AEP Vol. 15, No. 5
May 2005: 358–364

In the present study, we used self-reported tooth loss as a proxy for dental diseases, and we did not assess the validity of this methodology. However, Douglass and colleagues (23) showed that the self-reported residual number of teeth correlated highly with the actual number of teeth determined by clinical examination in the general population aged 70 years or over (Pearson correlation coefficient = 0.97). Axelesson and Helgadóttir (24) reported that the kappa statistic for agreement between the self-reported number of remaining teeth and the number found at a clinical examination in the 18-year-old group, 35- to 44-year-old group, and the group aged 65 years or older were 0.56, 0.60, and 0.63, respectively. Age is not likely to have a significant effect on the validity of self-reported information on the number of remaining teeth. In the US, the Erie County Periodontal Disease Study examined reliability of a self-reported health questionnaire (25). With respect to self-reported reasons for tooth loss, a substantial agreement at a 2-year interval was demonstrated among subjects aged 25 to 74 years (kappa value = 0.71 and 0.74 among women and men, respectively) (25). On the other hand, reliability of recall of past oral disorders such as tooth ache, sore or swollen gums, and sensitivity of teeth to cold or heat was moderate (kappa value = 0.57 and 0.56 among women and men, respectively) (25). These findings indicate that valid data in relation to oral health could be obtained from a self-reported oral health questionnaire regardless of age, and that persons are likely to be more knowledgeable about tooth loss than about signs and symptoms of disturbances of oral health. Thus, the use of self-reported tooth loss as a key indicator of dental health status can be considered satisfactory in epidemiological research.

A prospective study of Swedish women aged 38 to 60 years demonstrated that the number of cigarettes consumed per day was significantly positively correlated with the number of teeth lost during the 12-year follow-up period (3). A cross-sectional study in the US also showed that current and former smokers had a significantly higher number of missing teeth than non-smokers, and that the mean number of missing teeth among current, former, and non-smokers was 5.1, 3.9, and 2.8, respectively (9). Compared with non-smoking, active smoking for more than 10 years or consuming at least 11 or more cigarettes per day was significantly positively associated with the prevalence of tooth loss among Japanese men aged 20 to 59 years (5). Our results were partially consistent with these observations.

A few cross-sectional studies have examined the association of passive smoking with oral health status (17–19). A cross-sectional study in US children aged 4 to 11 years showed a significantly positive dose–response relationship between serum cotinine levels and caries in deciduous teeth (18). Serum cotinine is an objective and quantitative biomarker of ETS. In the UK National Diet and Nutrition Survey, maternal smoking was significantly positively related to the prevalence of caries in children (19). As far as we know, only one study in US adults aged 18 years and older examined the issue of exposure to ETS and periodontal disease and found that the OR for periodontal disease in relation to exposure to ETS was 1.6 (95% CI, 1.2–2.2), compared with those not exposed to ETS (17). In the present study, ETS exposure at home but not at work was significantly associated with an increased prevalence of tooth loss. This finding may be partially attributable to the fact that the proportions of housewives, part-time workers, and full-time workers among the present study subjects were 71.3%, 11.1%, and 17.7%, respectively. Japanese women tend to leave employment or become part-time workers after marriage or while bringing up their children.

Numerous tobacco smoke byproducts may affect oral health among both active and passive smokers (17). Potential mechanisms for the effect of smoking on oral health include immunosuppression and exaggerated inflammatory cell responses (26). Both local and systemic effects by tobacco smoke are pointed out (26). A number of tobacco smoke byproducts such as nicotine may promote local vasoconstriction, edema, and inflammation (26). Systemic alterations of the host response may include decreased levels of salivary IgA and serum IgG and decreased T-helper cell functions (26).

This investigation had methodological strengths. Study subjects were homogeneous in terms of all being pregnant. In addition, the extensive information collected allowed for the investigation of potential confounding factors. We also obtained detailed data on active and passive smoking such as the duration of tobacco exposure in spite of not using an objective and quantitative biomarker. Weaknesses of this study should be taken into account when interpreting the results. Of a total of 3639 eligible pregnant women in Neyagawa City, only 627 (17.2%) took part in this study. We were uncertain whether there was a difference between participants and non-participants in Neyagawa City, because data on personal characteristics such as age, socioeconomic status, and experience of extraction of permanent teeth among the non-participants were not available. With regard to the remaining 375 participants, we were not able to calculate the participation rate because the exact number of eligible subjects was not available. Our subjects were not representative of Japanese females in the general population and the present findings may not be generalized. Educational levels in the present study population were higher than in the general population. According to the 2000 population census of Japan, the proportions of women aged 30 to 34 years in Osaka Prefecture with years of education of < 13, 13 to 14, 15+, and unknown were 49.2%, 32.3%, 13.6%, and 4.9%, respectively (27). The corresponding figures for the present

