) z-score and waist circumference, which had a strong influence on insulin resistance.

II. MATERIALS AND METHODS

1. Survey Overview and Study Population

This was a cross-sectional study that used data obtained from the 2007-2010 Korean National Health and Nutrition Examination Survey (KNHANES), which was performed by the Korea Centers for Disease Control and Prevention. The KNHANES is a nationwide, representative, population-based survey to evaluate the health and nutrition status of Koreans. The survey consists of a Health Interview Survey, a Nutrition Survey, and a Health Examination Survey. The target population of the survey included non-institutionalized civilians in South Korea. Sampling units consisted of households that were selected through a stratified, multistage probability sampling design based on geographic area, sex distribution, and age. Sampling weights that were representative of the probability of being sampled were assigned to each participant to ensure that the results represented the overall South Korean population.

A total of 33,829 participants were included in the KNHANES conducting during 2007-2010 and this survey gathered data from 3,153 adolescents aged 12-18 years. Of these 3,153 subjects, we excluded participants who had not fasted 8 hours prior to blood sampling (n=496) and participants with missing data (n=4). Subjects who had a history of diabetes mellitus and/or a plasma glucose level ≥ 126 mg/dL were also excluded (n=4). After these exclusions, 2,649 subjects (1416 boys and 1233 girls) were included in the final analysis. The KNHANES was approved by the Institutional Review Board of the Korea

Centers for Disease Control and Prevention (Board approval numbers: 2007-02CON-04-P, 2008-04EXP-01-C, 2009-01CON-03-2C, 2010-02CON-21-C). In addition, the study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

2. Measurement of anthropometric and laboratory data

At the time of the 2007-2010 KNHANES, citizens were informed that they had been randomly selected as a household to voluntarily participate in a nationwide representative survey performed by the Korea Centers for Disease Control and Prevention and that they had the right to withdraw at any time in accordance with the National Health Enhancement Act supported by the National Statistics Law of Korea. Written informed consent was obtained from all of the citizens who agreed to participate. Blood tests were performed in participants aged 10 years or older, and participants' consent to use blood samples for further studies was also obtained.

Trained medical staff performed anthropometric measurements following a standardized procedure. Height and body weight were measured to the nearest 0.1 cm and 0.1 kg, respectively, while participants were wearing light clothing without shoes. BMI was calculated as the ratio of body weight (kg) to height squared (m^2). BMI z-score was calculated via the modified lambda, mu, sigma (LMS) statistical method used in the 2007 Korean Children and Adolescents Growth Standard. Waist circumference was measured to the nearest 0.1 cm at the midpoint between lower border of the rib cage and iliac crest at the end stage of a normal expiration. Systolic blood pressure and diastolic blood pressure were

measured three separate times at five-minute intervals using a standard mercury sphygmomanometer (Baumanometer, W.A. Baum Co., Inc., Copiague, NY, USA), and the average of the second and third measurements was used for analysis.

Blood samples were obtained from the antecubital vein after each participant had fasted overnight for a minimum of 8 hours. Fasting plasma glucose, total cholesterol, TG and HDL-C were measured using an Automatic Analyzer (Hitachi 7600, Hitachi Co., Tokyo, Japan). Leucocyte counts were determined by an automated blood cell counter (XE-2100D, Sysmex, Kobe, Japan). Fasting serum insulin levels were analyzed using a 1470 WIZARD gamma-counter (PerkinElmer, Turku, Finland) by radioimmunoassay.

3. Definition of each term

HOMA-IR was calculated using the following formula: fasting plasma glucose (mg/dL) x fasting insulin (μ IU/mL)/405. Insulin resistance was defined as the values greater than the 80th percentile of the HOMA-IR (> 3.65 in boys and > 3.70 in girls) in the current study.

