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Association of Atopic Dermatitis with Dyslipidemia in Adolescents: A Cross-Sectional Study

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Dear Editor:

Epidemiologic studies have suggested atopic dermatitis (AD) in adults may be a risk factor for cardiovascular disease (CVD), the link remains controversial[1]. However, few studies have been done in children and adolescents with a high prevalence of AD. In particular, dyslipidemia is a major cause of CVD, approximately half of children and adolescents with hyper-low density lipoprotein cholesterol (LDL-C) and hypo-high density lipoprotein cholesterol (HDL-C) have persistent disease at 10 years[2]. Therefore, dyslipidemia in adolescence act as major risk factors for CVD in adulthood, so it is important to diagnose and manage these cases early. Therefore, we analyzed the relationship between AD and dyslipidemia in adolescent AD patients using nationally representative Korean data.

We analyzed data from the 2010～2013 Korea National Health and Nutrition Examination Survey (KNHANES). Of the 33,552 individuals included in the KNHANES, we identified and enrolled 2,914 adolescents aged 12 to 18 years as potential candidates for this study in the preliminary analysis. Of these, we excluded subjects with missing data for variables (n=805) or insufficient fasting time (n=74). Adolescents with triglyceride levels ≥400 were excluded (n=2) as were those with congenital heart disease (n=2) and type 1 diabetes mellitus (n=19). Finally, we analyzed 2,012 participants in this study. Height, body weight and waist circumference measurements were obtained for all participants by trained staff. Blood sampling was performed in the morning after fasting for at least 8 hours. According to the criteria for diagnosis of dyslipidemia in adolescents in Korea, hypercholesterolemia, hypertriglyceridemia, and hyper-LDL-C and hypo-HDL-C were defined as ≥200, ≥130, ≥130, and <40 mg/dl, respectively[3]. Dyslipidemia was defined as the presence of ≥1 risk factors of hypercholesterolemia, hypertriglyceridemia, and hyper-LDL-C or hypo-HDL-C[3]. The sociodemographic factors of the participants were obtained from a self-reported questionnaire including age, sex, household income, and region. The presence or absence of AD was limited to those who were diagnosed by a doctor for life. Detailed information regarding the KNHANES has been reported previously[4]. The study was approved by the institutional review board of Inje University Ilsan Paik Hospital (No. ISPAIK 2020-06-011).

Since the KNHANES was collected through stratification and group sample selection methods for populations living in Korea, statistical analysis was conducted via a method of analyzing complex sample data considering weights. Categorical or ordinal variables were expressed as the proportions and standard errors (SE). Statistical differences were calculated by the design-based Wilcoxon rank-sum test for complex sample survey data or the Pearson χ^2 test with Rao-Scott adjustment. To confirm the relationship be-

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tween dyslipidemia and AD, we performed simple and multiple logistic regression analyses using the generalized linear model for a complex survey design. Model 1 was performed to determine the association between dyslipidemia and AD with adjusting for age, sex, region, household income, education, allergic rhinitis, and asthma. Model 2 was analyzed adjusting for the same variables in model 1 plus family history (diabetes, hypertension, dyslipidemia, stroke, ischemic heart disease), physical activity, smoking status, alcohol consumption, obesity, and central obesity. Statistical analysis was performed using IBM SPSS Statistics ver. 21.0 (IBM Corp., Armonk, NY, USA). Statistical significance was defined as $p<0.05$.

A total of 2,012 adolescents (1,068 boys, 944 girls; mean age 14.8±2.0 years) are analyzed (Supplementary Table 1). In total, 11.4% (230/2,012) of the participants were diagnosed with AD by a physician. Mean fasting blood glucose, total cholesterol, triglycerides, LDL-C, and HDL-C values were not significantly different between the two groups, after adjusting for confounding factors (Table 1). However, when the two groups were compared by applying the criteria for dyslipidemia, the proportion of hyper-LDL-C (≥130 mg/dl) in the AD group (8.0%±0.6%) was statistically significantly higher than that of the control group (4.2%±0.4%, $p=0.041$). There were no significant differences in hypercholesterolemia, hypo-HDL-C, hypertriglyceridemia between the two groups. In Table 2, without adjusting for potential confounders, AD was associated with hyper-LDL-C (odds ratio [OR]=2.0, 95% confidence interval [CI]=1.0~4.0). AD was associated with hyper-LDL-C even in the multivariate analyses model 1 (OR=2.0, 95% CI=1.0~3.9) and model 2 (OR=2.2, 95% CI=1.1~4.5). There was no significant association between AD and other hyperlipidemia.

