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Fermented food intake is associated with a reduced likelihood of atopic dermatitis in an adult population (Korean National Health and Nutrition Examination Survey 2012–2013)

Sunmin Park^a, Ji-Hyun Bae^{b,*}^a Department of Food and Nutrition, Diabetes/Obesity Center, Hoseo University, Asan, Republic of Korea^b Department of Food Science and Nutrition, Keimyung University, Daegu, Republic of Korea

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ABSTRACT

The prevalence of atopic dermatitis (AD) has continuously increased throughout the world in every age group, and the recent increase in AD in Korean adults may be related to changes in nutrient intakes due to westernization of dietary patterns. We hypothesized that the prevalence of AD is associated with the different dietary patterns and fermented food intakes of the Korean adult population. We examined the hypothesis using 9763 adults 19 years or older using the 2012–2013 Korean National Health and Nutrition Examination Survey. We identified 4 dietary patterns in addition to that including fermented foods using principal component analysis on data obtained from a 116-item validated semiquantitative food frequency questionnaire: meat and processed foods; vegetables, fruits, legumes, seafood, and seaweed; rice and grains; and coffee, chocolate, and ice cream. Adjusted odds ratios (ORs) for AD were calculated according to dietary patterns after adjusting for potential confounders. High levels of consumption (>92 times/month) of fermented foods such as doenjang, chungkookjang, kimchi, fermented seafood, makgeolli, and beer were associated with a lower prevalence of AD (OR, 0.56; 95% confidence interval [CI], 0.37–0.84). In contrast, high levels of consumption of meat and processed foods were strongly associated with the prevalence of AD (OR, 2.42; 95% CI, 1.48–3.94). Interestingly, the consumption of coffee, chocolate, and ice cream was significantly negatively associated with the prevalence of AD (OR, 0.53; 95% CI, 0.34–0.82). In conclusion, the hypothesis was accepted. The results can be applied to nutrition education programs for the general population to decrease risk factors for AD.

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Abbreviations: AD, atopic dermatitis; BMI, body mass index; CC, coffee, chocolate, and ice cream; CI, confidence interval; FF, fermented foods; IL, interleukin; KNHANES, Korean National Health and Nutrition Examination Survey; MP, meat and processed foods; OR, odds ratio; RG, rice and grains; Th, T-helper cell; VF, vegetables, fruits, legumes, seafoods, and seaweeds.

* Corresponding author at: Food Science and Nutrition, Dean of Faculty in Food & Health Sciences, Keimyung University, 1000 Shindang-dong, Dalseo-gu, Daegu, 704-701, Republic of Korea. Tel.: +82 53 580 5875; fax: +82 53 580 5885.

E-mail addresses: jhb@kmu.ac.kr, drjhbae@hanmail.net (J.-H. Bae).

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1. Introduction

Atopic dermatitis (AD) is more common in infants and children than in adults (approximately 20% vs 3%–6% prevalence in the United States) [1]. There are also ethnic differences in the prevalence of AD, and it occurred in approximately 2.5% of Korean adults during 2008 to 2010, which was greater than 30 years ago [2]. However, the prevalence of AD has continuously increased throughout the world in every age group, even in adults in industrialized countries, including Korea [3]. Its increase might also be associated with dietary patterns due to industrialization. The etiology of AD remains unknown, but it is related to immune dysfunction and epidermal barrier dysfunction [1,4]. Especially, in infants, AD is related to the immature intestinal and skin barriers, and certain foods act as antigens to activate unnecessary immune response [1]. Even in adults, certain foods and environmental factors induce overreactive immune responses, although intestinal barriers are intact and their overactivation by various mechanisms may be associated with AD in adults [4].

Many studies have been conducted in infants, children, and adults that evaluate allergenic foods and environmental factors, but the aggravating and relieving factors remain controversial [4–7]. Therefore, it is important to examine AD risk factors and preventive measures for AD especially in adults. The use of probiotics, mainly *Lactobacillus* species, has demonstrated preventive effects on the development of AD in infants [5], children [6], and adults [7]. According to a meta-analysis of 6 randomized clinical trials of infants, the combined risk ratio of the prevalence of AD associated with the long-term use of supplementary probiotics was 0.86 (95% confidence interval [CI], 0.77–0.96) compared with the placebo control [7]. In addition, a double-blinded, randomized clinical trial with adult AD patients demonstrate that the consumption of heat-killed *Lactobacillus acidophilus* strain L-92 decreased the incidence of skin lesions and eosinophil counts in comparison to the consumption of placebo. These results suggest that *L. acidophilus* strain L-92 is effective for AD symptoms in adult patients [7]. Thus, the use of probiotics is likely to have long-term preventive effects on AD even in adults.