study were 32.2%, 41.2%, 26.6%, and 0.0%, respectively. However, cigarette-smoking status in these study subjects was likely to be similar to that in the general population. In a national nutrition survey in 1998, percentages of current, former, and non-smoking in women aged 20 to 29 years were 19.1%, 4.9%, and 76.0%, respectively (28). The corresponding figures for the present subjects were 18.4%, 12.1%, and 69.6%, respectively. The prevalence of tooth extraction in this study population (25.5%) is also similar to that in a sample that consisted of Japanese women aged 25 to 30 years for a survey of dental diseases in 1999 (27.3%) (29). According to a report on reasons for extraction of teeth in Japanese aged 9 to 35 years, the proportions of extractions resulting from caries, periodontal disease, eruption problems, orthodontic indications, trauma, and others were 51.5%, 6.2%, 21.9%, 5.1%, 0.1%, and 15.2%, respectively (30). More than 90% of extractions for eruption problems were third molars (30). In the current population, one half of tooth loss is likely to be ascribed to caries and periodontal disease. Tooth loss cannot explain the condition of the teeth at the early stage of dental disease, i.e., tooth loss is mainly explained as a result of severe dental caries and periodontal diseases. Thus, the reported ORs associated with tooth loss would have been underestimated compared with a true relationship between smoking and dental health. In the present study, information regarding the point in time when the teeth were lost was not available. Therefore, the time sequence between smoking status and tooth loss could not be determined. We were not able to take into account oral health behaviors, such as frequency of tooth brushing and pattern of dental visits. If participants were not aware of the possible effects of smoking exposure with regard to tooth loss, misclassification of the outcome would be unlikely to differ among all categories of active and passive smoking. The consequence would have given rise to an underestimation of our findings.

In conclusion, the results of this cross-sectional study support previous observations showing a positive association between active smoking and tooth loss. We also found evidence of a clear relationship between current passive smoking at home and tooth loss among pregnant women who had never smoked. However, the reasons underlying this association are still unclear. Further investigations with more precise and objective indicators of dental diseases and exposure to smoking are needed to draw a conclusion as to whether active and passive smoking exposure are independent risk factors for dental diseases.

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APPENDIX

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ELSEVIER

Dietary Intake of Seaweed and Minerals and Prevalence of Allergic Rhinitis in Japanese Pregnant Females: Baseline Data From the Osaka Maternal and Child Health Study

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PURPOSE: It may be worthwhile to assess the possible protective effect of the traditional Japanese diet on allergic disorders. This cross-sectional study investigated the relationship between dietary intake of seaweed, vegetables, fruit, antioxidants, fiber, and minerals and the prevalence of allergic rhinitis.
METOHDS: Study subjects were 1002 Japanese pregnant women. Allergic rhinitis (including cedar pollinosis) was defined as present if subjects had received drug treatment at some point during the previous 12 months. Information on dietary factors was collected by using a self-administered diet history questionnaire.
RESULTS: Seaweed intake was associated independently with a decreased prevalence of allergic rhinitis. Significant inverse dose–response relationships were found between calcium and phosphorus intake and allergic rhinitis prevalence. There also was a tendency for an inverse association between magnesium consumption and allergic rhinitis. Additional adjustment for calcium or magnesium intake apparently did not influence the inverse association with seaweed consumption. Consumption of vegetables, fruit, vitamins C and E, fiber, and zinc showed no association with allergic rhinitis, whereas a significant positive relationship was observed between β-carotene intake and allergic rhinitis.
CONCLUSIONS: High dietary intake of seaweed, calcium, magnesium, and phosphorus may be associated with a decreased prevalence of allergic rhinitis.
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KEY WORDS: Calcium, Cross-Sectional Studies, Japan, Magnesium, Phosphorus, Pregnant Women, Rhinitis, Seaweed.

INTRODUCTION

Allergic rhinitis, especially Japanese cedar pollinosis, is a major public health problem in Japan. A recent cross-sectional survey throughout Japan showed that the age-adjusted prevalence of Japanese cedar pollinosis was 19.4% and almost 60% of those affected visited physicians (1). High exposure to cedar pollen in Japan is the result of forestation policies favoring planting of cedar trees for housing construction after World War II. However, the prevalence of allergic rhinitis in urban areas is high compared with that in rural areas in Japan (1–3). The prevalence of hay fever increased significantly between 1991 to 1992 and 1995 to 1996 in school children in the former East Germany (4). Thus, factors in relation to the Western lifestyle also may be of importance in the cause of allergic rhinitis. For example, the joint effect of cedar pollen and automobile exhaust is indicated (5, 6).

Several epidemiologic studies paid attention to the relationship between dietary factors and allergic rhinitis (4, 7–16). Associations of allergic rhinitis with fatty acids, foods high in fatty acids (4, 7–16), fruit, and antioxidants (15, 16) were examined, but results were inconsistent. It may be worthwhile to assess the possible protective effect of the traditional Japanese diet on allergic disorders. Seaweed is a food commonly eaten by all people in Japan and rarely eaten by people in Western countries. Seaweed is an important source of trace minerals, as well as fiber and

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Selected Abbreviations and Acronyms

OMCHS = Osaka Maternal and Child Health Study
BMI = body mass index
OR = odds ratio
CI = confidence interval
Th1 = T-Helper cell subtype 1
Th2 = T-Helper cell subtype 2
IL-12 = interleukin 12
IgE = immunoglobulin E

antioxidants. The role of seaweed as an anticarcinogen is suggested (17, 18). Two case–control studies in Japan found inverse associations between seaweed intake and stomach and colorectal cancer (19, 20), whereas a prospective study of Hawaiian Japanese men showed significant positive relationships between seaweed consumption and cancer of the upper aerodigestive tract and prostate (21, 22).

