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Dietary habits in adult Japanese patients with atopic dermatitis

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ABSTRACT

Dietary habits can modulate the pathogenesis of atopic dermatitis. We evaluated these habits in adult Japanese patients with atopic dermatitis using a validated, brief-type self-administered diet history questionnaire and compared the results to those of age- and sex-matched healthy controls. Patients with atopic dermatitis showed higher intakes of carbohydrate and potatoes and lower intakes of alcohol, niacin, meat and oils/fats compared with those of the healthy controls. The results of logistic regression analysis showed that the intake of alcohol was negatively associated with atopic dermatitis (odds ratio, 0.905; 95% confidence interval, 0.832–0.983; $P = 0.0181$). The intakes of vitamin B₆ and fruit were positively correlated with the severity scoring of atopic dermatitis. Multiple regression analysis revealed that vitamin B₆ intake was a predictor of the severity scoring of atopic dermatitis ($\beta = 26.98508709$, $t = 2.3995292$, $P = 0.01933781$). The intakes of vegetable fat, *n*-6 polyunsaturated fatty acid, and confections were lower in the severe atopic dermatitis group (severity scoring of atopic dermatitis, ≥ 33) than those in the mild group. Atopic dermatitis is negatively associated with alcohol intake, and intake of vitamin B₆ is a predictor of severity scoring of atopic dermatitis. The intake of *n*-6 polyunsaturated fatty acid is lower in the severe atopic dermatitis group than that in the mild group. Further study is warranted on the relationships of these results with abnormal immune responses, impaired skin barrier or pruritus in atopic dermatitis.

Key words: alcohol, atopic dermatitis, brief-type self-administered diet history questionnaire, *n*-6 polyunsaturated fatty acid, vitamin B₆.

INTRODUCTION

Atopic dermatitis (AD) is a chronic eczematous disease characterized by abnormal immune responses mainly skewed to T-helper (Th)2-phenotype, pruritis and skin barrier impairment.¹ A variety of genetic and environmental factors are involved in the pathogenesis of AD. The environmental factors include dietary habits as certain nutrients from the diet can modulate the disease course of AD patients. An excessive intake of *n*-6 polyunsaturated fatty acid (PUFA) promotes the Th2-skewed immune responses and exacerbates the symptoms of AD, while *n*-3 PUFA opposes the effects of *n*-6 PUFA.² The intakes of pro- or prebiotics³ or green/yellow vegetables,⁴ containing antioxidant nutrients, vitamin C or β -carotene, restore the balance between Th1/Th2-cell responses and have prophylactic or ameliorating effects on AD. To clarify the excessive or deficient nutrients related to the disease course, dietary habits in child or adult patients with AD have been analyzed mostly in Western countries.

Adult AD patients in Norway showed a lower intake of vitamin D and *n*-3 PUFA and a higher intake of saturated fatty acid compared with those in the reference group.⁵ In Germany, a lower intake of α -linolenic acid (α -LA) and a higher intake ratio of linoleic acid (LA) to α -LA were associated with the prevalence of AD in women.⁶ In Korea, the consumption of instant noodles, meat and processed foods was associated with an increased prevalence of AD.⁷ However, there are few studies on dietary habits in adult Japanese patients with AD. The traditional Japanese diet includes a high intake of rice, miso soup, sea products and fish. The dietary habits in Japan differ from those in Western countries that include high intakes of vegetable oil, salt-containing seasonings, meat and processed meat as well as from those in the other Asian countries. We herein investigated the dietary habits of adult Japanese patients with AD compared with healthy controls, using a previously validated brief-type self-administered diet history questionnaire (BDHQ).⁸ The BDHQ is based on the Japanese style of diet; thus, the findings based on the

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Table 1. Demographic characteristics and intake of nutrients and food in controls and patients with atopic dermatitis