Overweight was defined as a $85^{\text{th}} \leq \text{BMI} < 95^{\text{th}}$ percentile for age and sex and obesity was defined as a $\text{BMI} \geq 95^{\text{th}}$ percentile for age and sex according to the 2007 Korean Children and Adolescents Growth Standard.²⁵

Physical activity was assessed with a 7-day recall method using the Korean version of the short form International Physical Activity Questionnaire. According to the questionnaire, individuals who participated in vigorous-intensity physical activity lasting ≥ 20 minutes per session more than

three times per week, or participated in moderate-intensity physical activity lasting ≥ 30 minutes per session more than five times per week were categorized into the regular exercise group.

4. Statistical analysis

Sampling weights were used to account for complex survey design of KNHANES; therefore, we obtained valid estimates that represented the total Korean adolescents and avoided biased estimates. TG/HDL-C quartiles were categorized as follows: Q1, ≤ 1.05 ; Q2, 1.06-1.59; Q3, 1.60-2.35; and Q4, ≥ 2.36 in boys, and Q1, ≤ 1.06 ; Q2, 1.07-1.51; Q3, 1.52-2.19; and Q4, ≥ 2.20 in girls. Participant characteristics according to TG/HDL-C quartiles were summarized using a weighted one-way analysis of variance (ANOVA) test for continuous variables and a weighted chi-square test for categorical variables. A general linear model was used to test the trends across quartiles. The age-adjusted mean HOMA-IR was calculated by analysis of covariance (ANCOVA) test according to TG/HDL-C quartiles. The odds ratio (OR) and 95% confidence intervals (CIs) for insulin resistance were calculated using multiple logistic regression analysis after adjusting for confounding factors across TG/HDL-C quartiles. All statistical analyses were performed with SPSS statistical software (version 20.0; SPSS Inc., Chicago, IL, USA). Statistical significance was set at p values < 0.05 .

III. RESULTS

1. Characteristics of study subjects

The subject characteristics according to sex are presented in Table 1. In all, 1416 boys and 1233 girls were included. The prevalence of overweight and obesity was 12.6% and 5.9% among boys and 10.9% and 6.4% among girls.

Table 1. Characteristics of study subjects according to gender

	boys	girls
Unweighted N	1416	1233
Age (years)	15.0 (0.1)	15.1 (0.1)
BMI (kg/m ²)	21.3 (0.1)	20.6 (0.1)
BMI z-score	-0.02 (0.03)	-0.04 (0.04)
Overweight (%)	12.6 (1.0)	10.9 (1.0)
Obesity (%)	5.9 (0.7)	6.4 (1.0)
Waist circumference (cm)	73.1 (0.3)	68.4 (0.3)
WtHR	0.43 (0.00)	0.43 (0.00)
SBP (mmHg)	108.0 (0.4)	102.2 (0.4)
DBP (mmHg)	67.4 (0.3)	65.5 (0.3)
FPG (mg/dL)	89.1 (0.2)	87.9 (0.2)
Total cholesterol (mg/dL)	151.1 (1.0)	161.3 (0.8)
TG (mg/dL)	88.1 (1.9)	86.0 (1.6)
HDL-C (mg/dL)	47.4 (0.3)	50.9 (0.3)
TG/HDL-C	2.01 (0.06)	1.82 (0.05)
Insulin (μ IU/mL)	13.4 (0.3)	13.5 (0.3)
HOMA-IR	2.99 (0.06)	2.96 (0.06)
WBC count (cells/ μ L)	6360 (60)	6320 (60)
Regular exercise (%)	51.5 (1.5)	28.1 (1.5)
Residence in rural area (%)	18.0 (2.1)	18.8 (1.5)

Data are presented as mean (standard error) or percentage (standard error).