To our knowledge, there is no epidemiologic information on the effect of seaweed consumption on allergic disorders; therefore, we investigated the relationship between dietary intake of seaweed and prevalence of allergic rhinitis in Japanese pregnant women by using baseline data from the Osaka Maternal and Child Health Study (OMCHS). Associations of dietary intake of vegetables, fruit, fiber, and selected antioxidants and minerals with allergic rhinitis also were investigated.

METHODS

Study Population

The OMCHS, a prospective cohort study that examines preventive and risk factors for such maternal and child health problems as allergic disorders, started in November 2001. Details of the OMCHS were described elsewhere (23, 24). Briefly, eligible women were those who became pregnant in Neyagawa City, which is one of the 44 municipalities in Osaka Prefecture, a metropolis in Japan with a total population of approximately 8.8 million. Of 3639 eligible women in Neyagawa City, 627 women (17.2%) participated in this study between November 2001 and March 2003. Eight pregnant women 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 regarding the OMCHS from public health nurses in six other municipalities between August 2002 and March 2003. From October 2002 to March 2003, a total of 290 participants were recruited from a university hospital and three obstetric hospitals in three other municipalities; these women were recommended for participation in the OMCHS by an obstetrician. Finally, 1002 pregnant women gave their fully informed consent in writing and completed the baseline survey. The ethics committees of the Osaka City University School of Medicine and the Osaka Prefectural Institute of Public Health approved the present study.

Measurements

Baseline assessment of the cohort was composed of a set of two self-administered questionnaires and collection of a dust sample from a 1-m^2 area of the bedclothes for 1 minute by using a vacuum cleaner fitted with a collection apparatus. Participants 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 1 month. The structure and validity of the questionnaire were described in detail elsewhere (25, 26). In this instrument, intake of 147 food items was calculated by using an ad hoc computer algorithm developed to analyze the questionnaire. Seaweed consumption was calculated by using two semiquantitative frequency questions (Wakame or Hijiki and Nori). Green and yellow vegetable consumption included intake of carrot, pumpkin, tomato, sweet pepper, broccoli, and such dark-green leafy vegetables as spinach and komatsuna. Other vegetable intake included cabbage, cucumber, lettuce, Chinese cabbage, bean sprouts, Japanese radish, onion, cauliflower, eggplant, burdock, lotus root, vegetable juice, umeboshi, and salt pickles. Fruit consumption was defined as intake of raisins, canned fruits, fruit juice, tomato juice, citrus fruits, banana, apple, strawberry, grapes, peach, Japanese pear, Japanese persimmon, kiwifruit, melon, and watermelon. Energy-adjusted intake by the residual method was used for the analyses (27). Because of the small number who used calcium (5.0%), vitamin C (5.3%), and multivitamin supplements (3.8%) at least once a week, use of these dietary supplements was not incorporated into the analysis in this study.

A second self-administered questionnaire ascertained age, gestation, parity, smoking habits, passive smoking exposure, personal history of allergic rhinitis, family history of asthma, atopic eczema, allergic rhinitis, indoor domestic pets, family income, education, weight, height, and changes in diet in the previous 1 month. Allergic rhinitis (including Japanese cedar pollinosis) was defined as present when subjects had been treated with medications at some time in the previous 12 months. Current smokers were defined as respondents who reported smoking cigarettes every day at the time of the baseline survey. Body mass index (BMI) was calculated by dividing self-reported body weight (kilograms) by the square of self-reported height (meters).

Antigen levels from extracts of fine dust fractions were measured by means of a double-antibody sandwich enzyme-linked immunosorbent assay (Mitey checkerR; Shinto Fine Co., Ltd., Osaka, Japan) (28, 29). Antigen levels were

AEP Vol. 16, No. 8
August 2006: 614–621

semiquantitatively classified with scores of – (<2 μg/m^2), ± (5 μg/m^2), + (10 to 15 μg/m^2), and ++ (>35 μg/m^2).

Statistical Analysis

Intake of selected foods and nutrients was categorized at quartile points based on the distribution of all study subjects. Age was classified into three categories (<29, 29 to 31, and 32+ years); gestation, into three categories (<15, 15 to 20, and 21+ weeks); parity, into three categories (0, 1, and 2+); cigarette smoking, into three categories (never, former, and current); passive smoking at home, into three categories (never, former, and current); passive smoking at work, into three categories (never, former, and current); family income, into three categories (<4,000,000, 4,000,000 to 5,999,999, and 6,000,000+ yen/year); education, into three categories (<13, 13 to 14, and 15+ years); dust mite allergen levels, into four categories (–, ±, +, and ++); changes in diet in the previous 1 month, into three categories (none or seldom, slight, and substantial); and season when data were collected, into four categories (spring, summer, fall, and winter). BMI was used as a continuous variable.