	Control (n = 70)	AD (n = 70)	P
Sex			
Male	43	43	1 [†]
Female	27	27	
Age (years)	41.1 ± 13.24042	42.18571 ± 12.1552	0.612
BMI (kg/m ²)	21.76413 ± 3.252145	22.64006 ± 3.43968	0.116
Energy intake (kcal/day)	1869.7 ± 621.273	2028.582 ± 789.332	0.207
Animal protein (% energy)	8.247343 ± 2.41572	8.041153 ± 2.83445	0.664
Vegetable protein (% energy)	6.099639 ± 0.8623944	6.078655 ± 0.98969	0.895
Animal fat (% energy)	12.82646 ± 3.623226	13.71259 ± 4.37534	0.225
Vegetable fat (% energy)	14.84769 ± 3.3034	14.12376 ± 3.56981	0.22
Carbohydrate (% energy)	51.01657 ± 7.679207	54.38235 ± 7.87136	0.00954*
Na (mg/kcal)	2186.7 ± 443.0724	2165.134 ± 513.537	0.785
K (mg/kcal)	1272.837 ± 301.9767	1245.527 ± 388.201	0.584
Ca (mg/kcal)	254.248 ± 79.23635	262.9199 ± 110.372	0.601
Mg (mg/kcal)	127.6086 ± 22.76304	122.8613 ± 30.2152	0.241
Pi (mg/kcal)	529.3721 ± 96.73319	526.8739 ± 118.613	0.891
Fe (mg/kcal)	3.982085 ± 0.916113	3.851613 ± 1.01516	0.393
Zn (mg/kcal)	4.277569 ± 0.653158	4.196062 ± 0.57266	0.437
Cu (mg/kcal)	0.5748901 ± 0.0861178	0.5723515 ± 0.09498	0.861
Mn (mg/kcal)	1.676947 ± 0.5065394	1.68648 ± 0.55863	0.919
Retinol (μg/kcal)	265.2601 ± 167.9495	241.381 ± 192.085	0.456
β-Carotene (μg/kcal)	1602.996 ± 843.5811	1621.241 ± 1210.33	0.896
Vitamin D (μg/kcal)	5.360814 ± 3.091769	6.039013 ± 4.15422	0.247
α-Tocopherol (μg/kcal)	3.835388 ± 0.8694984	3.795572 ± 0.90204	0.768
Vitamin K (μg/kcal)	155.1837 ± 67.66738	136.9348 ± 67.5111	0.0722
Vitamin B ₁ (mg/kcal)	0.4027607 ± 0.0917601	0.3992519 ± 0.09082	0.805
Vitamin B ₂ (mg/kcal)	0.6881683 ± 0.1541188	0.6670331 ± 0.1782	0.456
Niacin (mg/kcal)	9.262182 ± 2.06242	8.581935 ± 2.26978	0.0452*
Vitamin B ₆ (mg/kcal)	0.6489259 ± 0.1336386	0.6174487 ± 0.16406	0.183
Vitamin B ₁₂ (μg/kcal)	4.277974 ± 2.119456	4.33464 ± 2.44849	0.883
Folic acid (μg/kcal)	170.3835 ± 47.80611	161.0256 ± 55.731	0.223
Pantothenic acid (mg/kcal)	3.423611 ± 0.6115838	3.285561 ± 0.63384	0.174
Vitamin C (mg/kcal)	53.51568 ± 22.86802	51.47884 ± 22.5448	0.539
SFA (% energy)	7.606745 ± 1.890501	8.159695 ± 2.19884	0.133
MUFA (% energy)	10.0741 ± 2.05794	10.00168 ± 2.27363	0.844
n-3 PUFA (% energy)	1.222347 ± 0.3114961	1.226045 ± 0.38554	0.951
n-6 PUFA (% energy)	5.350818 ± 1.115369	5.036539 ± 1.10962	0.0825
Cholesterol (mg/kcal)	193.8401 ± 68.41121	195.5022 ± 79.4166	0.897
Dietary fiber (g/kcal)	5.762522 ± 1.550002	5.718397 ± 1.77379	0.858
Salt (g/kcal)	5.518999 ± 1.123725	5.473507 ± 1.30063	0.821
Alcohol (% energy)	5.599146 ± 6.640783	2.316239 ± 3.71291	0.000691*
Food			
Cereals (g/kcal)	209.9119 ± 57.79546	214.5436 ± 64.9616	0.66
Potatoes (g/kcal)	19.65662 ± 15.47242	25.9588 ± 22.8374	0.0406*
Pulses (g/kcal)	2.266171 ± 1.783218	2.226416 ± 2.20181	0.911
Green and yellow vegetables (g/kcal)	52.10885 ± 30.56315	52.7933 ± 36.5882	0.887
Other vegetables (g/kcal)	72.91115 ± 36.02614	70.54822 ± 39.6466	0.688
Fruit (g/kcal)	58.44986 ± 64.37733	51.15563 ± 42.7354	0.404
Fish and shell fish (g/kcal)	32.4359 ± 17.73004	34.71008 ± 23.4425	0.503
Meat (g/kcal)	48.72827 ± 17.53693	41.23844 ± 19.9725	0.00754*
Eggs (g/kcal)	18.62017 ± 13.81898	19.34089 ± 15.8255	0.756
Dairy products (g/kcal)	70.62318 ± 48.977	77.08021 ± 58.4237	0.519
Oils and fats (g/kcal)	7.291804 ± 2.679864	6.303361 ± 2.51848	0.0257*
Confection (g/kcal)	24.30471 ± 16.85814	28.24408 ± 21.1552	0.192
Beverages (g/kcal)	462.8219 ± 195.4936	409.5413 ± 23.4616	0.149
Seasonings and spices (g/kcal)	126.5096 ± 72.39885	132.7449 ± 59.3284	0.586