BMI, body mass index; WtHR, waist-to-height ratio; SBP, systolic blood pressure;

DBP, diastolic blood pressure; FPG, fasting plasma glucose; TG, triglyceride;

HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model

Assessment of insulin resistance; WBC, white blood cell

2. Characteristics of study subjects according to TG/HDL-C quartiles

Table 2 shows the characteristics of study subjects according to sex-specific TG/HDL-C quartiles. The mean values of most cardiometabolic variables, such as BMI, BMI z-score, waist circumference, waist-to-height ratio, total cholesterol, TG, insulin, and HOMA-IR, all increased proportionally with TG/HDL-C quartiles. Additionally, the prevalence of overweight, obesity tended to increase proportionally with TG/HDL-C quartiles. WBC count, as shown by a nonspecific inflammatory marker, also tended to increase proportionally according to TG/HDL-C quartiles.²⁶

Table 2. Characteristics of study subjects according to TG/HDL-C quartiles in boys and girls

	TG/HDL-C quartiles in boys				p value	p for trend
	Q1 (≤1.05)	Q2 (1.06-1.59)	Q3 (1.60-2.35)	Q4 (≥2.36)		
Unweighted N	354	354	354	354		
Age (years)	14.7 (0.1)	15.0 (0.1)	15.3 (0.1)	15.2 (0.1)	0.008	0.003
BMI (kg/m ²)	20.1 (0.2)	20.3 (0.2)	21.8 (0.3)	23.1 (0.3)	<0.001	<0.001
BMI z-score	-0.33 (0.07)	-0.31 (0.06)	0.11 (0.08)	0.45 (0.07)	<0.001	<0.001
Overweight (%)	5.0 (1.3)	7.9 (1.5)	13.4 (2.3)	24.2 (2.5)	<0.001	<0.001
Obesity (%)	0.4 (0.3)	1.9 (0.7)	7.2 (1.7)	14.2 (2.2)	<0.001	<0.001
Waist circumference (cm)	69.2 (0.5)	70.5 (0.5)	74.6 (0.7)	78.1 (0.7)	<0.001	<0.001
WtHR	0.41 (0.00)	0.42 (0.00)	0.44 (0.00)	0.46 (0.00)	<0.001	<0.001
SBP (mmHg)	105.2 (0.6)	106.6 (0.6)	109.7 (0.8)	110.8 (0.7)	<0.001	<0.001
DBP (mmHg)	65.7 (0.6)	67.1 (0.5)	67.9 (0.6)	68.9 (0.6)	0.002	<0.001
FPG (mg/dL)	89.2 (0.5)	88.9 (0.4)	89.0 (0.5)	89.2 (0.4)	0.937	0.976
Total cholesterol (mg/dL)	145.2 (1.9)	145.3 (1.4)	151.6 (1.8)	162.2 (1.7)	<0.001	<0.001
TG (mg/dL)	42.9 (0.6)	64.3 (0.7)	87.5 (1.00)	158.2 (4.8)	<0.001	<0.001
HDL-C (mg/dL)	54.2 (0.5)	48.8 (0.5)	45.7 (0.5)	40.9 (0.4)	<0.001	<0.001
TG/HDL-C	0.80 (0.01)	1.32 (0.01)	1.92 (0.01)	4.00 (0.16)	<0.001	<0.001
Insulin (μIU/mL)	11.2 (0.3)	12.1 (0.3)	14.0 (0.7)	16.5 (0.6)	<0.001	<0.001
HOMA-IR	2.50 (0.08)	2.66 (0.06)	3.13 (0.17)	3.69 (0.14)	<0.001	<0.001
WBC count (cells/μL)	6100 (160)	6170 (80)	6490 (100)	6690 (90)	<0.001	<0.001
Regular exercise (%)	54.9 (3.0)	51.3 (3.1)	49.4 (3.2)	50.7 (3.0)	0.635	0.291
Residence in rural area (%)	19.9 (3.2)	16.4 (2.8)	18.8 (2.7)	16.9 (3.0)	0.702	0.518