Logistic regression analysis was used to estimate crude odds ratios (ORs) and their 95% confidence intervals (CIs) for allergic rhinitis relative to intake of vegetables, fruit, seaweed, fiber, and selected antioxidants and minerals. Multiple logistic regression analysis was used to control for potential confounders. Trend of association was assessed by means of a logistic regression model assigning scores to levels of the independent variable. Two-sided $p < 0.05$ is considered statistically significant. All computations were performed using the SAS software package, version 8.2 (SAS Institute, Inc., Cary, NC).

RESULTS

The prevalence of allergic rhinitis (including Japanese cedar pollinosis) in the previous 12 months was 14.1% among 1002 pregnant women. Tables 1 and 2 list the distribution of selected factors in the 1002 participants. Approximately 30% of subjects were aged 29 to 31 years. Approximately 70% of women were enrolled by the 20th week of gestation, and approximately half had a parity of one or more. Slight or substantial changes in diet in the previous 1 month were experienced by 702 pregnant women because of nausea gravidarum (585 women), maternal and fetal health (107 women), and other reasons (10 women). Mean total energy and energy-adjusted seaweed intake were 6815 kJ and 12.6 g/d, respectively.

Table 3 lists ORs and 95% CIs of allergic rhinitis in relation to vegetable, fruit, and seaweed intake in 1002 pregnant women. There was no measurable association of dietary

TABLE 1. Distribution of selected characteristics in 1002 pregnant women, Osaka Maternal and Child Health Study, Japan

Variable	
Age (years)	
<29	380 (37.9)
29–31	299 (29.8)
32+	323 (32.2)
Gestation (weeks)	
<15	357 (35.6)
15–20	329 (32.8)
21+	316 (31.5)
Parity	
0	489 (48.8)
1	399 (39.8)
2+	114 (11.4)
Cigarette smoking	
Never	697 (69.6)
Former	121 (12.1)
Current	184 (18.4)
Passive smoking at home	
Never	284 (28.3)
Former	224 (22.4)
Current	494 (49.3)
Passive smoking at work	
Never	344 (34.3)
Former	538 (53.7)
Current	120 (12.0)
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[a]	
–	436 (43.5)
±	297 (29.6)
+	196 (19.6)
++	73 (7.3)
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)

Values expressed as number (percent) or mean ± SD.
[a]Antigen levels were classified semiquantitatively with scores of – (<2 μg/m^2), ± (5 μg/m^2), + (10 to 15 μg/m^2), and ++ (>35 μg/m^2).

TABLE 2. Distribution of daily nutrients and food intake in 1002 pregnant women, Osaka Maternal and Child Health Study, Japan[a]

Variable	Mean ± SD
Total energy (kJ)	6815.3 ± 1793.7
Green and yellow vegetables (g)	69.5 ± 46.0
Other vegetables (g)	109.2 ± 68.9
Fruit (g)	173.2 ± 182.4
Seaweed (g)	12.6 ± 13.0
β-Carotene (mg)	1840.4 ± 1222.0
Vitamin C (mg)	120.7 ± 58.7
Vitamin E (mg)	7.5 ± 1.8
Fiber (g)	11.3 ± 3.4
Calcium (mg)	556.0 ± 182.9
Magnesium (mg)	194.4 ± 49.9
Phosphorus (mg)	890.0 ± 183.8
Zinc (μg)	7222.8 ± 1321.0

[a]Nutrients and food intake were adjusted for total energy intake by using the residual method.

intake of green and yellow vegetables, other vegetables, and fruit with allergic rhinitis prevalence. Compared with seaweed intake in the first quartile, seaweed consumption in the second and fourth quartiles, but not the third quartile, was statistically significantly related to a decreased prevalence of allergic rhinitis. After adjustment for age, gestation, parity, cigarette smoking, passive smoking at home and work, indoor domestic pets, family history of asthma, atopic eczema, allergic rhinitis, family income, education, and mite allergen level in house dust, changes in diet in the past 1 month, season when data were collected, and BMI, the inverse relation was slightly strengthened, showing a clear inverse dose–response relationship (p for trend = 0.03).

ORs for associations between antioxidant and fiber intake and allergic rhinitis are listed in Table 4. β-Carotene intake was associated independently with an increased prevalence of allergic rhinitis after multivariate adjustment: the OR for comparison of the highest with the lowest quartile was 1.98 (95% CI, 1.13–3.51). Consumption of vitamins C and E and fiber was not materially related to the prevalence of allergic rhinitis.