*Significant differences at $P < 0.05$. [†]Fisher's exact test was used to test the significance of differences in frequency distribution. Results are expressed as mean ± standard deviation. Differences between groups are analyzed by sample-paired *t* test. AD, atopic dermatitis; BMI, body mass index; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid.

Table 2. Association of atopic dermatitis with each variable analyzed by multiple logistic regression analysis

	OR	95% CI	P
(Intercept)	0.846	0.0015–477.000	0.959
BMI (kg/m ²)	1.12	1.0000–1.260	0.0505
Age (years)	1.01	0.9790–1.030	0.644
Sex (M = 1, F = 2)	0.568	0.2650–1.220	0.145
Carbohydrate (% energy)	0.994	0.9270–1.070	0.865
Niacin (mg/kcal)	0.866	0.6980–1.080	0.193
Alcohol (% energy)	0.905	0.8320–0.983	0.0181*
Potatoes (g/kcal)	1.02	1.000–1.040	0.0555
Meat (g/kcal)	0.987	0.9630–1.010	0.281

*Significant differences at $P < 0.05$. BMI, body mass index; CI, confidence interval; OR, odds ratio.

responses to this questionnaire reflect the dietary habits in Japanese participants.

METHODS

Study population

This study was performed in accordance with the Declaration of Helsinki (2004) and was approved by the ethics committees of Nippon Medical School Chiba Hokusoh Hospital and Nippon Medical School Hospital. The purpose of the protocol was explained to the patients and controls and written informed consent was obtained. Seventy patients with AD (43 men and 27 women), diagnosed according to the Japanese Dermatological Association criteria,⁹ were recruited to participate in this study. They were patients of the outpatient clinics of the dermatological departments of Nippon Medical School Chiba Hokusoh Hospital and Nippon Medical School Hospital. Among these, 68 and 32 patients were treated with topical steroids and topical tacrolimus, respectively. Fifty-two patients were treated with oral H₁ antihistamines, 18 with oral cyclosporin and three with oral corticosteroids. Eight patients were treated with s.c. dupilumab every 2 weeks. One patient had an allergy to shrimp and one to mackerel. Severity scoring of atopic dermatitis (SCORAD)¹⁰ was assessed for each patient. Seventy age- and sex-matched healthy subjects were chosen as controls among hospital volunteers and employees from the same geographical area. Body mass index (BMI) was calculated for each participant as the current bodyweight (kg) divided by the square of the body height (m).