Dyslipidemia is a key risk factor for CVD, particularly, oxidized LDL-C particles act as pro-oxidants in endothelial cells, causing atherosclerosis and acting as independent risk factors for CVD[5]. Therefore, regulation of LDL-C is very important to prevent CVD, and since AD is associated with hyper-LDL-C, active management of AD suggests the possibility of preventing morbidity in secondary CVD. Recently, when the lipid profile according to immunoglobulin (Ig) E level and allergic sensitization was examined in 654 children (11-year-old) in Japan, the higher the IgE and the higher rate of the allergic sensitization, the higher the total cholesterol and LDL-C[6]. Since the link between AD and dyslipidemia still shows inconsistent results from epidemiologic studies, the mechanism has not been clarified. Hyperlipidemia can cause release of proinflammatory cytokines and a Th2 response to external antigens, and a link between hyperlipidemia and asthma has

Table 1. Prevalence of adverse lipid profile

Variable	Total	non-AD (n=1,782)	AD (n=230)	*p*-value*
Dyslipidemia†				0.529
No	74.4±1.0	74.6±1.0	72.4±1.0	
Yes	25.7±1.0	25.4±1.0	27.6±1.0	
Hypercholesterolemia (≥200 mg/dl)				0.237
No	94.2±0.5	94.4±0.5	92.1±0.6	
Yes	5.8±0.5	5.6±0.5	7.9±0.6	
Low HDL-C (<40 mg/dl)				0.672
No	87.3±0.7	87.4±0.7	86.3±0.8	
Yes	12.7±0.7	12.6±0.7	13.7±0.8	
High LDL-C (≥130 mg/dl)				0.041*
No	95.4±0.5	95.9±0.4	92.1±0.6	
Yes	4.6±0.5	4.2±0.4	8.0±0.6	
Hypertriglyceridemia (≥130 mg/dl)				0.053
No	88.1±0.7	87.5±0.7	92.3±0.6	
Yes	12.0±0.7	12.5±0.7	7.7±0.6	

Values are presented as %±standard error. AD: atopic dermatitis, HDL-C: high density lipoprotein cholesterol, LDL-C: low density lipoprotein cholesterol. *p*-values were calculated by using Pearson χ^2 test with Rao-Scott adjustment. Statistically significant *$p<0.05$. †Dyslipidemia is defined as having 1 of the lipid abnormalities.

Table 2. Logistic regression analyses of dyslipidemia with atopic dermatitis

Variable	Unadjusted		Model 1		Model 2	
	OR (95% CI)	*p*-value†	OR (95% CI)	*p*-value‡	OR (95% CI)	*p*-value‡
Dyslipidemia	1.1 (0.8~1.6)	0.529	1.2 (0.8~1.7)	0.349	1.2 (0.9~1.8)	0.250
Hypercholesterolemia (≥200 mg/dl)	1.5 (0.8~2.7)	0.240	1.3 (0.7~2.4)	0.343	1.4 (0.8~2.7)	0.287
Low HDL-C (<40 mg/dl)	1.1 (0.7~1.8)	0.672	1.2 (0.8~1.9)	0.456	1.2 (0.8~2.0)	0.408
High LDL-C (≥130 mg/dl)	2.0 (1.0~4.0)	0.045*	2.0 (1.0~3.9)	0.038*	2.2 (1.1~4.5)	0.021*
Hypertriglyceridemia (≥130 mg/dl)	0.6 (0.3~1.0)	0.056	0.6 (0.4~1.1)	0.087	0.6 (0.3~1.1)	0.106

Model 1: adjusted for age, sex, region, household income, education, allergic rhinitis, and asthma, Model 2: Model 1+family history (hypertension, diabetes mellitus, dyslipidemia, stroke, ischemic heart disease), physical activity (walk, moderate, vigorous), smoking status, alcohol consumption, obesity, and central obesity. OR: odds ratio, CI: confidence interval, HDL-C: high density lipoprotein cholesterol, LDL-C: low density lipoprotein cholesterol. *Statistically significant ($p<0.05$). †*p*-values for unadjusted ORs. ‡*p*-values for adjusted ORs.

been suggested[7]. Therefore, controversy remains over the causality of whether the Th2 response due to hyperlipidemia increases the risk of AD, and conversely, whether systemic inflammation caused by AD causes dyslipidemia.

This cross-sectional study is not possible to confirm the causal relationship between AD and dyslipidemia, and genetic factors, diet, and stress could not be analyzed accurately, and differences according to the severity of AD could not be analyzed. KNHANES has no data on the pubertal development status that affects insulin resistance and lipid profiles, so it was not reflected in the analysis. Nevertheless, this study has significance that it analyzed standardized laboratory tests and demographic measurements in a nationally representative database.

In conclusion, we confirmed AD in adolescence was associated with hyper-LDL-C when analyzed based on large-scale national data in this study. Therefore, for treatment of AD in adolescence, it is necessary to be aware not only of skin symptoms, but also the possibility of potential cardiovascular complications in adulthood.

SUPPLEMENTARY MATERIALS

Supplementary data can be found via http://anndermatol.org/src/sm/ad-33-483-s001.pdf.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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