Results for mineral intake are listed in Table 5. A significant inverse dose–response association was observed between calcium intake and allergic rhinitis prevalence. The inverse association was slightly evident after controlling for the confounders under investigation, although the multivariate OR for comparison of the fourth with the first quartile was not statistically significant (p for trend = 0.03). For magnesium intake, an inverse association between the highest and lowest quartiles was statistically significant, but was just short of the significance level in the multivariate model. A clear inverse linear trend for phosphorus intake across quartiles was found, although only phosphorus consumption in the third quartile was associated with a statistically significant decreased prevalence of allergic rhinitis by the multivariate model. Dietary zinc intake showed no association with allergic rhinitis prevalence.

After further adjustment for calcium or magnesium consumption, an inverse association between seaweed intake and allergic rhinitis prevalence remained, albeit slightly attenuated: multivariate ORs for the second and fourth quartiles, but not the third quartile, were statistically significant (Table 6). After additional control for phosphorus intake, consumption of seaweed in the third and fourth quartiles, but not the second quartile, was not independently associated with the prevalence of allergic rhinitis.

DISCUSSION

The strengths of the current study include the homogeneity of study subjects in terms of all being pregnant and the comprehensive assessment of potential confounders. However, no allowance was made for such external factors as aeroallergens and air pollution.

TABLE 3. Odds ratios and 95% confidence intervals for allergic rhinitis by quartiles of vegetable, fruit, and seaweed intake, Osaka Maternal and Child Health Study, Japan

Variable[a]	Prevalence	Crude OR (95% CI)	Adjusted OR (95% CI)[b]
Green and yellow vegetables			
Q1 (28.6)	37/250 (14.8%)	1.00	1.00
Q2 (50.2)	28/251 (11.2%)	0.72 (0.42–1.22)	0.72 (0.41–1.25)
Q3 (71.2)	31/250 (12.4%)	0.82 (0.49–1.36)	0.88 (0.50–1.52)
Q4 (115.6)	45/251 (17.9%)	1.26 (0.78–2.03)	1.35 (0.80–2.29)
p for trend		0.28	0.18
Other vegetables			
Q1 (51.7)	36/250 (14.4%)	1.00	1.00
Q2 (80.6)	36/251 (14.3%)	1.00 (0.60–1.64)	0.94 (0.55–1.60)
Q3 (111.8)	25/250 (10.0%)	0.66 (0.38–1.13)	0.64 (0.36–1.13)
Q4 (171.6)	44/251 (17.5%)	1.26 (0.78–2.05)	1.27 (0.76–2.13)
p for trend		0.61	0.59
Fruit			
Q1 (44.3)	36/250 (14.4%)	1.00	1.00
Q2 (114.2)	30/251 (12.0%)	0.81 (0.48–1.36)	0.68 (0.39–1.19)
Q3 (174.3)	36/250 (14.4%)	1.00 (0.61–1.65)	1.05 (0.61–1.81)
Q4 (289.7)	39/251 (15.5%)	1.09 (0.67–1.79)	1.03 (0.60–1.78)
p for trend		0.55	0.55
Seaweed			
Q1 (2.4)	48/250 (19.2%)	1.00	1.00
Q2 (6.2)	29/251 (11.6%)	0.55 (0.33–0.90)	0.50 (0.29–0.84)
Q3 (12.9)	33/250 (13.2%)	0.64 (0.39–1.03)	0.59 (0.35–0.98)
Q4 (28.6)	31/251 (12.4%)	0.59 (0.36–0.96)	0.51 (0.30–0.87)
p for trend		0.06	0.03

OR = odds ratio, CI = confidence interval, Q = quartile.
[a]Quartile medians in grams per day adjusted energy intake by using the residual method are given in parentheses.
[b]Adjustment for age, gestation, parity, cigarette smoking, passive smoking at home and at work, indoor domestic pets, family history of asthma, atopic eczema, allergic rhinitis, family income, education, and mite allergen level in house dust, changes in diet in the previous 1 month, season when data were collected, and body mass index (continuous).

AEP Vol. 16, No. 8
August 2006: 614–621

TABLE 4. Odds ratios and 95% confidence intervals for allergic rhinitis by quartiles of antioxidant and fiber intake, Osaka Maternal and Child Health Study, Japan

Variable[a]	Prevalence	Crude OR (95% CI)	Adjusted OR (95% CI)[b]
β-Carotene			
Q1 (758.8)	26/250 (10.4%)	1.00	1.00
Q2 (1346.0)	40/251 (15.9%)	1.63 (0.97–2.80)	1.71 (0.98–3.02)
Q3 (1916.8)	31/250 (12.4%)	1.22 (0.70–2.13)	1.30 (0.72–2.37)
Q4 (3010.3)	44/251 (17.5%)	1.83 (1.10–3.12)	1.98 (1.13–3.51)
p for trend		0.07	0.05
Vitamin C			
Q1 (69.9)	29/250 (11.6%)	1.00	1.00
Q2 (97.2)	32/251 (12.8%)	1.11 (0.65–1.91)	1.12 (0.63–1.99)
Q3 (123.5)	40/250 (16.0%)	1.45 (0.87–2.44)	1.47 (0.85–2.57)
Q4 (179.6)	40/251 (15.9%)	1.45 (0.87–2.43)	1.54 (0.88–2.73)
p for trend		0.10	0.08
Vitamin E			
Q1 (5.7)	39/250 (15.6%)	1.00	1.00
Q2 (6.8)	35/251 (13.9%)	0.88 (0.53–1.44)	0.86 (0.50–1.45)
Q3 (7.8)	31/250 (12.4%)	0.77 (0.46–1.27)	0.68 (0.39–1.17)
Q4 (9.5)	36/251 (14.3%)	0.91 (0.55–1.48)	0.78 (0.46–1.33)
p for trend		0.59	0.27
Fiber			
Q1 (8.2)	33/250 (13.2%)	1.00	1.00
Q2 (10.0)	38/251 (15.1%)	1.17 (0.71–1.95)	1.18 (0.69–2.03)
Q3 (11.8)	32/250 (12.8%)	0.97 (0.57–1.63)	1.00 (0.57–1.74)
Q4 (14.7)	38/251 (15.1%)	1.17 (0.71–1.95)	1.14 (0.66–2.00)
P for trend		0.72	0.80

