Original Article

Relationship between dietary fat and fish intake and the prevalence of atopic eczema in pregnant Japanese females: baseline data from the Osaka Maternal and Child Health Study

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Dietary factors may be important in the development of atopic eczema. It remains controversial whether n-3 polyunsaturated fatty acid intake is preventive against allergic disorders and whether n-6 polyunsaturated fatty acid intake increases the risk of allergic disorders. The current cross-sectional study examined the association between intake of fatty acids and foods high in fatty acids and the prevalence of atopic eczema. Study subjects were 1002 pregnant Japanese females. Current atopic eczema and atopic eczema after age 18 were defined as present if subjects had been treated with medications at some time in the previous 12 months and after reaching the age of 18, respectively. Information on dietary factors was collected using a validated self-administered diet history questionnaire. Docosahexaenoic acid intake was statistically significantly related to a decreased prevalence of atopic eczema after age 18 and current atopic eczema. Inverse dose-response relationships with regard to consumption of n-3 polyunsaturated fatty acids, eicosapentaenoic acid, and fish and the ratio of n-3 to n-6 polyunsaturated fatty acids with atopic eczema were not observed although these dietary variables in the second tertile were inversely significantly associated with atopic eczema after age 18. Intake of total fat, saturated fatty acids, monounsaturated fatty acids, n-6 polyunsaturated fatty acids, cholesterol, meat, eggs, or dairy products was not related to either of the outcomes for atopic eczema. Docosahexaenoic acid intake may be associated with a reduced prevalence of atopic eczema in pregnant Japanese females.

Key Words: Atopic eczema, eating, fatty acids, fishes, Japan

INTRODUCTION

Many epidemiologic studies have focused on the association of fatty acids and/or foods high in fatty acids with allergic disorders.[1-22] Although the outcomes investigated were most often related to asthma and allergic rhinitis, the findings were not consistent. In particular, it remains controversial whether n–3 polyunsaturated fatty acid intake is preventive against allergic disorders and whether n–6 polyunsaturated fatty acid intake increases the risk of allergic disorders. A cross-sectional study in German adults reported that inverse dose-response relationships of α-linolenic acid intake and the ratio of n–3 to n–6 fatty acids with the prevalence of atopic eczema were statistically significant whereas consumption of butter and margarine was not related to atopic eczema in females.[1] In Finland a case-control study found that the children with atopic eczema consumed more margarine and less butter than nonatopic children and that serum docosahexaenoic acid and eicosapentaenoic acid levels were significantly lower in those with atopic eczema.[3] A case-referent study in Norway showed that among female adult patients with moderate to severe atopic dermatitis, intake of saturated fatty acids was higher whereas intake of docosahexaenoic acid and eicosapentaenoic acid was lower than in the reference group.[4] In the Childhood Asthma Prevention Study, a daily omega-3-rich tuna fish oil supplement in the first 18 months of life had no beneficial effect on the manifestation of eczema.[23] An intervention study demonstrated that fish oil supplementation significantly im

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proved some of the subjective manifestations of atopic dermatitis[24] whereas another intervention study concluded that linoleic acid, but not docosahexaenoic acid or eicosapentaenoic acid, intake was useful to treat atopic eczema.[25]

In view of the lack of epidemiologic studies of the relationship between intake of fatty acids and high-fat foods and atopic eczema in Japan where intake of fish is high, the present cross-sectional study examined the association with regard to the intake of specific types of fatty acids, cholesterol, and selected foods high in fatty acids with the prevalence of atopic eczema in pregnant Japanese females using baseline data from the Osaka Maternal and Child Health Study (OMCHS).