However, the effect of fermented foods (FF) on AD has not been studied in randomized clinical trials, although a beneficial effect has been reported in experimental animal models [8,9]. Kimchi contains several strains of *Lactobacillus plantarum*, some of which were shown to suppress AD-like skin lesions and epidermal thickening, with decreased serum immunoglobulin E levels and T-helper cell (Th)–producing cytokines, in house dust mite-induced dermatitis in NC/Nga mice [10]. In addition, treatment with chungkookjang, a Korean fermented soy food, has been demonstrated to reduce ear thickness, dermis thickness, auricular lymph node weight, and infiltration of mast cells in IL-4/Luc/CNS-1 transgenic mice with AD-like symptoms [9]. Thus, FF may play an important role in preventing AD. Koreans have traditionally consumed various FF such as chungkookjang, deonjang, kochjang, kimchi, and pickled vegetables, but consumption of these foods has decreased in the last decade.

Therefore, the decreased consumption of FF may be associated with the increased prevalence of AD. In addition to the consumption of FF, the westernization of food intake, such as increased consumption of meats and processed foods (MP) and decreased consumption of rice and grains (RG), may affect the prevalence of AD.

We hypothesized that the prevalence of AD is associated with the different dietary patterns and consumptions of FF in the Korean adult population. We tested the hypothesis independent of potential confounding factors, in adults 19 years or older using data from the 2012–2013 Korean National Health and Nutrition Examination Survey (KNHANES), a large South Korean population-level study based on a stratified multistage probability sampling design.

2. Methods and materials

2.1. Data collection

2.1.1. Data and participants

This study used data from the 2-year KNHANES conducted from 2012 to 2013, which was obtained from KNHANES V (2012) and KNHANES VI (2013). KNHANES is conducted annually using a rolling sampling design that involves a complex, stratified, multistage, probability-cluster survey of a representative sample of the civilian population in South Korea [11]. The survey is performed by the Korean Centers for Disease Control and Prevention and the Korean Ministry of Health and Welfare, and it has 3 components: health interviews, health examinations, and nutrition surveys [12]. The Institutional Review Board of the Korean Centers for Disease Control and Prevention and the Keimyung University Institutional Review Board reviewed and approved the survey (approval nos. 2012-01EXP-01-2C, 2013-07CON-03-4C, 2013-12EXP-03-5C, and 2015-01-HR-05-01) [13]. The study was carried out in accordance with the recommendations for strengthening the reporting of observational studies in epidemiology statement [14]. The present cross-sectional analysis was restricted to participants aged 19 years or older who completed the health examination and the nutrition survey ($n = 9763$; 3875 men and 5888 women). Information regarding age, educational level, income, residential area, smoking history, and alcohol consumption was collected during the health interview according to the KNHANES manual [12].

2.1.2. Variables for general information of participants

Age was categorized into 2 groups (19–50 and 51–65 years). Educational level was categorized into 3 groups: less than high school, high school, and college or more. Height and weight measurements were performed with the participants wearing light clothing without shoes. Body mass index (BMI) was calculated as weight (in kilograms) divided by the square of height (in meters). Waist circumference was measured midway between the costal margin and the iliac crest at the end of normal expiration [12]. Participants were categorized into 3 groups according to the obesity references for Asian populations [13]: lean ($\text{BMI} < 18.5$), normal ($18.5 \leq \text{BMI} < 25$),

and obese (BMI ≥ 25). Smoking status was divided into 3 categories based on self-reported cigarette consumption: nonsmoker, former smoker, and current smoker [11]. Nonsmokers had smoked less than 100 cigarettes in their lifetime, and participants who smoked greater than or equal to 100 cigarettes were categorized as former or current smokers based on their current cigarette consumption. Alcohol consumption was assessed by asking participants about their drinking behavior during the month before the interview. Participants were also asked about the frequency (servings/month) with which they consumed alcoholic beverages [12]. Alcohol consumption was categorized into 2 groups according to daily alcohol intake: nondrinker and drinker. Regular exercise was defined as participation in moderate exercise (slow swimming, doubles tennis, volleyball, or occupational or recreational activity involving carrying light objects) on a regular basis for more than 30 minutes at a time at least 5 times per week or participation in vigorous exercise (running, climbing, fast cycling, fast swimming, football, basketball, rope jumping, squash, singles tennis, or occupational or recreational activity involving carrying heavy objects) for more than 20 minutes at a time at least 3 times per week [12].

2.1.3. Definition of AD

The presence of AD was defined as a positive response to the following question in the health interview: “Have you been diagnosed with AD by a doctor?” [12].

2.1.4. Biochemical variables

Blood samples were collected after a 12-hour overnight fast. They were properly processed and transported in cold storage to the central laboratories (Seoul Medical Science Institute, Seoul, Korea, and Seegene Medical Foundation, Seoul, Korea) within 24 hours. Serum 25-OH-D levels were measured with a radioimmunoassay kit (DiaSorin, Stillwater, MN, USA) using a 1470 Wizard gamma counter (Perkin-Elmer, Turku, Finland). The interassay variation coefficients were 7.6% and 7.2% at 14.7 ng/mL and 52.5 ng/mL, respectively [15]. All clinical analyses were performed by the Neodin Medical Institute, a laboratory authorized by the Korean Ministry of Health and Welfare.