OR = odds ratio, CI = confidence interval, Q = quartile.
[a]Quartile medians in milligrams per day (except for fiber; grams per day) adjusted energy intake by using the residual method are given in parentheses.
[b]Adjustment for age, gestation, parity, cigarette smoking, passive smoking at home and at work, indoor domestic pets, family history of asthma, atopic eczema, allergic rhinitis, family income, education, and mite allergen level in house dust, changes in diet in the previous 1 month, season when data were collected, and body mass index (continuous).

In our current investigation, dietary information was derived from a self-administered semiquantitative dietary assessment questionnaire. Because we did not actually observe dietary habits of subjects, the possibility of misclassification might be a concern. According to the validation studies, correlation coefficients for nutrient intake between those estimated from the diet-history questionnaire and those observed by a 3-day dietary record were 0.45, 0.49, and 0.59 for vitamin C, calcium, and phosphorus in women, respectively (25). Correlation coefficients between intake and the corresponding concentrations in serum phospholipid fraction were 0.40 and 0.60 in men and women for β-carotene and −0.23 and −0.22 in men and women for vitamin E, respectively (26). Those with allergic rhinitis might not be aware of the ill effects of diet. Therefore, any misclassification would be nondifferential between cases and noncases and most likely would weaken any true relationship. Our diet-history questionnaire was designed to assess recent dietary intake, i.e., for 1 month before completing the questionnaire. However, adjustment for season when data were collected is likely to ease this limitation. Changes in diet in the past 1 month were controlled for because pregnant women are likely to change their diet for such reasons as nausea gravidarum.

Other weaknesses of this study should be clarified. Of 3639 eligible pregnant women in Neyagawa City, only 627 (17.2%) participated in this study. We were not able to assess a difference between participants and nonparticipants in Neyagawa City because information on personal characteristics of nonparticipants was not available. Also, we were not able to calculate the participation rate of subjects from other areas and data were not available for nonparticipants in those areas.

Our subjects were an unrepresentative sample of Japanese women in the general population, and the present findings may not be generalized. Educational levels were higher in the present study population than in the general population. According to the 2000 population census of Japan, proportions of women aged 30 to 34 years in Osaka Prefecture with years of education of less than 13, 13 to 14, 15+,

TABLE 5. Odds ratios and 95% confidence intervals for allergic rhinitis by quartiles of mineral intake, Osaka Maternal and Child Health Study, Japan

Variable[a]	Prevalence	Crude OR (95% CI)	Adjusted OR (95% CI)[b]
Calcium			
Q1 (368.0)	37/250 (14.8%)	1.00	1.00
Q2 (491.7)	46/251 (18.3%)	1.29 (0.81–2.08)	1.44 (0.86–2.43)
Q3 (590.3)	33/250 (13.2%)	0.88 (0.53–1.45)	0.89 (0.51–1.57)
Q4 (739.4)	25/251 (10.0%)	0.64 (0.37–1.09)	0.60 (0.33–1.07)
p for trend		0.05	0.03
Magnesium			
Q1 (150.8)	42/250 (16.8%)	1.00	1.00
Q2 (175.4)	36/251 (14.3%)	0.83 (0.51–1.35)	0.96 (0.57–1.61)
Q3 (199.4)	36/250 (14.4%)	0.83 (0.51–1.35)	0.83 (0.49–1.41)
Q4 (245.8)	27/251 (10.8%)	0.60 (0.35–1.00)	0.63 (0.36–1.10)
p for trend		0.07	0.10
Phosphorus			
Q1 (713.1)	39/250 (15.6%)	1.00	1.00
Q2 (828.7)	52/251 (20.7%)	1.41 (0.90–2.25)	1.42 (0.86–2.34)
Q3 (928.1)	22/250 (8.8%)	0.52 (0.30–0.90)	0.50 (0.27–0.90)
Q4 (1085.0)	28/251 (11.2%)	0.68 (0.40–1.14)	0.59 (0.33–1.04)
p for trend		0.01	0.005
Zinc			
Q1 (5936.5)	38/250 (15.2%)	1.00	1.00
Q2 (6816.2)	41/251 (16.3%)	1.09 (0.67–1.77)	1.09 (0.65–1.84)
Q3 (7493.8)	35/250 (14.0%)	0.91 (0.55–1.49)	0.90 (0.53–1.55)
Q4 (8608.4)	27/251 (10.8%)	0.67 (0.39–1.14)	0.71 (0.40–1.26)
P for trend		0.11	0.19

