Association Between Metabolic Syndrome and Atopic Dermatitis in Korean Adults

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Whether metabolic syndrome (MetS) and its components are risk factors for atopic dermatitis (AD) remains unclear. This study investigated the association between MetS and AD in Korean adults. Nationally representative data for 5,007 Korean adults, aged 19–40 years, from the cross-sectional Korea National Health and Nutrition Examination Survey 2010–2011 were analysed. AD in female patients was associated with MetS ($p = 0.02$) and increased triglyceride level ($p = 0.05$). After adjusting for confounding factors, the odds ratio for female participants with MetS was 2.92; for central obesity (waist circumference ≥ 85 cm), 1.73; and for hypertriglyceridaemia, 2.20. In this large-scale nationwide study in Korean adults, MetS and its components (central obesity and hypertriglyceridaemia) correlated positively with the presence of AD in women.

Key words: atopic dermatitis; metabolic syndrome; obesity; lipid; association; prevalence.

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Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disorder and part of the beginning of the atopic march. AD often accompanies various systemic or allergic diseases, such as asthma or allergic rhinitis. For example, autoimmune diseases, as well as ophthalmic, gastrointestinal, and renal diseases, have been reported to be associated with AD (1). Recently, metabolic diseases including obesity coexistent with chronic skin disorders, such as AD, have attracted more attention and thus warrant further research.

Metabolic syndrome (MetS) is a cluster of metabolic abnormalities and is well-known for its associations with diabetes and coronary artery disease. MetS is diagnosed if at least 3 of the following 5 metabolic risk factors are present: increased waist circumference (WC); increased serum triglycerides (TG); decreased serum high-density lipoprotein (HDL); increased fasting blood sugar; and hypertension (2). Although the pathophysiological mechanism of MetS is still not fully known, genetic as well as environmental factors have been reported to play a role (3). Association between MetS and asthma, one of the major respiratory allergic diseases, has been proposed (4, 5).

To date, the relationship between AD and MetS has not been understood. Although some prior reports suggested an association between AD with serum lipid profiles, obesity, or insulin resistance, the findings in the studies were not consistent (6–8). Therefore, in this study, we aim to investigate associations between AD and MetS, as well as AD and each component of MetS, by analysing data from the 2010 to 2011 Korea National Health and Nutrition Examination Survey (KNHANES).

METHODS

Study population

KNHANES is a cross-sectional survey comprising surveys in 3 categories: health interviews, dietary interviews, and health examination. KNHANES was organized by the Korean Ministry of Health and Welfare, and conducted by specially trained interviewers and examiners who were not provided with any information about the participants beforehand. KNHANES was performed using a complex, stratified, multistage cluster survey design and the rolling survey sampling method. Therefore, the samples in this study were nationally representative, non-institutionalized populations. A detailed description of the plan and operation of the survey is available on the KNHANES website (http://knhanes.cdc.go.kr/). The Institutional Review Board at the Korea Centers for Disease Control and Prevention approved the protocol of this study, and all participants signed informed consent forms. This study was also approved by the Institutional Review Board of the Catholic University of Korea (Approved No. KC15EASI0102). A total of 5,007 subjects (2,142 men and 2,865 women) were included in the analysis.

Study variables

We examined the prevalence of AD in the population, based on the responses to a question in the KNHANES, "Have you ever been diagnosed with AD by a physician?" According to the answers to the question, we divided the respondents into 2 groups: an AD group and a non-AD group. KNHANES data were analysed to calculate the prevalence of AD in the Korean population. Further investigation was performed to examine the influence of various factors that have previously been shown to correlate with the prevalence of AD in the USA and Europe. Such factors included age, sex, socioeconomic status, lifestyle, coexistence of allergic diseases (asthma or allergic rhinitis), and place of residence. The region of residence was grouped as follows: urban (Seoul, Busan, Daegu, Incheon, Gwangju, Daejeon, Ulsan, and Gyeonggi-do) and rural (Gangwon-do, Chungcheongbuk-do, Chungcheongnam-do,

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Jeollabuk-do, Jeollanam-do, Gyeongsangbuk-do, Gyeongsangnam-do, and Jeju-do). For economic status, we examined whether the subjects belonged to the highest income level (defined by those in the highest quartile).

Diagnosis of metabolic syndrome

MetS was defined based on the revised criteria of the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) (9). According to the guideline, 3 or more of the following 5 components constitute a diagnosis of MetS: (*i*) elevated WC (≥90 cm for men and ≥85 cm for women, according to the Korean Society for the Study of Obesity's cut-off point for central or abdominal obesity) (10); (*ii*) elevated TG level (≥150 mg/dl or taking medications for hypertriglyceridaemia); (*iii*) reduced HDL (<40 mg/dl in men and <50mg/dl in women); (*iv*) elevated blood pressure (systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg, or receiving antihypertensive treatment); and (*v*) elevated fasting glucose (≥100 mg/dl or taking medications for increased glucose).