2.1.5. Dietary variables

All participants were instructed to maintain their usual dietary habits before assessing their dietary intake. Daily energy intake was calculated with the Can-Pro 4.0 nutrient intake assessment software developed by the Korean Nutrition Society. Dietary intake information was collected by administering a validated semiquantitative food frequency questionnaire to each participant [16]. This questionnaire requested information regarding participants’ consumption of 116 food items, and the frequency of food intake was quantified using 9 categories: “never or seldom,” “once a month,” “2 to 3 times a month,” “once a week,” “2 to 4 times a week,” “5 to 6 times a week,” “once a day,” “twice a day,” and “3 times a day.”

Questions about the intake of FF, such as doenjang, cheonggukjang, kimchi, fermented seafood (crab, anchovies, shrimp, and squid), makgeolli, and beer, were asked, and the frequencies of the consumption of these foods were summed

for statistical analysis. Fermented food intake was divided into 3 categories (<54 times per month, 54 to 92 times per month, and >92 times per month) according to the frequency of the consumption of sum of FF.

2.2. Statistical analyses

Statistical analyses were performed using SPSS software (version 21; IBM SPSS Statistics, New York, NY, USA). Sample weights were used in all analyses to produce estimates that were representative of the Korean civilian population. The sample size was calculated using the G-power program ($\alpha = .05$; power = 0.95; effect size = 0.25); the total calculated sample size for χ^2 test and analysis of covariance was approximately 317 and 400, respectively. The sample size was sufficient for each group because non-AD and AD groups consisted of 9536 and 227 participants, respectively.

Dietary patterns were generated by using principal component analysis on the 24 predefined food groups. We determined the number of factors to retain based on eigenvalues greater than 1.0, and we were able to extract 4 major dietary patterns, which explained 52% of the total variance in adults [17]. The orthogonal rotation procedure (varimax) yielded 4 dietary patterns uncorrelated to each other. Foods with factor loading values greater than or equal to 0.48 were considered to have made important contributions to the specific pattern [18]: “meat and processed foods (MP) group”; “vegetables, fruits, legumes, seafood, and seaweed (VF) group”; “rice and grains (RG) group”; and “coffee, chocolate, and ice cream (CC) group”. An FF group was additionally generated as a separate group for examining the association with the prevalence of AD. The descriptive statistics for participants were determined by the frequency distribution of variables such as age, residential area, smoking and drinking status, regular exercise, and obesity. The frequency distribution according to the classification variable was analyzed using the χ^2 test. Data for continuous variables were presented as means $\pm$ SDs.

Odds ratios (ORs) and 95% CIs for having AD were calculated according to dietary patterns, while controlling for covariates (sex, age, educational level, income, BMI, energy intake, residential area, smoking status, alcohol consumption, and exercise) using logistic regression to incorporate the sample weights given the complex sample design of the survey [15]. Unadjusted and adjusted means and 95% CIs of BMI, serum 25-OH-D levels, and daily nutrient intakes according to the tertiles of food groups were calculated using analysis of covariance. The covariates used for adjusted means were age, sex, education level, income level, BMI, energy intake, residence area, the status of smoking, drinking, and exercise.

3. Results

3.1. General characteristics according to the prevalence of AD

Table 1 shows the demographic characteristics of the participants with and without AD. Of the 9763 participants aged 19 years or older, 2.3% (227) had AD. Participants with and

Table 1 – Demographic characteristics of participants according to AD in adults 19 years or older using the 2012–2013 KNHANES database

Variable	AD		P
	Without	With	
Sample sizes	9536	227	
Age (y) ^a	46.0 ± 0.3	33.3 ± 0.9	<.001
Age (y) ^b			<.001
19–50	4529 (71.7%)	171 (90.8%)	
51–65	2699 (28.3%)	30 (9.2%)	
Sex			.854
Male	3790 (49.1%)	85 (49.9%)	
Female	5746 (50.9%)	142 (50.1%)	
Residence area			.287
Urban	7583 (82.1%)	189 (85.0%)	
Rural	1953 (17.9%)	38 (15.0%)	
Education level			<.001
<High school	3507 (27.9%)	75 (13.5)	
High school	3178 (39.5%)	107 (57.8%)	
College and more	2828 (33.4%)	77 (30.6%)	
Obesity			.393
Lean	413 (4.7%)	15 (7.0%)	
Normal	6054 (63.0%)	140 (62.2%)	
Obese	3015 (32.2%)	70 (30.8%)	
Exercise			.683
No	8917 (93.6%)	210 (92.7%)	
Yes	567 (6.4%)	17 (7.3%)	
Smoking status			.706
Never	5865 (55.7%)	136 (58.4%)	
Former	1846 (20.3%)	38 (17.5%)	
Current	1683 (24.0%)	45 (24.1%)	
Drinking status			.173
No	4770 (43.5%)	104 (37.9%)	
Yes	4731 (56.5%)	123 (62.1%)	
Income level			.540
High	2385 (24.2%)	57 (24.6%)	
Middle	4878 (50.4%)	102 (46.2%)	
Low	2288 (25.5%)	64 (29.1%)	

^a Values are means ± SDs and calculated using the generalized linear model.