Dietary assessment

The dietary habits of the patients and controls were assessed using the BDHQ, which is a 4-page, fixed-portion questionnaire used to estimate the dietary intake of 58 food items. The food items and portion sizes contained in the BDHQ were derived from a food list used in the National Health and Nutrition Survey of Japan and from several recipe books for Japanese dishes. Estimates of the intakes of food items and of energy and nutrients were calculated using an ad hoc computer algorithm for the BDHQ which was based on the Standard Tables of Food Composition in Japan.¹¹

Table 3. Correlations of scoring of atopic dermatitis with nutrients/food in patients with atopic dermatitis

	γ	P
Age (years)	−0.0354	0.771
BMI (kg/m ²)	0.0459	0.706
Energy intake (kcal/day)	0.0445	0.714
Nutrients		
Animal protein (% energy)	0.169	0.162
Vegetable protein (% energy)	−0.214	0.0753
Animal fat (% energy)	0.0699	0.565
Vegetable fat (% energy)	−0.215	0.0733
Carbohydrate (% energy)	−0.0342	0.779
Na (mg/kcal)	0.141	0.243
K (mg/kcal)	0.224	0.0628
Ca (mg/kcal)	0.0595	0.625
Mg (mg/kcal)	0.179	0.138
Pi (mg/kcal)	0.142	0.241
Fe (mg/kcal)	0.00431	0.972
Zn (mg/kcal)	0.00334	0.978
Cu (mg/kcal)	0.0256	0.834
Mn (mg/kcal)	−0.0388	0.75
Retinol (μg/kcal)	0.0319	0.793
β-carotene (μg/kcal)	0.15	0.214
Vitamin D (μg/kcal)	0.142	0.24
α-Tocopherol (μg/kcal)	0.0818	0.501
Vitamin K (μg/kcal)	0.0529	0.664
Vitamin B ₁ (mg/kcal)	0.133	0.273
Vitamin B ₂ (mg/kcal)	0.0101	0.934
Niacin (mg/kcal)	0.23	0.0552
Vitamin B ₆ (mg/kcal)	0.296	0.0128*
Vitamin B ₁₂ (μg/kcal)	0.202	0.0937
Folic acid (μg/kcal)	0.0875	0.471
Pantothenic acid (mg/kcal)	0.122	0.314
Vitamin C (mg/kcal)	0.194	0.108
SFA (% energy)	−0.0264	0.828
MUFA (% energy)	−0.136	0.263
n-3 PUFA (% energy)	−0.0186	0.879
n-6 PUFA (% energy)	−0.184	0.127
Cholesterol (mg/kcal)	−0.0104	0.932
Dietary fiber (g/kcal)	0.102	0.402
Salt (g/kcal)	0.141	0.244
Alcohol (% energy)	0.221	0.0663
Food		
Cereals (g/kcal)	−0.121	0.319
Potatoes (g/kcal)	0.23	0.0553
Pulses (g/kcal)	0.0862	0.478
Green and yellow vegetables (g/kcal)	0.224	0.0618
Other vegetables (g/kcal)	0.172	0.154
Fruit (g/kcal)	0.247	0.0391*
Fish and shell fish (g/kcal)	0.177	0.142
Meat (g/kcal)	0.03	0.805
Eggs (g/kcal)	−0.0795	0.513
Dairy products (g/kcal)	0.00114	0.993
Oils and fats (g/kcal)	−0.0297	0.807
Confection (g/kcal)	−0.107	0.378
Beverages (g/kcal)	0.129	0.287
Seasonings and spices (g/kcal)	0.0884	0.467

*Significant differences at $P < 0.05$. Correlations between variables were performed using Spearman's correlation coefficients. BMI, body mass index; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid.

Table 4. Predictive factors for severity scoring of atopic dermatitis analyzed by linear multivariate analysis

	Estimate	SE	<i>t</i>	<i>P</i>
(Intercept)	31.61053	15.67092854	2.017145	0.04787908*
Age (years)	−0.15494	0.14741976	−1.05104	0.29719064
BMI (kg/m ²)	−0.02137	0.50723104	−0.04212	0.96653038
Fruit (g/kcal)	0.036329	0.04366037	0.832081	0.40845723
Sex (M = 1, F = 2)	−6.66749	3.56181176	−1.87194	0.06578603
Vitamin B ₆ (mg/kcal)	26.98509	11.24599197	2.3995292	0.01933781*

*Significant differences at $P < 0.05$. BMI, body mass index; SE, standard error.