	TG/HDL-C quartiles in girls				p value	p for trend
	Q1 (≤1.06)	Q2 (1.07-1.51)	Q3 (1.52-2.19)	Q4 (≥2.20)		
Unweighted N	308	308	309	308		
Age (years)	15.5 (0.1)	15.0 (0.1)	15.0 (0.1)	14.70 (0.1)	<0.001	<0.001
BMI (kg/m ²)	20.0 (0.2)	20.4 (0.2)	20.4 (0.2)	21.7 (0.3)	<0.001	<0.001
BMI z-score	-0.29 (0.06)	-0.11 (0.08)	-0.08 (0.07)	0.34 (0.09)	<0.001	<0.001
Overweight (%)	7.5 (1.6)	9.5 (1.8)	11.2 (2.2)	15.8 (2.3)	0.028	0.003
Obesity (%)	1.6 (0.8)	4.4 (1.1)	5.1 (1.8)	15.3 (3.0)	<0.001	<0.001
Waist circumference (cm)	66.5 (0.4)	68.0 (0.5)	68.5 (0.5)	70.8 (0.6)	<0.001	<0.001
WtHR	0.42 (0.00)	0.43 (0.00)	0.43 (0.00)	0.44 (0.00)	<0.001	<0.001
SBP (mmHg)	102.1 (0.7)	101.5 (0.5)	101.1 (0.7)	104.5 (0.7)	0.001	0.038
DBP (mmHg)	66.0 (0.6)	65.2 (0.5)	64.6 (0.7)	66.3 (0.7)	0.195	0.959
FPG (mg/dL)	86.7 (0.4)	88.0 (0.4)	87.8 (0.4)	89.1 (0.4)	0.001	<0.001
Total cholesterol (mg/dL)	158.6 (1.5)	160.5 (1.5)	161.2 (1.6)	165.2 (1.8)	0.043	0.007
TG (mg/dL)	47.0 (0.7)	67.1 (0.7)	87.9 (1.0)	146.1 (3.2)	<0.001	<0.001
HDL-C (mg/dL)	58.3 (0.6)	52.7 (0.5)	49.0 (0.4)	42.9 (0.5)	<0.001	<0.001
TG/HDL-C	0.81 (0.01)	1.28 (0.01)	1.80 (0.01)	3.52 (0.12)	<0.001	<0.001
Insulin (μIU/mL)	11.8 (0.4)	13.2 (0.3)	13.3 (0.4)	15.8 (0.7)	<0.001	<0.001
HOMA-IR	2.56 (0.09)	2.89 (0.07)	2.91 (0.09)	3.53 (0.17)	<0.001	<0.001
WBC count (cells/μL)	6020 (110)	6360 (110)	6180 (90)	6740 (110)	<0.001	<0.001
Regular exercise (%)	21.5 (2.8)	32.3 (2.9)	28.0 (2.8)	30.8 (3.2)	0.043	0.077
Residence in rural area (%)	15.5 (2.7)	17.3 (3.8)	19.4 (3.4)	19.2 (3.6)	0.649	0.179

Data are presented as mean (standard error) or percentage (standard error).

p values were determined for continuous variables by one-way ANOVA tests and for categorical variables by chi-square test.

BMI, body mass index; WtHR, waist-to-height ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment of insulin resistance; WBC, white blood cell

3. Age-adjusted HOMA-IR according to TG/HDL-C quartiles

Figure 1 illustrates the age-adjusted mean HOMA-IR according to TG/HDL-C quartiles. The mean values of age-adjusted HOMA-IR were progressively increased for the higher quartiles of TG/HDL-C for boys and girls (p for trend < 0.001).