^b Values are frequencies and percentages according to the presence of AD and the statistical differences were analyzed using the χ^2 test.

without AD differed significantly with respect to age and educational level but not with regard to sex, residential area, obesity, exercise, smoking status, and alcohol consumption. The average age of participants with AD was 33.3 years, and younger participants with a high school education developed AD more frequently.

Table 2 shows the unadjusted and adjusted mean values and 95% CIs of several biochemical parameters and markers of nutritional status associated with the prevalence of AD. Model 1 represented unadjusted means, model 2 described adjusted means calculated after adjusting for age and sex, and model 3 adjusted for age, sex, educational level, income, BMI, energy intake, residential area, smoking status, alcohol consumption, and exercise. Body mass index, an indicator of obesity, was not associated with the prevalence of AD with or without adjusting for potential confounders, whereas waist circumference was negatively related to AD without adjusting for potential confounders. Serum 25-OH-D, an index of

vitamin D status, was not significantly associated with AD. The daily energy intake of participants with and without AD differed significantly after adjusting for age and sex. In the absence of adjustment for these covariates, fat intake was positively associated with AD (21.3%, 20.0–22.6) in comparison with non-AD (19.4%, 19.1–19.7), but protein intake was negatively associated with AD (14.0%, 13.2–14.8) after adjusting for all covariates in model 3. Thus, protein intake may influence the development of AD.

3.2. Consumption of each food category according to AD

Using food frequency data, 4 different dietary patterns (MP, VF, RG, and CC groups) were generated by using principal component analysis, and the FF group was included separately. The unadjusted and adjusted frequencies with which the food groups, corresponding to the dietary patterns, were consumed are presented in Table 3 according to food categories. Adjusted frequencies in models 2 and 3 were calculated after adjusting for the covariates of age and sex in model 2 and for all covariates in model 2 plus education level, income level, BMI, energy intake, residence area, the status of smoking, drinking, and exercise, respectively. The frequency with which foods in the FF group were consumed was significantly higher in participants without AD (72.3 and 73.2 servings consumed per month) than in those with AD (65.7 and 67.2 servings consumed per month) in models 1 and 3, respectively. The frequency with which foods in the MP group were consumed was significantly higher in participants with AD (93.7, 78.8, and 80.7 servings consumed per month) than in those without AD (73.4, 64.8, and 66.5 servings consumed per month) in models 1, 2, and 3, respectively, after adjusting for potential confounders. Participants without AD consumed more foods in the RG group than did those with AD without adjusting for the potential covariates. However, the frequencies for the CC group were much higher in participants without AD (114.8, 115.8, and 122.0 servings consumed per month) than in those with AD (87.5, 89.5, and 96.8 servings consumed per month) in models 1, 2, and 3, respectively.

3.3. Biochemical parameters and nutrient intakes according to dietary patterns

The participants were divided into tertiles according to the frequency of consumption of different dietary patterns. The participants in the high-tertile groups for FF, VF, and RG were older than those in the low-tertile groups, whereas participants in the high-tertile group for MP were younger than those in the low-tertile group (Table 4). A higher percentage of men consumed FF, MP, and coffee and desserts, but men consumed less dietary fiber-rich foods and RG. Nondrinking participants ate less FF, MP, RG, and coffee, and those who consumed alcohol ate more MP.

Participants with a high BMI consumed more in all food categories except MP than those with a low BMI (Table 5). Serum levels of 25-OH-D, an indicator of vitamin D status, were higher participants in the high-tertile groups for FF, VF, RG, and CC, but 25-OH-D levels were lower in the high-tertile group for MP. As expected, participants whose diets were high in MP had a higher intake of protein and fat than did those

Table 2 – Biochemical parameters and nutrient intakes according to AD after covariate adjustment in adults 19 years or older using the 2012–2013 KNHANES database

	Model 1 ^a			Model 2 ^b			Model 3 ^c		
	Without AD	With AD	P	Without AD	With AD	P	Without AD	With AD	P
Sample sizes	9536	227		9536	227		9536	227	
FF	72.3 (71.0–73.6)	65.7 (60.0–71.5)	.027	74.0 (77.7–75.3)	68.7 (63.1–74.4)	.071	73.2 (70.9–75.5)	67.2 (61.4–73.1)	.035
Meat processed foods	73.4 (71.8–75.1)	93.7 (85.7–101.6)	<.001	64.8 (63.4–66.2)	78.8 (71.2–86.5)	<.001	66.5 (63.7–69.2)	80.7 (73.0–88.4)	<.001
VF	232.9 (229.1–236.7)	228.0 (209.0–247.0)	.615	237.3 (233.4–241.2)	235.7 (216.7–254.6)	.866	241.9 (234.7–249.0)	238.7 (220.2–257.2)	.737
RG	71.6 (70.8–72.4)	67.0 (63.4–70.5)	.010	73.8 (73.1–74.6)	70.9 (67.4–74.4)	.099	73.8 (72.4–75.2)	70.6 (67.1–74.1)	.060
CC	114.8 (111.7–118.0)	87.5 (71.9–103.2)	.001	115.8 (112.6–119.0)	89.5 (74.1–104.8)	.001	122.0 (116.0–128.1)	96.8 (81.2–112.4)	.001

Values are unadjusted and adjusted means and 95% CIs analyzed by analysis of covariance without and with various covariates.