Statistical analyses

Results are expressed as mean $\pm$ standard deviation (SD). Differences in the intakes of nutrients or foods between case–control pairs with and without AD were tested by paired-sample *t*-tests. The AD patients were divided into mild and severe groups according to the SCORAD. The differences between the mild and severe groups were analyzed by Student's *t*-tests. Fisher's exact test was used to assess the significance of differences in frequency distributions. In the group of AD patients, the correlations between SCORAD and each variable were evaluated using Spearman's rho correlation coefficients. $P < 0.05$ was considered statistically significant.

The association of each variable with AD was analyzed using multiple logistic regression analysis adjusted for age, sex and BMI. The predictive factors for SCORAD were analyzed using linear multivariate analysis adjusted for age, sex and BMI. These analyses included only those variables with a *P*-value of less than 0.05 in univariate analysis. To avoid multicollinearity, variables with a variance inflation factor of more than 10 were excluded. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, it is a modified version of R commander designed to add statistical functions frequently used in biostatistics.¹²

RESULTS

Comparison of dietary habits between AD patients and controls

There was no difference in BMI between AD patients and controls (Table 1). AD patients showed a higher intake of carbohydrates and lower intakes of alcohol and niacin compared with those of the controls. Among food items, AD patients showed lower intakes of meat and oils/fats and a higher intake of potatoes compared with those of the controls. In logistic regression analysis (Table 2), the intake of alcohol was negatively associated with AD (odds ratio, 0.905; 95% confidence interval, 0.832–0.983; $P = 0.0181$).

Correlation studies

Among AD patients, the mean $\pm$ SD of the SCORAD was 33.87 ± 14.87 and there was no difference between male (35.98 ± 14.42) and female (30.52 ± 15.22 , $P = 0.136$, by Student's *t*-test) patients.

Scoring of atopic dermatitis was positively correlated with the intakes of vitamin B₆ and of fruit (Table 3). In the linear multivariate analysis adjusted for age, sex and BMI, SCORAD was predicted by the intake of vitamin B₆ (Table 4; $\beta = 26.98508709$, $t = 2.39952929$, $P = 0.01933781$).

Comparison between mild and severe groups of AD

The AD patients were subdivided by the median SCORAD into mild (SCORAD, <33 ; $n = 35$) and severe (SCORAD, ≥ 33 ; $n = 35$) groups, and intakes of nutrients and foods were compared between the two groups. There were no differences in sex ratio, age and BMI between the two groups (Table 5). The intakes of vegetable fat, *n*-6 PUFA and confections were lower in the severe group than those in the mild group.

DISCUSSION

In this study, alcohol intake was negatively associated with AD. AD patients may avoid alcohol because it generates an itch by increasing blood flow.¹³ Alternatively, the lower intake of alcohol may be because most patients (74.2%) used H₁ antihistamines to relieve pruritus; concomitant use of these medicines with alcohol may increase psychomotor impairment related to alcohol intake.¹⁴ Previous findings on alcohol intake in AD patients are conflicting; Siverberg *et al.*¹⁵ and Egeberg *et al.*¹⁶ reported increased alcohol intake in AD patients compared with that in the reference group, while Drucker *et al.*¹⁷ reported no difference. The conflicting results may be due to the differences in patient backgrounds including comorbidities, education, occupation, religion or physical activity. Further analysis on alcohol intake in Japanese AD patients in a variety of facilities is necessary.