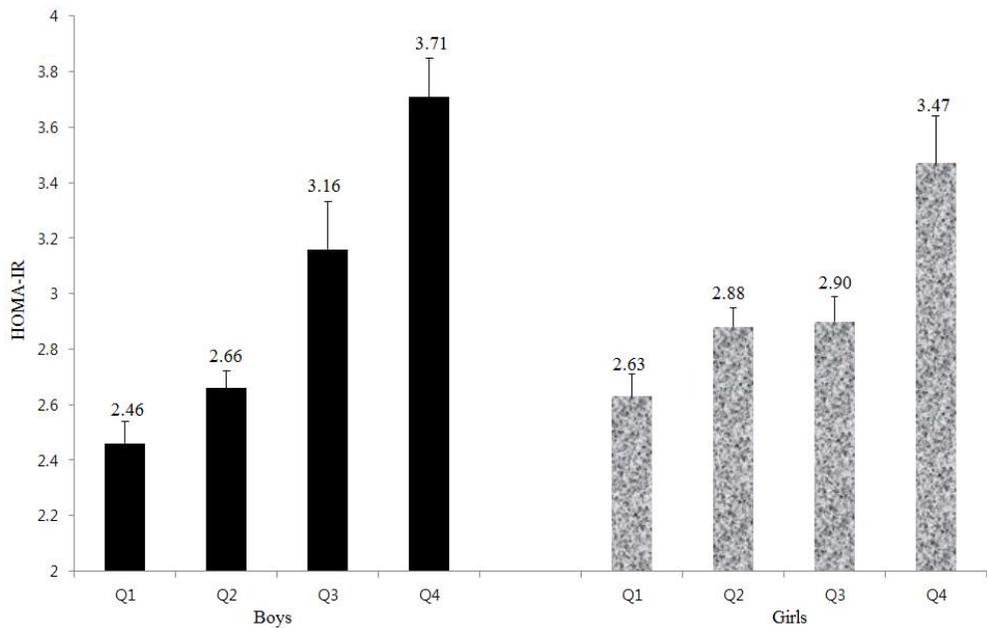


Figure 1. Age-adjusted mean HOMA-IR according to TG/HDL-C quartiles (Bars mean standard errors).

4. Odds ratios and 95% confidence intervals for insulin resistance

Table 3 shows the risk of insulin resistance in terms of TG/HDL-C quartiles using multiple logistic regression analysis. In model 1, the ORs (95% CIs) were calculated after adjusting for age. In model 2, we adjusted for additional potential confounding variables, such as systolic blood pressure, physical activity, and residential area. In model 3, we examined the relationship between TG/HDL-C and insulin resistance independently of obesity effects by adjusting for additional confounding variables, such as BMI z-score and waist circumference. Compared with the lowest quartile, the ORs (95% CIs) for insulin resistance in the highest quartiles of TG/HDL-C, were 6.84 (4.08, 11.46) and 3.62 (2.22, 5.90) in model 1, 5.69 (3.30, 9.80) and 3.44 (2.07, 5.72) in model 2, and 2.91 (1.68, 5.05) and 2.38 (1.39, 4.06) in model 3 for boys and girls, respectively.

Table 3. Odds ratios and 95% confidence intervals for insulin resistance (HOMA-IR >80%, 3.65 in boys and 3.70 in girls) according to TG/HDL-C quartiles in boys and girls

		Boys			
		Q1	Q2	Q3	Q4
		(≤ 1.05)	(1.06-1.59)	(1.60-2.35)	(≥ 2.36)
			1.86	3.38	6.84
Model 1	1		(1.08, 3.20)	(1.94, 5.90)	(4.08, 11.46)
Model 2	1		1.64 (0.94, 2.86)	2.77 (1.55, 4.95)	5.69 (3.30, 9.80)
Model 3	1		1.50 (0.85, 2.66)	1.84 (0.99, 3.40)	2.91 (1.68, 5.05)

		Girls			
		Q1	Q2	Q3	Q4
		(≤ 1.06)	(1.07-1.51)	(1.52-2.19)	(≥ 2.20)
			1.54	3.38	3.62
Model 1	1		(0.90, 2.66)	(0.91, 2.71)	(2.22, 5.90)
Model 2	1		1.53 (0.87, 2.70)	1.65 (0.94, 2.89)	3.44 (2.07, 5.72)
Model 3	1		1.36 (0.74, 2.50)	1.37 (0.75, 2.51)	2.38 (1.39, 4.06)

Model 1 adjusted for age.

Model 2 adjusted for systolic blood pressure, physical activity, and residential area, in addition to the factor in Model 1.

Model 3 adjusted for BMI z-score and waist circumference, in addition to the factors in Model2.