^a Model 1, no adjustment.

^b Model 2, adjusted for sex and age.

^c Model 3, adjusted for all covariates in model 2 plus education level, income level, BMI, energy intake, residence area, the status of smoking, drinking, and exercise.

whose diets were low in those types of foods, whereas those whose diets were high in RG and in coffee and desserts had lower protein and fat intake.

3.4. Association between AD and FF and different dietary patterns

The adjusted ORs and 95% CI values for the prevalence of AD were calculated according to the tertiles of consumption of FF, MP, VF, RG, or CC group with and without adjustment for covariates (Table 6). The covariates in model 2 were age and sex, and those in model 3 were age, sex, educational level, income, BMI, residential area, smoking status, alcohol consumption, and exercise. Those who frequently consumed (>92 times/month) FF showed significantly lower ORs (0.58) for AD compared with those who consumed these foods less frequently (reference group) regardless of the adjustment for potential confounders. The ORs for the MP groups were opposite to those in the FF groups, as the participants in the high-tertile group for MP were 3.06 times more likely to develop AD according to the analysis conducted without adjusting for covariates, 2.27 times more likely to do so when adjusting for sex and age, and 2.42

times more likely to do so with adjustment for sex, age, educational level, income, BMI, energy intake, residential area, smoking status, alcohol consumption, and exercise. However, the ORs for having AD were not affected by the frequency of consuming VF and RG after adjustment for covariates. Surprisingly, the ORs for having AD were significantly lower in participants in the high tertile of the CC group.

4. Discussion

We hypothesized that the prevalence of AD is associated with the different dietary patterns and FF intake of the Korean adult population. The results indicated that the hypothesis was correct: the prevalence of AD was positively associated with the dietary pattern that includes a high consumption of MP, whereas it was negatively related to the dietary pattern that includes a high consumption of RG and a high consumption of FF. Thus, the westernization of dietary patterns may be a risk factor for AD in the Korean adult population. This is a novel finding that shows the association between the dietary pattern changes and the prevalence of AD.

Table 3 – The consumption frequencies of each food category according to AD

	Model 1 ^a			Model 2 ^b			Model 3 ^c		
	Without AD	With AD	P	Without AD	With AD	P	Without AD	With AD	P
Sample size	9536	227		9536	227		9536	227	
BMI (kg/m ²)	23.7 (23.6–23.8)	23.8 (23.0–24.5)	.927	23.9 (23.8–24.0)	24.1 (23.3–24.8)	.853	24.1 (23.9–24.4)	24.3 (23.5–25.1)	.711
Waist circumferences (cm)	77.2 (76.8–77.6)	68.6 (119–685)	<.001	81.0 (80.1–81.4)	80.9 (79.1–82.8)	.925	80.7 (80.4–81.1)	80.2 (79.5–81.0)	.161
Serum 25-OH-D (ng/mL)	16.8 (16.5–17.1)	16.0 (14.9–17.0)	.082	17.1 (16.7–17.4)	16.9 (15.8–17.9)	.658	18.4 (17.8–19.1)	18.0 (16.8–19.2)	.365
Energy intake (kcal/d)	2067 (2037–2094)	2188 (1979–2397)	.252	2146 (2120–2172)	2373 (2220–2525)	.004	2331 (2164–2298)	2204 (1988–2421)	.798
Fat intake (%)	19.4 (19.1–19.7)	21.3 (20.0–22.6)	.005	19.2 (18.9–19.5)	19.3 (17.9–20.7)	.889	19.1 (18.5–19.6)	19.4 (17.9–20.9)	.690
Carbohydrate intake (%)	65.8 (65.4–66.2)	64.2 (62.6–65.8)	.043	65.9 (65.5–66.3)	66.5 (64.8–68.1)	.500	66.2 (65.5–66.9)	66.7 (64.8–68.6)	.587
Protein intake (%)	14.8 (14.7–15.0)	14.5 (13.9–15.1)	.392	14.9 (14.7–15.1)	14.2 (13.6–14.9)	.053	14.8 (14.4–15.1)	14.0 (13.2–14.8)	.034

Values were servings consumed per month. They were unadjusted or adjusted means and 95% CIs analyzed by analysis of covariance without and with various covariates.

^a Model 1, no adjustment.

^b Model 2, adjusted for sex and age.

^c Model 3, adjusted for all covariates in model 2 plus education level, income level, BMI, energy intake, residence area, the status of smoking, drinking, and exercise.