MATERIALS AND METHODS

Study population

The OMCHS, an ongoing prospective cohort study, investigates preventive and risk factors for maternal and child health problems such as allergic disorders and postpartum depression. Details of the OMCHS have been described elsewhere.[26,27] Briefly, eligible females were those who became pregnant in Neyagawa City, which is one of the 43 municipalities in Osaka Prefecture, a metropolis in Japan with a total population of approximately 8.8 million. Of the 3639 eligible females in Neyagawa City, 627 (17.2%) participated in this study between November 2001 and March 2003. Eight pregnant females who did not live in Neyagawa City but who had become aware of the present study at an obstetric clinic before August 2002 decided by themselves to participate in this study. Also, there were 77 participants who received explanations of the OMCHS from public health nurses in 6 other municipalities from August 2002 to March 2003. From October 2002 to March 2003, 290 participants were recruited from a university hospital and three obstetric hospitals in 3 other municipalities; these women were recommended for participation in the OMCHS by an obstetrician. Finally, a total of 1002 pregnant women gave their fully informed consent in writing and completed the baseline survey. The OMCHS was approved by the ethics committees of the Osaka City University School of Medicine and the Osaka Prefectural Institute of Public Health.

Measurements

In the baseline survey, each participant filled out a set of two self-administered questionnaires and collected two dust samples from a 1 m^2 area of the bedclothes and flooring for 1 minute using a vacuum cleaner fitted with a collection apparatus. Participants then mailed these materials to the data management center. Research technicians completed missing or illogical data by telephone interview.

A validated self-administered diet history questionnaire was used to assess dietary habits over a period of 1 month. The structure and validity of the questionnaire were described in detail elsewhere.[28, 29] In this instrument, intake of 147 food items was calculated using an ad-hoc computer algorithm developed to analyze the questionnaire. Information on dietary supplements was not used in the calculation of dietary intake. According to the validation studies, the correlation coefficients for nutrient intake between those estimated from the diet history questionnaire and those observed by a 3-day dietary record were 0.75, 0.50, 0.37, and 0.49 for saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids, and cholesterol, respectively, in women.[28] A highly positive correlation was also observed between marine-origin n–3 polyunsaturated fatty acid intake estimated by the diet history questionnaire and the corresponding concentration in the serum phospholipid fraction in women ($r = 0.69$).[29] Energy-adjusted intake by the residual method was used for the analyses.[30]

A second self-administered questionnaire asked about age, gestation, parity, smoking habits, personal history of atopic eczema, family history of asthma, atopic eczema, and allergic rhinitis, indoor domestic pets, family income, education, weight, height, and changes in diet in the previous 1 month. Current atopic eczema was defined as present when subjects had received any medical treatment for atopic eczema at any time during the previous 12 months. Atopic eczema after age 18 was considered to be present if subjects had received any medical treatment for atopic eczema at any time after reaching the age of 18. However, data on the types of medications and topical therapy and the duration of their use were not available. A family history of asthma, atopic eczema, and allergic rhinitis (including Japanese cedar pollinosis) was considered to be present if one or more parents or siblings of the study subject had manifested any of these allergic disorders. Body mass index was calculated by dividing self-reported body weight (kg) by the square of self-reported height (m).

Antigen levels from extracts of fine dust fractions were measured by a double-antibody sandwich enzyme-linked immunosorbent assay using a soluble antigen prepared from whole *Dermatophagoides farinae* mite bodies as a reference standard and were expressed as antigen equivalent in $\mu g/m^2$ of surface area (Mitey checker®, Shinto Fine Co., Ltd., Osaka, Japan).[31,32] Antigen levels were semiquantitatively classified with scores of – (< 2 $\mu g/m^2$), ± (5 $\mu g/m^2$), + (10 to 15 $\mu g/m^2$), and ++ (> 35 $\mu g/m^2$). In the present study, we used only antigen levels in the sample collected from the bedclothes because the correlation between antigen levels from the bedclothes and flooring was collinear (Spearman correlation coefficient = 0.54, $p < 0.0001$).