OR = odds ratio, CI = confidence interval, Q = quartile.
[a]Quartile medians in milligrams per day (except for zinc; micrograms per day) adjusted energy intake by using the residual method are given in parentheses.
[b]Adjustment for age, gestation, parity, cigarette smoking, passive smoking at home and at work, indoor domestic pets, family history of asthma, atopic eczema, allergic rhinitis, family income, education, and mite allergen level in house dust, changes in diet in the previous 1 month, season when data were collected, and body mass index (continuous).

TABLE 6. Adjusted odds ratios and 95% confidence intervals for allergic rhinitis by quartiles of seaweed intake, Osaka Maternal and Child Health Study, Japan[a]

Variable[b]	OR (95% CI)[c]	OR (95% CI)[d]	OR (95% CI)[e]
Seaweed			
Q1 (2.4)	1.00	1.00	1.00
Q2 (6.2)	0.51 (0.30–0.87)	0.50 (0.29–0.84)	0.51 (0.29–0.87)
Q3 (12.9)	0.62 (0.36–1.04)	0.61 (0.35–1.03)	0.65 (0.38–1.11)
Q4 (28.6)	0.58 (0.33–0.99)	0.56 (0.32–0.98)	0.62 (0.35–1.08)
p for trend	0.08	0.07	0.16

OR = odds ratio, CI = confidence interval, Q = quartile.
[a]Adjustment for age, gestation, parity, cigarette smoking, passive smoking at home and at work, indoor domestic pets, family history of asthma, atopic eczema, allergic rhinitis, family income, education, and mite allergen level in house dust, changes in diet in the previous 1 month, season when data were collected, and body mass index (continuous).
[b]Quartile medians in grams per day adjusted energy intake by using the residual method are given in parentheses.
[c]Further adjustment for energy-adjusted calcium intake (quartiles).
[d]Further adjustment for energy-adjusted magnesium intake (quartiles).
[e]Further adjustment for energy-adjusted phosphorus intake (quartiles).

and unknown were 49.2%, 32.3%, 13.6%, and 4.9%, respectively (30). Japanese cedar pollinosis is a seasonal disorder with a high prevalence that is often undiagnosed (1). We did not use validated diagnostic criteria for allergic rhinitis, such as those reported in the International Study of Asthma and Allergies in Childhood. Because the definition of allergic rhinitis is based on drug treatment, there was a loss of those with milder cases. Moreover, women who want to become pregnant or are pregnant might tend to avoid drugs. The consequence would introduce a bias toward the null. However, median and 95th percentile values of total serum immunoglobulin E (IgE) concentrations were 123 and 761 IU/mL in 139 cases and 68 and 734 IU/mL in 842 noncases, respectively, although data for specific IgE levels were not available in this study. In addition, our study used cross-sectional data; thus, the data cannot be used to discriminate cause from effect. Symptoms of allergic rhinitis might have affected food preference and food consumption patterns. Nonetheless, important associations can be noted.

A relationship between pregnancy and a shift to the T-helper cell subtype 2 (Th2) side of the immune response has been indicated (31), whereas the importance of the role of natural killer and interleukin 12 (IL-12), IL-15, and IL-18 tripods in successful or failed pregnancy in humans was suggested beyond the Th1/Th2 paradigm (32). Rhinitis symptoms during pregnancy may be attributable to hormonal changes in pregnancy. However, rhinitis solely ascribed to pregnancy may not be a distinct entity because most pregnant women do not have significant nasal symptoms (31). In the present study, 105 of 141 persons current affected with allergic rhinitis (74.5%) had been treated with medications at some time for 1 or more years.

The European Prospective Investigation into Cancer and Nutrition among German adults found that high β-carotene intake significantly increased the risk for hay fever, whereas a significant inverse relationship was observed between vitamin E intake and hay fever, especially among women and former or current smokers (15). The Nutrition and Health Survey in Taiwan showed no association between calcium, phosphorus, and vitamin C and E intake and allergic rhinitis prevalence in teenagers (16). A cross-sectional study of UK adults showed that vitamin E intake was not associated independently with hay fever, but was related significantly to lower total serum IgE concentrations and lower frequency of allergy sensitization (33). Another cross-sectional study in Norway reported that vitamin C intake was not measurably related to prevalence of asthma attack in the previous 12 months among young adults, although a significant inverse association was observed between vitamin C intake and wheeze only in exsmokers (34). No differences in daily vitamin A, C, and E; magnesium; and zinc intakes were seen between patients with asthma and healthy subjects in a case–control study of prevalence in Spain (35).