Table 4 – Demographic characteristics according to the tertile categories of FF consumption and dietary patterns in adults 19 years or older using the 2012-2013 KNHANES

Servings/month	FF				MP				VF				RG				CC			
	Times/mo	Times/mo	Times/mo	P	T1	T2	T3	P	T1	T2	T3	P	T1	T2	T3	P	T1	T2	T3	P
	<54	54-92	>92		<44	44-80	>80		<186	186-271	>271		<62	62-90	>90		<48	48-168	>168	
Sample size	2385	2368	2369		2410	2376	2366		2367	2377	2378		2600	2571	1951		2390	2381	2351	
Age (%)				<.001				<.001				<.001				<.001				.001
19-50	35.6 ^a	35.9	28.5		20.6	34.0	45.4		38.7	31.7	29.6		45.3	36.0	18.7		35.5	31.3	33.2	
50-65	29.1	31.4	39.6		55.5	30.7	13.7		29.2	35.6	35.3		25.5	38.1	36.4		30.4	33.2	36.4	
Sex (male %)	28.8	36.9	34.3	<.001	25.9	32.4	41.7	<.001	37.3	32.6	30.0	.184	38.5	40.4	21.0	<.001	30.1	27.3	42.6	<.001
Exercise (%)				.634				.007				.037				.183				.420
Yes	31.9	37.0	31.1		26.2	28.0	45.8		29.7	35.0	35.3		39.1	33.3	27.6		37.4	28.8	33.9	
No	34.1	34.6	31.2		29.9	33.3	36.8		36.8	32.3	30.9		40.1	36.6	23.2		34.4	32.2	33.4	
Smoking status (%)				<.001				<.001				.001				<.001				<.001
Current	29.9	37.3	32.8		23.2	34.3	42.5		41.0	31.6	27.4		48.8	35.4	15.8		21.9	26.1	52.0	
Former	31.1	34.8	34.1		32.1	30.0	37.8		35.8	30.1	34.1		34.1	39.6	26.3		34.3	29.9	35.8	
Never	36.9	33.6	29.5		31.7	33.3	34.9		34.4	33.7	31.9		38.1	35.8	26.2		40.5	35.4	24.1	
Drinking status (%)				.009				<.001				.465				<.001				<.001
Yes	32.4	35.2	32.5		25.3	33.0	41.7		36.8	32.7	30.5		43.5	36.3	20.3		32.4	32.5	35.1	
No	36.5	34.2	29.3		36.2	32.9	30.8		35.7	32.0	32.2		34.9	36.6	28.6		38.0	31.1	30.9	

^a Values were means for servings per month. The statistical differences were analyzed using the χ^2 test.

Table 5 – Biochemical parameters and nutrient intakes according to tertiles of FF consumption and dietary patterns in adults 19 years or older using the 2012-2013 KNHANES

Servings/month	FF				MP				VF				RG				CC			
	Times/mo	Times/mo	Times/mo	P	T1	T2	T3	P	T1	T2	T3	P	T1	T2	T3	P	T1	T2	T3	P
	<54	54-92	>92		<44	44-80	>80		<186	186-271	>271		<62	62-90	>90		<48	48-168	>168	
Sample size	2385	2368	2369		2410	2376	2366		2367	2377	2378		2600	2571	1951		2390	2381	2351	
BMI (kg/m ²)	23.3 ± 0.1	23.8 ± 0.1	24.0 ± 0.1	<.001	24.1 ± 0.1	23.6 ± 0.1	23.5 ± 0.1	<.001	23.5 ± 0.1	23.8 ± 0.1	23.9 ± 0.1	.002	23.5 ± 0.1	23.9 ± 0.1	23.9 ± 0.1	.002	23.5 ± 0.1	23.8 ± 0.1	23.9 ± 0.1	.005
Serum 25-OH-D (ng/mL)	16.1 ± 0.2	16.4 ± 0.2	17.1 ± 0.3	.002	17.1 ± 0.2	16.2 ± 0.2	16.3 ± 0.2	.001	16.1 ± 0.2	16.6 ± 0.2	16.8 ± 0.2	.020	15.9 ± 0.2	16.5 ± 0.2	17.5 ± 0.2	<.001	16.2 ± 0.2	16.3 ± 0.2	17.0 ± 0.2	.001
Energy intake (kcal/d)	2029 ± 28	2156 ± 23	2267 ± 29	<.001	1924 ± 24	2114 ± 25	2355 ± 28	<.001	2048 ± 23	2183 ± 25	2225 ± 29	<.001	2081 ± 24	2221 ± 25	2148 ± 32	<.001	2062 ± 29	2066 ± 24	2310 ± 26	<.001
Carbohydrates (%)	63.5 ± 0.34	63.5 ± 0.3	65.7 ± 0.3	<.001	68.2 ± 0.3	64.2 ± 0.3	61.0 ± 0.3	<.001	63.8 ± 0.3	64.4 ± 0.3	64.5 ± 0.3	.241	62.3 ± 0.3	64.4 ± 0.3	67.1 ± 0.3	<.001	63.4 ± 0.3	64.1 ± 0.3	65.1 ± 0.3	<.001
Protein (%)	14.9 ± 0.1	15.2 ± 0.1	15.1 ± 0.1	.105	14.6 ± 0.1	15.0 ± 0.1	15.6 ± 0.1	<.001	14.9 ± 0.1	15.2 ± 0.1	15.3 ± 0.1	.077	15.3 ± 0.1	15.1 ± 0.1	14.7 ± 0.1	.007	15.4 ± 0.1	15.2 ± 0.1	14.7 ± 0.1	<.001
Fat (%)	21.6 ± 0.27	21.2 ± 0.2	19.1 ± 0.2	<.001	17.2 ± 0.3	20.8 ± 0.3	23.4 ± 0.2	<.001	21.4 ± 0.3	20.4 ± 0.2	20.3 ± 0.2	.005	22.4 ± 0.2	20.5 ± 0.2	18.1 ± 0.3	<.001	21.2 ± 0.3	20.7 ± 0.3	20.2 ± 0.2	.012
Sodium (mg/d)	4265 ± 92	4723 ± 75	5301 ± 91	<.001	4380 ± 91	4656 ± 81	5125 ± 83	<.001	4298 ± 73	4906 ± 82	5111 ± 95	<.001	4486 ± 73	4973 ± 88	4853 ± 101	<.001	4554 ± 100	4572 ± 76	5112 ± 79	<.001