Statistical analysis

Intake of dietary factors under investigation was categorized at tertile points based on the distribution of all study subjects. Age, gestation, parity, cigarette smoking, indoor domestic pets, family history of asthma, atopic eczema, and allergic rhinitis, family income, education, mite allergen level in house dust, changes in diet in the past 1 month, the season when data were collected, and body mass index were selected *a priori* as potential confounding factors. Age was classified into 2 categories (< 30 and 30+ years); gestation into 2 (< 18 and 18+ weeks); parity into 2 (0 and 1+); cigarette smoking into 3 (never, former, and current); family income into 3 (< 4,000,000, 4,000,000–5,999,999, and 6,000,000+ yen per year); education into 3 (< 13, 13–14, and 15+ years); dust mite allergen levels into 3 (–, ±, and + or ++); changes in diet in

Table 1. Distribution of selected characteristics in 1002 pregnant females, Osaka Maternal Child Health Study, Japan

Variable	n (%) or mean (SD)
Age (% years)	
< 30	473 (47.2)
30+	529 (52.8)
Gestation (% weeks)	
< 18	508 (50.7)
18+	494 (49.3)
Parity of 1 or more (%)	513 (51.2)
Cigarette smoking (%)	
Never	697 (69.6)
Former	121 (12.1)
Current	184 (18.4)
Family history of asthma (%)	101 (10.1)
Family history of atopic eczema (%)	138 (13.8)
Family history of allergic rhinitis (%)	429 (42.8)
Indoor domestic pets (cats, dogs, birds, or hamsters) (%)	114 (11.4)
Family income (% yen/year)	
< 4,000,000	301 (30.0)
4,000,000–5,999,999	403 (40.2)
6,000,000+	298 (29.7)
Education (% years)	
< 13	323 (32.2)
13–14	413 (41.2)
15+	266 (26.6)
Mite allergen level in house dust (%)†	
–	436 (43.5)
±	297 (29.6)
+ or ++	269 (26.9)
Body mass index (kg/m^2)	21.4 (2.8)
Changes in diet in the previous 1 month (%)	
None or seldom	300 (29.9)
Slight	435 (43.4)
Substantial	267 (26.7)
Season when data were collected (%)	
Spring	318 (31.7)
Summer	162 (16.2)
Fall	223 (22.3)
Winter	299 (29.8)

† Antigen levels were semi-quantitatively classified with scores of – (< 2 μg/m^2), ± (5 μg/m^2), + (10 to 15 μg/m^2), and ++ (> 35 μg/m^2).

the previous 1 month into 3 (none or seldom, slight, and substantial); and season when data were collected into 4 categories (spring, summer, fall, and winter). Body mass index was used as a continuous variable.

Logistic regression analysis was used to compare the prevalence of atopic eczema associated with intake of specific types of fatty acids, cholesterol, and selected foods high in fatty acids. Multiple logistic regression analysis was used to control for the potential confounding factors under study. Trend of association was assessed by a logistic regression model assigning scores to the levels of the independent variable. Two-sided *p*-values less than 0.05 were considered statistically significant. All computations were performed using the SAS software package version 9.1 (SAS Institute, Inc., Cary, NC, USA).

RESULTS

Table 2. Distribution of daily nutrients and food intake in 1002 pregnant females, Osaka Maternal Child Health Study, Japan†

Variable	Mean (SD)
Daily nutrient intake	
Total energy (kJ)	6815.3 (1793.7)
Total fat (g)	54.3 (10.3)
Saturated fatty acids (g)	16.6 (3.5)
Monounsaturated fatty acids (g)	19.0 (4.2)
n-3 Polyunsaturated fatty acids (g)	2.3 (0.8)
n-6 Polyunsaturated fatty acids (g)	11.0 (2.8)
Cholesterol (mg)	265.2 (105.3)
Daily intake	
Meat (g)	59.8 (29.2)
Eggs (g)	28.3 (20.3)
Dairy products (g)	192.5 (123.1)
Fish (g)	48.3 (27.4)

† Nutrients and food intake were adjusted for total energy intake using the residual method.