Atopic dermatitis patients showed a lower intake of niacin compared with that in the controls. Oral or topical nicotinamide, a metabolite of niacin, reduces transepidermal water loss and restores epidermal barrier integrity,^{18–20} nicotinamide also attenuates the overexpression of aquaporin-3, a water-permeable channel upregulated in AD patients,^{21,22} and increases ceramide synthesis in the stratum corneum.²⁰ Because AD patients are associated with skin barrier impairment and increased transepidermal water loss,²¹ the reduced intake of niacin in AD patients may be related to their skin barrier impairment through decreased systemic nicotinamide level.

n-6 PUFA is present in significant quantities in vegetable fats such as vegetable oils or margarine. In the *n*-6 PUFA

Table 5. Demographic characteristics and intake of nutrients and food in mild and severe groups of patients with atopic dermatitis

	Mild AD (SCORAD, <33; n = 35)	Severe AD (SCORAD, ≥33; n = 35)	P
Sex			
Male	19	24	0.326 [†]
Female	16	11	
Age (years)	43.77143 ± 13.50182	40.6 ± 10.60022	0.278
BMI (kg/m ²)	22.51332 ± 3.781661	22.76681 ± 3.110754	0.76
Energy intake (kcal/day)	2070.924 ± 925.7937	1986.239 ± 635.3188	0.657
Nutrients			
Animal protein (% energy)	7.837187 ± 2.460465	8.245119 ± 3.188251	0.551
Vegetable protein (% energy)	6.306413 ± 0.991761	5.850898 ± 0.9472977	0.0535
Animal fat (% energy)	13.60696 ± 4.312644	13.81821 ± 4.497587	0.842
Vegetable fat (% energy)	15.20423 ± 3.585392	13.04329 ± 3.256274	0.0103*
Carbohydrate (% energy)	53.87241 ± 6.805536	54.89229 ± 8.8819	0.591
Na (mg/kcal)	2145.222 ± 526.3817	2185.046 ± 507.2501	0.748
K (mg/kcal)	1218.149 ± 354.0399	1272.904 ± 423.019	0.559
Ca (mg/kcal)	257.4224 ± 83.72875	268.4175 ± 132.85071	0.68
Mg (mg/kcal)	121.9065 ± 28.27179	123.816 ± 32.42824	0.794
Pi (mg/kcal)	519.7121 ± 96.57498	534.0358 ± 138.27365	0.617
Fe (mg/kcal)	3.991473 ± 0.9852549	3.711753 ± 1.0394269	0.252
Zn (mg/kcal)	4.192845 ± 0.5035435	4.199279 ± 0.6418255	0.963
Cu (mg/kcal)	0.5787417 ± 0.0925341	0.5659613 ± 0.0982821	0.577
Mn (mg/kcal)	1.761011 ± 0.6081906	1.61195 ± 0.5019805	0.267
Retinol (μg/kcal)	228.2796 ± 179.3411	254.4825 ± 205.8198	0.572
β-Carotene (μg/kcal)	1565.649 ± 1123.512	1676.834 ± 1305.46	0.704
Vitamin D (μg/kcal)	5.837754 ± 3.739589	6.240273 ± 4.57763	0.688
α-Tocopherol (μg/kcal)	3.848171 ± 0.8406549	3.742974 ± 0.9689538	0.629
Vitamin K (μg/kcal)	144.2065 ± 74.02675	129.6632 ± 60.50384	0.371
Vitamin B ₁ (mg/kcal)	0.3939632 ± 0.072444	0.4045406 ± 0.1069244	0.63
Vitamin B ₂ (mg/kcal)	0.6796589 ± 0.1518608	0.6544072 ± 0.2026162	0.557
Niacin (mg/kcal)	8.462603 ± 2.269158	8.701267 ± 2.297162	0.663
Vitamin B ₆ (mg/kcal)	0.6347137 ± 0.1532803	0.6347137 ± 0.1746785	0.382
Vitamin B ₁₂ (μg/kcal)	4.243268 ± 2.595231	4.426012 ± 2.326822	0.757
Folic acid (μg/kcal)	164.1384 ± 55.70956	157.9129 ± 56.38916	0.644
Pantothenic acid (mg/kcal)	3.278268 ± 0.6168839	3.292854 ± 0.659289	0.924
Vitamin C (mg/kcal)	51.21328 ± 22.55222	51.74439 ± 22.86349	0.922
SFA (% energy)	8.295217 ± 1.986541	8.024174 ± 2.414094	0.61
MUFA (% energy)	10.381282 ± 1.966108	9.622069 ± 2.515672	0.164
n-3 PUFA (% energy)	1.276689 ± 0.3821505	1.1754 ± 0.3877359	0.275
n-6 PUFA (% energy)	5.319171 ± 1.086103	4.753908 ± 1.074548	0.032*
Cholesterol (mg/kcal)	199.0733 ± 73.4644	191.9312 ± 85.88488	0.71
Dietary fiber (g/kcal)	5.623057 ± 1.508291	5.813737 ± 2.022762	0.656
Salt (g/kcal)	5.42383 ± 1.333334	5.523183 ± 1.284594	0.752
Alcohol (% energy)	1.780391 ± 3.140417	2.852087 ± 4.186112	0.23
Food			
Cereals (g/kcal)	213.2231 ± 59.39539	215.8642 ± 70.94174	0.866
Potatoes (g/kcal)	20.90377 ± 17.00259	31.01382 ± 26.77194	0.0636
Pulses (g/kcal)	2.018712 ± 2.154231	2.434121 ± 2.260315	0.434
Green and yellow vegetables (g/kcal)	51.97662 ± 39.26848	53.60999 ± 34.25465	0.853
Other vegetables (g/kcal)	67.33548 ± 31.59382	73.76096 ± 46.58884	0.502
Fruit (g/kcal)	48.87809 ± 48.70668	53.43317 ± 36.37755	0.659
Fish and shell fish (g/kcal)	32.81187 ± 22.68832	36.60829 ± 24.35331	0.502
Meat (g/kcal)	41.25709 ± 19.9571	41.21979 ± 20.27927	0.994
Eggs (g/kcal)	20.39768 ± 14.85906	18.2841 ± 16.88694	0.58
Dairy products (g/kcal)	71.17352 ± 47.01813	82.9869 ± 68.15069	0.402
Oils and fats (g/kcal)	6.57691 ± 2.274438	6.029811 ± 2.746797	0.367
Confection (g/kcal)	33.26493 ± 24.4343	23.22324 ± 16.10311	0.0463*