IV. DISCUSSION

In this nationally representative cross-sectional study, we found that TG/HDL-C was positively associated with insulin resistance in Korean children and adolescents after adjusting for potential confounding variables. These positive associations were maintained regardless of the effects of obesity, even after controlling for BMI z-score and waist circumference. Our findings are in agreement with the results of previous studies showing that TG/HDL-C is a reliable indicator of insulin resistance and atherosclerotic disease in adult populations.¹⁵⁻¹⁸ Our results suggest that this association can be applied to adolescent populations. Pacifico et al. reported that TG/HDL-C ratio was positively associated with carotid artery intima-media thickness, insulin resistance, and nonalcoholic fatty liver disease.²³ However, in that study, sex difference was not fully considered since it did not present separate data on both sexes. As shown in the present study, there is a significant sex difference in TG/HDL-C distribution. Our study showed that these associations between TG/HDL-C and HOMA-IR can be applied to both boys and girls through sex-specific multiple logistic regression analyses. The authors used TG/HDL-C as a surrogate marker of insulin resistance, which is widely and rapidly accessible to clinicians as part of the patient's lipid profile. Lipid profile is incorporated in the pediatric population as a universal screening for dyslipidemia. Although, the HOMA-IR is considered a traditional marker of insulin resistance, it is not routinely evaluated in standard clinical practice. In

addition, the cut-off values of the fourth quartiles are similar to those of other studies in which the values of 2.2 and 2.05 resulted to be the best marker of metabolic complications in children and adolescents with and without other cardiovascular risk factors, respectively.^{26,27}

There are several possible mechanisms for the significant association between TG/HDL-C and HOMA-IR in adolescents. Insulin resistance mediates visceral obesity, type 2 diabetes mellitus, hypertension, and atherosclerosis, all of which are linked to the development of cardiovascular disease.²⁸ Moreover, insulin resistance promotes atherogenic dyslipidemia, as manifested by increased TG and small dense low-density lipoprotein cholesterol levels and decreased levels of HDL-C.²⁹ Thus, a higher TG/HDL-C may be a phenotype of insulin resistance and cardiometabolic risk factors. In the present study, cardiometabolic risk factors, such as BMI, waist circumference, waist-to-height ratio and total cholesterol, increased proportionally with increasing TG/HDL-C quartiles. Another important factor to consider is subclinical, low-grade inflammation. Insulin resistance is increasingly recognized as a chronic, low-grade, inflammatory state.³⁰⁻³² A study of 1,008 subjects in the U.S. from the insulin resistance atherosclerosis study reported that three inflammatory markers, including C-reactive protein, fibrinogen, and WBC count, were positively correlated with insulin resistance.³³ In the current study, WBC count tended to increase proportionally according to TG/HDL-C quartiles. WBC count is widely considered to be a marker of inflammation and is also an independent predictor of metabolic syndrome and cardiovascular disease.³⁴⁻³⁶ Based on this evidence, the interrelationship between TG/HDL-C and insulin

resistance may be explained by chronic subclinical inflammation.

This study has several limitations that should be considered when interpreting the results. First, this study used a cross-sectional study design that makes it difficult to establish a causal relationship between TG/HDL-C and insulin resistance. Although a significant relationship between TG/HDL-C and insulin resistance exists in the present study, whether TG/HDL-C is a risk factor actively involved in the development of insulin resistance or just an epiphenomenon remains unclear. Second, we defined insulin resistance as a value greater than the 80th percentile of HOMA-IR. As described previously, HOMA-IR is a generally accepted method used to quantify insulin resistance in epidemiological studies. However, there are no clear cut-off points for HOMA-IR values that meet the definition of insulin resistance and defining insulin resistance as HOMA-IR greater than the 80th percentile was commonly practiced.^{18,37} Third, we did not compare TG/HDL-C with another tool for predicting insulin resistance such as the waist-to-height ratio or BMI. Waist-to-height is also known to be associated with insulin resistance and low-grade inflammation in pediatric population.^{38,39} However, we did not intend to indicate that TG/HDL-C is better tool than waist-to-height ratio when identifying insulin resistance. We would like to demonstrate that the positive association between TG/HDL-C and insulin resistance remains after controlling for BMI z-score and waist circumference, which had a strong influence on insulin resistance. Lastly, this study did not take into account the physiological effect of puberty on insulin levels. Specifically, insulin resistance increases at the onset of puberty and stays elevated through Tanner stage 4.⁴⁰ Unfortunately,