The prevalence values for current atopic eczema and atopic eczema after age 18 were 5.7% and 10.2%, respectively, among the 1002 pregnant females. About 50% of the women were aged 30 years or over and enrolled by the 17th week of gestation and had a parity of one or more (Table 1). Slight or substantial changes in diet in the previous 1 month were experienced by 702 pregnant females due to nausea gravidarum (585 females), maternal and fetal health (107 females), and other reasons (10 females). Mean daily total energy, energy-adjusted total fat and n–3 and n–6 polyunsaturated fatty acid intake were 6815 kJ, 54.3 g, 2.3 g, and 11.0 g, respectively (Table 2).

Odds ratios (ORs) and their 95% confidence intervals (CIs) for the prevalence of atopic eczema in relation to dietary intake of specific types of fatty acids and cholesterol are presented in Table 3. Compared with n–3 polyunsaturated fatty acid intake in the first tertile, consumption of that in the second tertile was independently associated with a decreased prevalence of atopic eczema after age 18, after adjustment for age, gestation, parity, cigarette smoking, indoor domestic pets, family history of asthma, atopic eczema, and allergic rhinitis, family income, education, mite allergen level in house dust, changes in diet in the past 1 month, the season when data were collected, and body mass index, although the adjusted OR for the highest tertile was almost unity in the multivariate model (p for trend = 0.86). No such association was noted for current atopic eczema. We found an inverted J-shaped relationship between eicosapentaenoic acid intake and atopic eczema after age 18: only eicosapentaenoic acid intake in the second tertile was independently inversely associated with the prevalence of atopic eczema after age 18. Dietary intake of docosahexaenoic acid was independently associated with a decreased prevalence of atopic eczema after age 18 and current atopic eczema: the multivariate ORs for comparison of the highest with the lowest tertile were 0.52 (95% CI: 0.30 to 0.88; p for trend = 0.01) and 0.50 (95% CI: 0.24 to 1.00; p for trend = 0.04), respectively. For the ratio of n–3 to n–6 polyunsaturated fatty acids, a significant inverse association with atopic eczema after age 18 was

Table 3. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for atopic eczema by tertiles of specific types of dietary fat, Osaka Maternal Child Health Study, Japan[†]