Values are means ± SDs and calculated using the generalized linear model.

Table 6 – Association between AD and the consumption of FF and dietary patterns in adults 19 years or older using the 2012–2013 KNHANES

Servings/ month	FF	MP			VF			RG			CC		
		T1	T2	P	T1	T2	P	T1	T2	P	T1	T2	P
		44	44–80	>80	<186	186–271	>271	<62	62–90	>90	<48	48–168	>168
Sample size		2385	2368	2369	2367	2377	2378	2600	2571	1951	2390	2381	2351
Model 1 ^a	1	0.75 (0.51–1.11)	0.58 (0.36–0.83)	.016	1	1.04 (0.73–1.48)	0.83 (0.54–1.27)	.556	1	0.81 (0.55–1.18)	0.49 (0.30–0.80)	0.56 (0.36–0.88)	0.50 (0.33–0.78)
Model 2 ^b	1	0.76 (0.51–1.12)	0.60 (0.40–0.91)	.051	1	1.12 (0.78–1.60)	0.89 (0.58–1.37)	.583	1	0.88 (0.60–1.29)	0.60 (0.38–0.99)	0.58 (0.37–0.91)	0.52 (0.34–0.80)
Model 3 ^c	1	0.77 (0.52–1.14)	0.56 (0.37–0.84)	.022	1	1.13 (0.80–1.61)	0.86 (0.56–1.33)	.450	1	0.85 (0.58–1.24)	0.58 (0.36–0.93)	0.61 (0.39–0.97)	0.53 (0.34–0.82)

Unadjusted and adjusted ORs and 95% CIs and statistical differences were analyzed using logistic regression without and with adjusting for covariates.

^a Model 1, no adjustment.

^b Model 2, adjusted for sex and age.

^c Model 3, adjusted for all covariates in model 2 plus education level, income level, BMI, energy intake, residence area, the status of smoking, drinking, and exercise.

Recent studies have suggested that FF might be useful in the management of AD [10,19]. Chungkukjang, a Korean fermented soybean product including *Bacillus subtilis*, contains a high concentration of γ -aminobutyric acid and has been found to be effective for the treatment of AD in an animal study [9]. Although some soybean proteins are known food allergens, these allergens may have been completely removed by the fermentation, salting-out, and cooking procedures in preparing fermented soybean pastes [20]. Doenjang, a Korean FF product made from rice or barley with soybeans fermented by the fungal *Aspergillus* species, has been reported to contain orthohydroxydaidzein and orthohydroxygenistein, which are soy isoflavones that are known to inhibit lipopolysaccharide-induced nitric oxide, tumor necrosis factor α , and interleukin (IL) 6 production, which have been suggested as targets for treating AD in NC/Nga mice [21,22]. *L. plantarum* and *Lactobacillus sakei* probio 65 isolated from kimchi in that study were also found to be potentially useful for preventing AD by altering the balance of the Th1/Th2 ratio and increasing the IL-10, which has a suppressive effect on AD [10,23].

Heavy metal pollution in the ocean has become a serious problem in contemporary society, and consumers avoid seafood because of this threat. The use of microbial biosorbents to sequester metals from diluted aqueous solutions has been studied, and this process could occur naturally during seafood fermentation [24]. The anchovies, shrimp, and squid products examined in this study were washed and packed with salt in wooden boxes to ferment and slowly pressed, yielding the salty, fishy liquid along with the fermented seafood. During this washing and pickling process, considerable quantities of harmful chemicals, such as heavy metals, can be removed. The elimination of heavy metals from contaminated food during fermentation could ameliorate inflammatory or allergic conditions such as AD or eczema [25]. The salting process during fermentation induces osmosis in the cell, which effectively removes the heavy metals by osmotic pressure across the cell membrane [26]. This might explain why the salty fermented seafood in this study was associated with fewer symptoms of AD.