because information on the pubertal stage was not included in the KNHANES dataset, we could not determine whether the participants had reached puberty. However, to minimize this limitation, we analyzed data subdivided by sex and included age as a confounding variable in the multiple logistic regression analysis. Further studies that elucidate TG/HDL-C and insulin resistance according to pubertal stage, with a comparison between girls and boys, are needed. Despite these potential limitations, the general applicability of the results is supported by the utilization of a national representative sample. The large sample of subjects for each gender has allowed for an appropriate empirical study on the relationship between TG/HDL-C and insulin resistance. Most previous studies investigating the association between TG/HDL-C and insulin resistance in children and adolescents included only subjects who were overweight or obese, or these studies used a small participant population.

V. CONCLUSION

In conclusion, a higher TG/HDL-C was positively associated with a higher risk of insulin resistance in Korean adolescents. In clinical practice, TG/HDL-C, which is widely accessible on routine laboratory tests, could be a convenient surrogate marker for identifying adolescents with insulin resistance.

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ABSTRACT (IN KOREAN)

한국 청소년에서 고밀도 지단백 콜레스테롤에 대한 중성지방의 비율과 인슐린 저항성과의 연관성: 전국 인구 기반 연구

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목적: 고밀도 지단백 콜레스테롤에 대한 중성지방의 비율은 인슐린저항성의 대리 마커로서 여러 연구들을 통해 제시되었다. 그러나, 일반 청소년 인구집단에서 고밀도 지단백 콜레스테롤에 대한 중성지방의 비율과 인슐린 저항성과의 연관성을 조사한 연구는 거의 이루어 지지 않았다. 따라서 본 연구는 고밀도 지단백 콜레스테롤에 대한 중성지방의 비율과 인슐린 저항성과의 연관성을 한국 청소년의 국가 대표 샘플을 통해 조사하였다.

재료 및 방법: 2007년부터 2010년까지 시행된 국민건강영양조사 자료로부터 12-18세의 2649명의 청소년이 연구 대상으로 선정되었다. 인슐린 저항성은 인슐린 저항성의 항상성 모델 평가의 80th 퍼센트 이상 값으로 정의하였다. 인슐린 저항성의 교차비와 95% 신뢰구간은 다중 로지스틱 회귀분석을 사용하여 계산하였다.

결과: 대부분의 심혈관대사 변수들의 평균값은 고밀도 지단백 콜레스테롤에 대한 중성지방의 비율 사분위수의 증가에 따라

증가하였다. 나이를 보정한 인슐린 저항성의 항상성 모델 평가의 평균값 역시 고밀도 지단백 콜레스테롤에 대한 중성지방의 비율 사분위수가 높아짐에 따라 지속적으로 증가하였다. 가장 낮은 고밀도 지단백 콜레스테롤에 대한 중성지방의 비율 사분위수와 비교하여 가장 높은 고밀도 지단백 콜레스테롤에 대한 중성지방의 비율 사분위수의 인슐린 저항성의 교차비는 나이, 수축기 혈압, 신체 활동, 거주 지역, 체질량지수 z-점수, 허리 둘레를 보정한 후에도, 소년들에서는 2.90, 소녀들에서는 2.34였다.

결론: 한국 청소년에서 높은 고밀도 지단백 콜레스테롤에 대한 중성지방의 비율은 높은 인슐린 저항성과 양의 관계가 있다. 본 연구는 고밀도 지단백 콜레스테롤에 대한 중성지방의 비율이 인슐린 저항성이 있는 한국 청소년들을 확인하는데 편리한 마커가 될 수 있다는 것을 제안한다.

핵심되는 말: 고밀도 지단백 콜레스테롤에 대한 중성지방의 비율,
인슐린 저항성, 인슐린 저항성의 항상성 모델 평가, 청소년