Table 5. (continued)

	Mild AD (SCORAD, <33; <i>n</i> = 35)	Severe AD (SCORAD, ≥33; <i>n</i> = 35)	<i>P</i>
Beverages (g/kcal)	398.2104 ± 238.852	420.8722 ± 209.8196	0.675
Seasonings and spices (g/kcal)	121.3903 ± 43.62075	144.0994 ± 70.53388	0.11

*Significant differences at $P < 0.05$. †Fisher's exact test was used to test the significance of differences in frequency distribution. Results are expressed as mean ± standard deviation. Differences between groups are analyzed by paired *t*-test. AD, atopic dermatitis; BMI, body mass index; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SCORAD, severity scoring of atopic dermatitis; SFA, saturated fatty acid.

biosynthesis pathway, LA is converted to γ -LA by δ -6-saturase, to dihomono- γ -linolenic acid (DGLA) by elongase-5, and then to arachidonic acid (AA) by δ -5-desaturase.² An increased intake of *n*-6 PUFA, especially LA, leads to increased AA in the cell membranes of various immune cells such as mast cells or macrophages.² The increased AA is then converted to two-series prostaglandins (PG) such as PGD₂, activating Th2-type responses, or to four-series leukotrienes (LT) such as LTB₄, promoting immunoglobulin E production by B cells, leading to the exacerbation of Th2-type immune responses in AD.² There is some epidemiological evidence associating high *n*-6 PUFA intake with AD, in which the intake ratio of *n*-6 PUFA/*n*-3 PUFA was positively associated with the prevalence of AD in female adults in Germany.⁶ Margarine consumption was higher in Australian schoolchildren with AD compared with that in controls.²³ Thus, the reduced intake of *n*-6 PUFA in the severe AD group compared with that in the mild group is contrary to our expectation. However, *n*-6 PUFA plays an essential role in the assembly of the skin permeability barrier; LA is the predominant ω -O-esterified fatty acid species located on acylceramide in the stratum corneum.²⁴ An LA-supplemented diet reduced transepidermal water loss and scratching behavior in AD-like dermatitis of hairless mice.²⁵ DGLA also acted on mast cells and induced their release of PGD₁, which suppressed degranulation of mast cells and production of thymic stromal lymphopoietin in keratinocytes.²⁶ DGLA-supplemented diet reduced scratching behavior and severity score in AD-like dermatitis of NC/Tnd mice.²⁶ The intake of *n*-6 PUFA may thus improve skin barrier impairment and/or pruritus in AD. Therefore, the reduced intake of *n*-6 PUFA in the severe AD group may be related to enhanced skin barrier disruption or pruritus compared with that in the mild group.