The health benefits of FF can be acquired either directly from ingested live microorganisms, such as bacteria or yeast, or indirectly from the ingestion of biogenic metabolites produced during the fermentation process. Bioactive peptides (biogenic peptides released from food proteins by microbial proteolysis during fermentation) have been known to have immunostimulating effects, such as increasing immunoglobulin A-producing cells and macrophage activity, leading to the prevention of infectious diseases [27]. Conjugated linoleic acid produced during fermentation has been found to be effective for treating AD [28]. During fermentation, vitamins such as vitamin K and vitamin B₁₂ could be synthesized by microbes; these vitamins play an important role in host health, including the prevention of atopic diseases. For example, vitamin K₂ or menaquinone, which is a lipophilic vitamin that can be found in FF, has been reported to be useful for the treatment of AD [29]. Vitamin B₁₂, which is found only in foods fermented by B₁₂-producing probiotic lactic acid bacteria, such as *L. plantarum*, has also been shown to exert a protective effect against AD [30,31].

Of interest is that the vegetable and fruit pattern and the RG pattern showed no significant effect on AD, although the

RG pattern appeared more effective for reducing the prevalence of AD than the vegetable and fruit pattern. During fermentation, residual pesticides have been reported to be degraded by microorganisms, such as *Saccharomyces cerevisiae* and lactic acid bacteria [32,33]. Beer consumption in Korea has been continuously increasing since 2010, and an average annual consumption of 2.01 L per person was reported in 2012 [34]. Oral administration of the water extract of hops, one of the main ingredients in beer, has been reported to ameliorate AD in the NC/Nga mice model [35]. Makgeolli, a traditional Korean fermented alcohol, has been reported to contain probiotics such as *L. plantarum*, *Lactobacillus brevis*, *Lactobacillus casei*, *Lactobacillus parabuchneri*, *Bifidobacterium longum*, and *Pediococcus pentosaceus* [36,37]. The probiotics that are primarily used in FF have been reported to be effective for treating AD in young children as well as adults [38,39]. *Lactobacillus paracasei*, *Lactobacillus acidophilus*, *Lactobacillus salivaris*, *Bifidobacterium animalis*, *Bifidobacterium lactis*, and *Bifidobacterium breve* were effective in the treatment of patients with AD by modulating gut microbial translocation, Th17/regulatory T cells, and Th1/Th2 cytokine profiles [39,40].

Coffee consumption in Korea has also significantly increased recently (338 cups per capita per year in 2013), and coffee is the most frequently consumed single food item (12.3 times per week per capita), which is higher than the frequency of rice (7 times per week) and kimchi (11.8 times per week) consumption in Korea [41]. Coffee has been controversial with regard to AD, although diterpene, an antioxidant contained in coffee, has been reported to have anti-inflammatory effects in vitro and in animal studies [42,43]. Arabinogalactan protein obtained from freeze-dried *Coffea arabica* instant coffee powders was found to have a significant immunostimulatory effect on the production of Th1 cytokines, IL-2, IL-12, and interferon γ , which terminate inflammatory immune responses and thereby inhibit allergic dermatitis [44]. The present study did not show what type of coffee, for example, instant or brewed coffee, was consumed; hence, a limitation of the study was the inability to identify which component of coffee was possibly beneficial for preventing AD.

There are some other limitations in this study. First, the results did not indicate cause-and-effect relationships because this was a cross-sectional study. The results demonstrated the association between certain dietary patterns such as MP and FF and the prevalence of AD in the adult population. Second some of the FF consumed in Korea are seasonings such as kochujang, doenjang, cheonggukjang, and fermented seafoods; their intake may have been underestimated or overestimated because 1-serving size is difficult to measure. In addition, the amounts of their consumption might not be high, although the total frequencies of their consumption were high. In addition, individual FF consumption was varied on a daily basis. Thus, individual FF may not be sufficient to affect AD prevalence and symptoms. Third, the adults with AD might not be accurately categorized because the question used to determine AD status was “Have you been diagnosed with AD by a doctor?” Some adults might be diagnosed as AD previously, but it was healed. By contrast, other adults may have had undiagnosed and unrecognized AD. Finally, we could not eliminate the possibility that having AD caused some participants to change their diets in an effort to remedy the condition, therefore resulting in a reverse causality.

In conclusion, high consumption (>92 times/month) of FF such as doenjang, chungkookjang, kimchi, fermented seafood, makgeolli, and beer was associated with a lower prevalence of AD. In contrast, the dietary patterns of mainly consuming MP were very strongly associated with a higher prevalence of AD. The dietary patterns of consuming high amounts of CC and intake of RG were significantly associated with a lower prevalence of AD. However, interestingly, the dietary patterns of consuming high amounts of raw vegetable, fruits, legumes, and seafood did not significantly affect the prevalence of AD. These results suggest that the westernization of dietary patterns, including less consumption of FF, was highly associated with the increased prevalence of AD. This information can be used to develop nutrition education programs for the general population designed to decrease risk factors for AD.

Conflicts of interest

The authors declare no conflicts of interest.

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