Variable[‡]	Atopic eczema after age 18		Current atopic eczema	
	Prevalence	Adjusted OR (95% CI)	Prevalence	Adjusted OR (95% CI)
Total fat				
< 50.49	34/334 (10.2%)	1.00	16/334 (4.8%)	1.00
50.49–57.64	35/334 (10.5%)	1.01 (0.60–1.71)	20/334 (6.0%)	1.17 (0.58–2.41)
> 57.64	33/334 (9.9%)	1.09 (0.64–1.85)	21/334 (6.3%)	1.42 (0.70–2.91)
p for trend		0.75		0.33
Saturated fatty acids				
< 15.108	29/334 (8.7%)	1.00	13/334 (3.9%)	1.00
15.108–17.77	37/334 (11.1%)	1.47 (0.86–2.55)	20/334 (6.0%)	1.71 (0.81–3.75)
> 17.77	36/334 (10.8%)	1.34 (0.77–2.33)	24/334 (7.2%)	1.93 (0.93–4.20)
p for trend		0.31		0.09
Monounsaturated fatty acids				
< 17.48	39/334 (11.7%)	1.00	19/334 (5.7%)	1.00
17.48–20.21	31/334 (9.3%)	0.71 (0.42–1.19)	17/334 (5.1%)	0.74 (0.36–1.51)
> 20.21	32/334 (9.6%)	0.89 (0.53–1.49)	21/334 (6.3%)	1.15 (0.59–2.29)
p for trend		0.61		0.68
n-3 Polyunsaturated fatty acids				
< 2.0196	41/334 (12.3%)	1.00	18/334 (5.4%)	1.00
2.0196–2.4789	25/334 (7.5%)	0.54 (0.31–0.93)	17/334 (5.1%)	0.87 (0.42–1.79)
> 2.4789	36/334 (10.8%)	0.98 (0.59–1.61)	22/334 (6.6%)	1.42 (0.72–2.82)
p for trend		0.86		0.31
Eicosapentaenoic acid				
< 0.137	44/334 (13.2%)	1.00	26/334 (7.8%)	1.00
0.137–0.2232	28/334 (8.4%)	0.54 (0.32–0.91)	15/334 (4.5%)	0.51 (0.25–1.01)
> 0.2232	30/334 (9.0%)	0.63 (0.37–1.06)	16/334 (4.8%)	0.56 (0.27–1.11)
p for trend		0.07		0.08
Docosahexaenoic acid				
< 0.2475	46/334 (13.8%)	1.00	26/334 (7.8%)	1.00
0.2475–0.3616	29/334 (8.7%)	0.53 (0.32–0.89)	16/334 (4.8%)	0.53 (0.26–1.04)
> 0.3616	27/334 (8.1%)	0.52 (0.30–0.88)	15/334 (4.5%)	0.50 (0.24–1.00)
p for trend		0.01		0.04
n-6 Polyunsaturated fatty acids				
< 9.89	38/334 (11.4%)	1.00	19/334 (5.7%)	1.00
9.89–11.72	27/334 (8.1%)	0.66 (0.38–1.13)	16/334 (4.8%)	0.75 (0.36–1.55)
> 11.72	37/334 (11.1%)	1.15 (0.69–1.92)	22/334 (6.6%)	1.40 (0.71–2.77)
p for trend		0.61		0.33
n-3/n-6 Polyunsaturated fatty acid ratio				
< 0.1914	43/334 (12.9%)	1.00	24/334 (7.2%)	1.00
0.1914–0.2218	24/334 (7.2%)	0.55 (0.31–0.94)	14/334 (4.2%)	0.54 (0.25–1.09)
> 0.2218	35/334 (10.5%)	0.81 (0.49–1.35)	19/334 (5.7%)	0.77 (0.39–1.50)
p for trend		0.39		0.41
Cholesterol				
< 215.70	39/334 (11.7%)	1.00	21/334 (6.3%)	1.00
215.70–303.76	36/334 (10.8%)	0.92 (0.55–1.53)	18/334 (5.4%)	0.84 (0.42–1.66)
> 303.76	27/334 (8.1%)	0.63 (0.36–1.07)	18/334 (5.4%)	0.74 (0.37–1.48)
p for trend		0.09		0.40

[†] Based on multiple logistic regression controlling for age (< 30 and 30+ years), gestation (< 18 and 18+ weeks), parity (0 and 1+), cigarette smoking (never, former, and current), indoor domestic pets, family history of asthma, atopic eczema, and allergic rhinitis, family income (< 4,000,000, 4,000,000–5,999,999, and 6,000,000+ yen per year), education (< 13, 13–14, and 15+ years), mite allergen level in house dust (–, ±, and + or ++), changes in diet in the previous 1 month (none or seldom, slight, and substantial), season when data were collected (spring, summer, fall, and winter), and body mass index (continuous).

[‡] Tertiles were based on intake in g/day (except for cholesterol; mg/day) adjusted for energy intake using the residual method, except for tertiles of the ratio of n-3 to n-6 polyunsaturated fatty acids, which were based on crude intake in g/day.

observed only when comparing the second with the first tertile in the multivariate model. The prevalence of current atopic eczema was lower in the second ratio category than in the lowest ratio category, although the multivariate OR for the second tertile was not statistically significant. Consumption of total fat, saturated fatty acids, monounsaturated fatty acids, n–6 polyunsaturated fatty acids, and cholesterol was not materially associated with the prevalence of both outcomes for atopic eczema.

We then evaluated the prevalence of atopic eczema based on intake of selected high-fat foods (Table 4). Compared with fish intake in the first tertile, only consumption of fish in the second tertile was independently related to a reduced prevalence of atopic eczema after age 18 in the multivariate model (p for trend = 0.13). We found no significant association for the consumption of meat, eggs, or dairy products.