Statistical analysis

Statistical analyses were performed using an SAS survey procedure (version 9.2; SAS Institute, Inc., Cary, NC, USA) to take into account the complex sampling design using the KNHANES sampling weights and to provide nationally representative prevalence estimates. In order to minimize the variations in survey components and methods between survey years, all analyses performed in this study were adjusted for survey years. We evaluated differences in categorical variables between groups using the χ^2 test, while examined differences between 2 groups in continuous variables using 2-sample *t*-tests. All data are presented as the mean ± standard error (SE) and % ± SE. The odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated by logistic analysis. AD prevalence was also compared by the presence of MetS and each factor of MetS, using multivariate logistic regression after adjusting for potentially confounding variables (age, smoking status, alcohol consumption, exercise, and vitamin D). A p-value <0.05 was considered statistically significant.

RESULTS

A total of 5,007 subjects was included in the analysis of this study. Table SI[1] summarizes the demographic characteristics of the data, divided by sex and AD group and non-AD group, subsequently. Both AD groups were on average 2–3 years younger than the non-AD groups. Serum levels of TG were higher in the female AD group than the female non-AD group, although the difference was not statistically significant. Body mass index (BMI) and other components of MetS, including WC, serum cholesterol, HDL, and LDL, did not show any differences between AD and non-AD group.

Table I shows the correlation between MetS and AD in men and women. Women with AD had more MetS and MetS components than women without AD ($p=0.02$). Table I also shows the results of multiple logistic regression analyses. We adjusted for confounders (age for Model 1; age, smoking status, alcohol consumption, exercise and vitamin D for Model 2) and calculated ORs and 95% CIs for AD according to the presence of MetS, high WC, high BP, low HDL, and hypertriglyceridaemia. In both adjusted models, female subjects with AD were more likely to have MetS, central obesity, or hypertriglyceridaemia. For female patients with MetS, the OR was 2.92 (95% CI 1.49–5.73); for women with abdominal obesity, 1.73 (95% CI 1.09–2.75); for women with hypertriglyceridaemia, 2.20 (95% CI 1.19–4.05). In addition, after adjusting for all confounding factors (Model 2), the adjusted ORs were similar to those of Model 1. Women with AD were also more likely to have high BP, hyperglycaemia, and low HDL, yet the association was not statistically significant. In contrast, in male subjects with AD, there was no association between these components.

Table SII[1] shows data including components of MetS divided into 3 groups: subjects without AD and any allergic diseases (A1); subjects with AD and without any other allergic diseases (A2); and subjects with AD and other allergic diseases, such as allergic rhinitis or asthma (A3). In female subjects, mean values of BMI, WC, total body fat (BF) percentage, HDL, and TG were statistically significantly different among the 3 groups. The mean values of TG in the 3 women groups showed an increasing pattern from A1 to A3. Fig. S1[1] shows a synergy between hypertriglyceridaemia and abdominal obesity in female patients with AD ($p<0.0017$).

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Table I. Correlation between metabolic syndrome (MetS) and atopic dermatitis (AD) by sex and odds ratios with 95% confidence intervals for AD according to components of MetS

	Male			Female			Male		Female	
	Non-AD Mean (SD)	AD Mean (SD)	*p*	Non-AD Mean (SD)	AD Mean (SD)	*p*	Model 1	Model 2	Model 1	Model 2
MetS	4.8 (0.6)	2.7 (1)	0.11	4.8 (0.5)	9.5 (2.9)	0.02	0.72 (0.33, 1.58)	0.75 (0.34, 1.66)	2.92 (1.49, 5.73)	2.82 (1.45, 5.52)
Increased WC	4.8 (0.6)	3.7 (1)	0.37	4.8 (0.5)	6.6 (1.3)	0.14	0.87 (0.48, 1.57)	0.91 (0.50, 1.65)	1.73 (1.091, 2.75)	1.71 (1.071, 2.73)
Hypertension	4.8 (0.6)	3.9 (1)	0.44	5 (0.5)	7.1 (2.4)	0.29	0.93 (0.55, 1.59)	0.94 (0.56, 1.60)	1.77 (0.86, 3.65)	1.74 (0.84, 3.61)
Hyperglycaemia	4.8 (0.6)	3 (1.1)	0.22	5.1 (0.5)	5.2 (1.9)	0.94	0.81 (0.37, 1.81)	0.83 (0.37, 1.86)	1.44 (0.65, 3.16)	1.42 (0.63, 3.19)
Decreased HDL	4.6 (0.6)	4.3 (1.3)	0.84	5 (0.6)	5.5 (1)	0.58	1.05 (0.56, 1.98)	1.01 (0.53, 1.89)	1.31 (0.86, 1.99)	1.31 (0.86, 1.99)
Increased triglyceridaemia	4.8 (0.7)	4.1 (0.8)	0.50	4.8 (0.5)	8.3 (2.1)	0.05	1.06 (0.64, 1.75)	1.12 (0.67, 1.86)	2.20 (1.19, 4.05)	2.20 (1.20, 4.03)

Increased waist circumference (WC) (≥90 cm for men and ≥85 cm for women); hypertension (systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg, or receiving antihypertensive treatment); hyperglycaemia (≥100 mg/dl or taking medications for increased glucose); decreased high-density lipoprotein (HDL) (<40 mg/dl in men and <50 mg/dl in women); increased triglyceridemia (≥150 mg/dl or taking medications for hypertriglyceridaemia). Model 1: adjustment for age; Model 2: adjustment for age, smoking, alcohol consumption, exercise, and vitamin D. SD: standard deviation.