In this study, vitamin B₆ intake was the predictor of SCORAD in AD patients. Vitamin B₆ promotes Th1-type immune responses.^{8,27} Acute AD lesions are characterized by the enhanced expression of Th2 (interleukin [IL]-4, IL-13, IL-31)/Th22 (IL-22) cytokines, while progression to chronic AD is associated with intensification of Th2/Th22 and significant increases in Th1-related products like interferon (IFN)- γ , C-X-C motif chemokine (CXCL)9 and CXCL10.²⁸ Especially, lesions of adult patients with long-standing AD reveal extremely enhanced expression of Th1-associated mediators (CXCL9, CXCL10, signal transducer and activator of transcription 1, IL-12RB2), which is not seen in the lesions of pediatric AD patients with early onset.¹ The enhanced Th1 activity may be related to the decreased expression of epidermal differentiation

complex like filaggrin, and of ceramides with long-chain fatty acids in the stratum corneum in chronic adult AD lesions.¹ IFN- γ is reported to inhibit the expression of filaggrin^{29,30} and ceramides with long-chain fatty acids in keratinocytes,³¹ and thus contribute to barrier defects. The positive correlation between vitamin B₆ intake and SCORAD thus indicates that higher intake of vitamin B₆ may enhance Th1 activity, disrupting the skin barrier and resultantly aggravating the disease.

The intakes of oils/fats and meat were lower while those of carbohydrate and potatoes were higher in AD patients compared with those in the controls. Studies in other countries have reported results different from ours; a higher intake of meat was associated with a higher prevalence of AD in a Korean study.⁷ A high-fat and low-carbohydrate diet was also associated with a higher prevalence of allergic diseases such as allergic rhinitis in Korean children, although not of AD.³² Our present study showed that the intake of fruit was correlated with SCORAD in Japanese AD patients, indicating that patients with more severe disease may consume higher amounts of fruit. This is also a distinctive result; studies in Norway and Korea reported that adult AD patients showed significantly lower intakes of fruit compared with those of the controls.^{5,33} Overall, our present results indicate that adult Japanese patients with AD may have rather healthy dietary habits, somewhat different from those of studies in other countries. Whether these differences may represent the characteristics of adult Japanese AD patients requires further study. Adult Japanese patients with AD may prefer a healthy diet pattern rich in fruit and potatoes to a Western diet pattern featuring high fat, high meat or low carbohydrate consumption. Adult Japanese patients with AD may also have a greater awareness of health and diseases.

This study was performed in a limited number of places; namely Chiba and Tokyo in the Kanto region. Dietary habits, especially the intakes of carbohydrate or salt, may vary regionally in Japan. Therefore, we should further extend this study to a variety of regions in Japan. Besides, dietary habits may alter according to the seasons because sorts of vegetables, fruit or fish and recipes vary with the four seasons in Japan. This study was performed in summer (June, July and August), and thus we should further examine dietary habits of patients and controls in different seasons and evaluate the seasonal change. Previous studies on the relationship between diet and AD focused on the allergic or immunological aspects; however, other aspects of AD, such as skin barrier impairment or pruritus, should also be assessed.

In conclusion, adult Japanese patients with AD showed higher intakes of carbohydrate and potatoes and lower intakes of alcohol, niacin, meat and oils/fats compared with those of controls. The intake of alcohol was negatively associated with AD. The intakes of vitamin B₆ and fruit were correlated with SCORAD and the former was a predictor of SCORAD. The intakes of vegetable fat, *n*-6 PUFA and confections were lower in the severe AD group than those in the mild group. The significance of these results in the pathogenesis of AD should be identified in further extended studies.

CONFLICT OF INTEREST: None declared.

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