Table 4. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for atopic eczema by tertiles of intake of selected foods high in fat, Osaka Maternal Child Health Study, Japan[†]

Variable[‡]	Atopic eczema after age 18		Current atopic eczema	
	Prevalence	Adjusted OR (95% CI)	Prevalence	Adjusted OR (95% CI)
Fish				
< 36.14	42/334 (12.6%)	1.00	25/334 (7.5%)	1.00
36.14–54.44	28/334 (8.4%)	0.59 (0.34–0.99)	14/334 (4.2%)	0.50 (0.24–1.01)
> 54.44	32/334 (9.6%)	0.67 (0.40–1.13)	18/334 (5.4%)	0.64 (0.32–1.24)
p for trend		0.13		0.17
Meat				
< 46.16	35/334 (10.5%)	1.00	18/334 (5.4%)	1.00
46.16–67.13	37/334 (11.1%)	1.01 (0.60–1.69)	20/334 (6.0%)	0.94 (0.47–1.90)
> 67.13	30/334 (9.0%)	0.85 (0.49–1.47)	19/334 (5.7%)	0.96 (0.47–1.97)
p for trend		0.58		0.92
Eggs				
< 17.99	37/334 (11.1%)	1.00	18/334 (5.4%)	1.00
17.99–37.76	35/334 (10.5%)	0.95 (0.57–1.59)	22/334 (6.6%)	1.18 (0.60–2.34)
> 37.76	30/334 (9.0%)	0.82 (0.48–1.39)	17/334 (5.1%)	0.91 (0.44–1.88)
p for trend		0.46		0.81
Dairy products				
< 129.74	33/334 (9.9%)	1.00	19/334 (5.7%)	1.00
129.74–221.79	36/334 (10.8%)	1.05 (0.62–1.78)	19/334 (5.7%)	0.99 (0.49–1.98)
> 221.79	33/334 (9.9%)	0.86 (0.49–1.49)	19/334 (5.7%)	0.86 (0.42–1.77)
p for trend		0.58		0.68

[†] Based on multiple logistic regression controlling for age (< 30 and 30+ years), gestation (< 18 and 18+ weeks), parity (0 and 1+), cigarette smoking (never, former, and current), indoor domestic pets, family history of asthma, atopic eczema, and allergic rhinitis, family income (< 4,000,000, 4,000,000–5,999,999, and 6,000,000+ yen per year), education (< 13, 13–14, and 15+ years), mite allergen level in house dust (–, ±, and + or ++), changes in diet in the previous 1 month (none or seldom, slight, and substantial), season when data were collected (spring, summer, fall, and winter), and body mass index (continuous).
[‡] Tertiles were based on intake in g/day adjusted for energy intake using the residual method.

DISCUSSION

The proinflammatory eicosanoids prostaglandin E_2 and leukotriene B_4 are derived from n–6 fatty acid arachidonic acid, which is maintained at high cellular concentrations by the high n–6 polyunsaturated fatty acid content of the modern Western diet.[33] Prostaglandin E_2 is an important immune regulator known to suppress Th1 activation and enhance Th2 activation thereby enhancing the formation of IgE in B cells.[34] On the other hand, eicosapentaenoic acid, the n–3 homologue of arachidonic acid, can inhibit arachidonic acid metabolism competitively via enzymatic pathways and, thus, can suppress production of n–6 eicosanoid inflammatory mediators.[33] A balance between n–3 and n–6 polyunsaturated fatty acid metabolism may be important. In the typical Western diet, 20 to 25-fold more n–6 fats than n–3 fats are consumed.[33] In a case-control study of fat intake and risk of squamous cell carcinoma of the skin in the USA,[35] the 90th percentile value of the ratio of n–3 to n–6 polyunsaturated fatty acid intake among 267 controls was 0.06; this value was much lower than 0.1914, the lowest tertile point in this study. In contrast, the median values of the ratio of n–3 to n–6 polyunsaturated fatty acids were 0.145 and 0.206 in the previously cited German study[1] and the present study, respectively. Neither study showed a relationship between n–6 polyunsaturated fatty acid intake and atopic eczema. Thus, a potential ill effect of n–6 polyunsaturated fatty acids on atopic eczema may be detected when intake of n–3 polyunsaturated fatty acids is very low. A cross-sectional study in Japanese females showed that dietary intake of n–6 polyunsaturated fatty acids was significantly positively associated with seasonal allergic rhinoconjunctivitis in spring, however.[14]