DISCUSSION

Notably, after adjusting for confounding factors, MetS and its components, such as central obesity and hypertriglyceridaemia, were found to be significantly correlated with AD in female subjects. Moreover, central obesity and hypertriglyceridaemia had a synergistic effect on having AD in women. In addition, both A2 and A3 groups were statistically significantly associated with central obesity, low HDL and hypertriglyceridaemia.

AD and MetS, have , in common, some environmental factors, such as recent changes of lifestyle (11, 12). We propose several other mechanisms to explain the association between MetS and AD.

The first point, which we considered, was that there might be a link between MetS and AD, based on the previously reported associations between MetS and allergic diseases. For example, MetS has reportedly been associated with allergic asthma. MetS including high WC and elevated glucose was associated with asthma in adults in the HUNT study (13). Furthermore, it was suggested that nitric oxide-arginine metabolism abnormalities in patients of MetS might lead to development of asthma. It suggests a possible link between the two diseases. Therefore, we suggest that, in AD, these cells act in a similar mechanism, implying a link between MetS and AD. Another point that we considered was that the association between each MetS component and AD or allergic diseases has been proposed previously (5, 14–18). The factors of MetS include central obesity, hypertension, dyslipidaemia, and hyperglycaemic tendencies, which are characterized by insulin resistance and hyperinsulinism. Abdominal obesity, in particular, is a strong risk component of MetS. Silverberg et al. (19) showed that AD may have an association with central obesity. In some studies, obesity has been suggested to be a chronic low-grade inflammatory condition and influences the immune system through various channels affecting adipose tissue, leukocytes, endothelial cells, and mast cells. Also, obesity promotes the production of proinflammatory mediators, such as TNF-α and IL-6, and alteration of adipokine and leptin profile (20). Chitinase 3–like 1, a glycoprotein associated with a number of inflammatory disease, is involved in the development of Th2 response in asthma and the genetic variation of encoding gene (CHI3L1) has also been known to be associated with atopy. (21). Ahangari et al. (22) showed that Chi3l1 also plays an important role in white adipose tissue accumulation as well as Th2 inflammation. It has been reported that Sirtuin1-Chi3l1 is involved in the pathogenesis of obesity. The positive association between central obesity and the presence of AD, as demonstrated in this study, may be understood in the same way. Although lipid profiles are other critical factor of MetS, there have been only a few studies with limited samples (6, 7). In this larger study, we found that female patients with AD were more likely to have hypertriglyceridaemia than non-AD females. Moreover, Yeh & Huang (23) showed that dyslipidaemia enhances Th2 response and allergic inflammation. In addition, HDL levels are inversely related to AD, while LDL levels are positively related to IgE level, AD, and allergic sensitization (6, 24). Recently, Seino et al. (7) also found that TG accumulation was promoted in the liver of mouse with AD. The authors suggested that stress triggered by AD might influence lipid and sugar metabolism, which resulted in MetS. Notably, this study showed a synergy between central obesity and hypertriglyceridaemia in AD. Insulin resistance, which is thought to be linked with MetS, has been proposed to be a risk factor for allergic diseases (5, 25). In addition, Singh et al. showed that insulin resistance is a strong, independent risk factor for asthma, explaining a connection between asthma and MetS (26). However, in the present study, an association between hyperglycaemia and AD was not demonstrated.

Furthermore, in our study, BMI, WC, BF, and TG level were higher in the group with AD coexistent with AR or asthma than in the group with AD alone. Takeuchi et al. (27) reported that HDL levels were lower in AD with allergic diseases than those in AD alone. Several genome-wide association studies have shown that AD and asthma have partially overlapping genes (28). Kim et al. (29) reported that *FLG* p.P478S variant significantly increased the risk of AD, AR, and asthma in general. In this respect, we suggest that patients with AD who have other allergic diseases are more likely to have MetS than patients with AD alone.

In our study, a statistically significant association between MetS (and increased WC and TG) and the presence of AD was demonstrated in only female subjects. Oestrogen is generally known to enhance the activity of eosinophil and inhibit the production of cortisol (30). Therefore, females are more prone to have more severe allergy. Such a mechanism might play a role in the sex differences found in this study.

To date, the association between MetS and AD has been unclear. The results of this study demonstrate that MetS and its components, including increased WC and TG, had a positive association with AD in Korean women. Moreover, a synergy between WC and TG was found in the prevalence of AD.

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The authors declare no conflicts of interest.

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