Our observations of an inverse association between docosahexaenoic acid intake and atopic eczema may be attributable to anti-inflammatory effects of marine-derived n–3 polyunsaturated fatty acids although clear inverse relationships of consumption of eicosapentaenoic acid and fish with atopic eczema were not found in the current study. We have no immediate explanation as to the underlying mechanisms for those observations. Unknown active substances in fish might have interfered with the benefit of fish or marine origin n–3 polyunsaturated fatty acids on atopic eczema. For example, methylmercury and dioxins are accumulated in fish and shellfish through the marine food web. Alternatively, the findings regarding docosahexaenoic acid intake may simply be a chance phenomenon. However, our previous results using baseline data from the OMCHS showed a significant inverse relationship between intake of eicosapentaenoic and docosahexaenoic acids and the prevalence of allergic rhinitis whereas fish consumption and high ratio of n–3 to n–6 polyunsaturated fatty acid intake were associated with a decreased prevalence of asthma.[36, 37]

The present study had several methodological advantages in that study subjects were homogeneous in terms of all being pregnant and in that this study incorporated extensive information on potential confounding factors. Since we did not actually observe the dietary habits of the subjects, the results should be interpreted cautiously. Our diet history questionnaire was designed to assess recent dietary intake, i.e. for 1 month prior to completing the

questionnaire. Adjustment for the season when data were collected is likely to mitigate this disadvantage, however. It is uncertain whether our diet history questionnaire reflects the diet over a long period of time, which would be relevant to the presence of atopic eczema. However, it seems probable that all subjects had the same probability of being misclassified in relation to their true long-term dietary exposure. The consequence would have been an underestimation of values in our results. Changes in diet in the past 1 month were controlled for because pregnant females are likely to change their diet for reasons such as nausea gravidarum.

Other limitations also should be discussed. Our subjects were an unrepresentative sample of Japanese females in the general population, and the present findings may not be generalized. In fact, educational levels were higher in the present study population than in the general population. According to the 2000 population census of Japan, the proportions of females aged 30 to 34 years in Osaka Prefecture with years of education of < 13, 13–14, 15+, and unknown were 49.2, 32.3, 13.6, and 4.9%, respectively.[38] The prevalence of atopic eczema might be higher among our subjects than among the general population. Muto et al. reported that the lifetime prevalence of atopic eczema was 4.4% for Japanese women aged 30 to 39 years according to UK Working Party's diagnostic criteria.[39] We did not use validated diagnostic criteria for atopic eczema such as those reported in the International Study of Asthma and Allergies in Childhood. Because the definition of atopic eczema was based on drug treatment, there was a loss of milder sufferers. Moreover, females who want to become pregnant or who are pregnant might tend to avoid drugs. The consequence could be a bias toward the null. However, median and 95th percentile values for total serum immunoglobulin E concentrations were 201 and 2215 IU/ml in 54 current atopic eczema sufferers and 70 and 633 IU/ml in 927 females without current atopic eczema, respectively. The corresponding values were 162 and 2215 IU/ml in 99 atopic eczema sufferers after age 18 and 67 and 586 IU/ml in 882 noncases, respectively. Our study did not have substantial statistical power, although a statistically significant association with intake of docosahexaenoic acid was detected. However, this cross-sectional data cannot demonstrate a causal relationship between intake of fatty acids and foods high in fatty acids and atopic eczema.

The interface between allergy/immunology and pregnancy should be discussed, as it may have an influence on the association of interest. It has been suggested that pregnancy involves a shift to the Th2 side of the immune response,[40] although Chaouat et al pointed out the importance of the role of NK and IL-12, IL-15, and IL-18 tripods in successful or failed pregnancy in humans beyond the Th1/Th2 paradigm.[41] Symptoms of atopic eczema may worsen with pregnancy in some patients and appear to improve in others.[42] Atopic eczema in pregnancy is not likely to be a distinct entity. In the present study, 54 of 57 current patients with atopic eczema (94.7%) had been treated with medications at some time for 1 or more years.

Seventeen of 102 atopic eczema sufferers after age 18 (16.7%) and 10 of 57 current atopic eczema sufferers (17.5%) had received medical treatment due to allergies such as food allergy, but with the exception of asthma, atopic eczema, and allergic rhinitis, at some time after reaching the age of 18 although data on the precise diagnosis were not available. Some of those with atopic eczema in this study might have made a conscious decision to have a low dietary intake of fish because of a fear of sensitivity to fish. If correct, such a hypothesis would have given rise to an overestimation of our findings. During the time period of this study, patients with atopic eczema might not have been aware of the beneficial effects of fat intake. This could lead to bias toward the null.

This is the first epidemiological study on the association of intake of fat and high-fat foods with atopic eczema in Japan. Our results suggest that a daily intake of more than 0.36 g of docosahexaenoic acid may be associated with a reduced prevalence of atopic eczema in young female Japanese adults. Further investigations are needed to draw a conclusion as to whether consumption of fish and n–3 polyunsaturated fatty acids is independently protective against atopic eczema, taking into consideration additional environmental factors as well as genetic factors. Research regarding biological mechanisms is also warranted.

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AUTHOR DISCLOSURES

All authors declare no conflict of interest in this manuscript.

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Original Article

Relationship between dietary fat and fish intake and the prevalence of atopic eczema in pregnant Japanese females: baseline data from the Osaka Maternal and Child Health Study

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日本孕婦在飲食脂肪和魚的攝取與遺傳過敏性溼疹之盛行率之相關性：大阪母親與孩童健康研究之基綜資料

在遺傳過敏性溼疹發展過程中，飲食因子可能是重要的。不論是攝取 n-3 多元不飽和脂肪酸可防止過敏的論點，或攝取 n-6 多元不飽和脂酸會增加過敏性的風險都仍然是有爭議的。本篇橫斷性研究就是在檢測脂肪酸和高脂肪食物攝取與遺傳過敏性溼疹之盛行率的相關性。研究對象是 1002 位日本孕婦。目前的遺傳過敏性溼疹和 18 歲之後的遺傳過敏性溼疹，被定義為當受試者分別在 12 個月前和滿 18 歲後已經接受藥物治療，那就是有遺傳過敏性溼疹。飲食因子資訊，是使用一個有效的自我填答飲食史問卷收集得來的。DHA 攝取顯著性地與 18 歲之後和目前的遺傳過敏性溼疹盛行率的降低有相關。不論 n-3 多元不飽和脂肪酸、EPA、魚和 n-3/ n-6 多元不飽和脂肪酸比值對遺傳過敏性溼疹並沒有負的劑量效應，但這些飲食變項的第二個參等分與 18 歲之後的遺傳過敏性溼疹呈顯著地負相關。總脂肪、飽和脂肪酸、單元不飽和脂肪酸、n-6 多元不飽和脂肪酸、膽固醇、肉、蛋或是乳製品攝取與任一項遺傳過敏性溼疹都沒有相關。在日本孕婦中，DHA 攝取可能與遺傳過敏性溼疹盛行率的減少有相關性存在。

關鍵字：遺傳過敏性溼疹、飲食、脂肪酸、魚類、日本