These results are partially consistent with the present findings. In the present study, the multivariate OR for comparison of the fourth with the first quartile of β-carotene intake was 1.84 (95% CI, 0.92–3.79) in the sample of 697 never-smoking pregnant women. The possibility of a smoking-related harmful effect of β-carotene is not likely to explain our results (36). An intervention study in Germany showed that tomato or carrot juice supplementation significantly increased IL-2 levels, whereas IL-4 levels were not changed in healthy men (37). The present results also are incompatible with this Th1/Th2 imbalance toward Th1 function. Conversely, an animal study in mice showed that in vitro treatment of naive Th0 cell cultures with vitamin A strongly enhanced the development of IL-4–secreting Th2 (38). Environmental exposure, such as cigarette smoking, increases oxidant stress, and the effect of vitamins C and E may be more beneficial in smokers compared with others. Preventive effects of antioxidants on allergic rhinitis might only be identified in a larger population that would include males or middle-aged subjects in contrast to our study population. A laboratory study showed that vitamin E suppressed IL-4, but not IL-2, protein levels in human peripheral-blood T cells in a dose-dependent manner (39).

Persons who frequently consume seaweed tend to follow traditional Japanese dietary customs or behaviors that could protect against allergic disorders. Although the present study incorporates extensive information on potential confounding factors, the possibility of residual confounding caused by unmeasured dietary or behavioral factors cannot be excluded completely. Adjustment for confounders under investigation slightly strengthened the inverse association between seaweed intake and allergic rhinitis prevalence. Thus, residual confounding is not likely to fully explain the robust observed inverse association.

AEP Vol. 16, No. 8
August 2006: 614–621

As a complex plant food, seaweed contains many nutrients and other bioactive compounds. Because of the lack of association of vitamin C and E and fiber intake with allergic rhinitis prevalence in the present study, the decrease in prevalence of allergic rhinitis through dietary seaweed intake probably cannot be explained by vitamins C and E and fiber in seaweed. Moreover, because an inverse association persisted after adjustment for calcium or magnesium intake, the inverse association is unlikely to be ascribed to the calcium or magnesium in seaweed. Further control for consumption of phosphorus almost completely removed the inverse association, although the multivariate OR for comparison of the second with the first quartile was statistically significant. The beneficial association between seaweed intake and allergic rhinitis may be attributable to some extent to phosphorus or unmeasured constituents in relation to phosphorus, although phosphorus is contained in a number of foods. Seaweed also is a source of selenium and iodine, which might contribute to the decreased prevalence of allergic rhinitis. However, data for selenium and iodine intake were not available in the present study. A recent laboratory study showed that alginate oligosaccharides, which are cleaved from alginic acid polysaccharides of seaweed, enhanced Th1 differentiation through the upregulation of IL-12 production in murine lymphocyte cultures and that alginate oligosaccharides also inhibited in vivo IgE production (40).

To the best of our knowledge, there has been no epidemiologic study on the relationship between calcium or phosphorus consumption and allergic disorders. In the present study, dairy products were not associated statistically significantly with allergic rhinitis prevalence (data not shown). An intervention study of US healthy premenopausal women showed that 3 months of yogurt consumption did not enhance ex vivo cell-mediated immune function (41).

In conclusion, our results suggest that greater dietary intake of seaweed, calcium, magnesium, and phosphorus was associated with a decreased prevalence of allergic rhinitis in female Japanese young adults. The inverse association between seaweed intake and prevalence of allergic rhinitis appears to be independent of calcium or magnesium intake. Future studies are needed to prospectively assess the beneficial effects of seaweed, calcium, magnesium, and phosphorus on allergic disorders. Confirmation of the current findings would lend further support to the public health benefit of seaweed.

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APPENDIX

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Risk of postpartum depression in relation to dietary fish and fat intake in Japan: the Osaka Maternal and Child Health Study

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ABSTRACT

Background. An ecological analysis found that the docosahexaenoic acid content in mother's milk and seafood intake were inversely correlated with postpartum depression. This prospective study investigated the relationship of consumption of selected high-fat foods and specific types of fatty acids with the risk of postpartum depression.

Method. The subjects were 865 Japanese women. Dietary data were obtained from a self-administered diet history questionnaire during pregnancy. The Edinburgh Postnatal Depression Scale (EPDS) was used for the evaluation of postpartum depression. Adjustment was made for age, gestation, parity, cigarette smoking, family structure, family income, education, changes in diet in the previous month, season when data at baseline were collected, body mass index, time of delivery before the second survey, medical problems in pregnancy, baby's sex and baby's birthweight.

Results. The percentage of women with high depression scores was 14·0%. No evident dose–response associations were observed between intake of fish, meat, eggs, dairy products, total fat, saturated fatty acids, monounsaturated fatty acids, n-3 polyunsaturated fatty acids, n-6 polyunsaturated fatty acids, linoleic acid, α-linolenic acid, arachidonic acid, eicosapentaenoic acid or docosahexaenoic acid and the ratio of n-3 to n-6 polyunsaturated fatty acids and the risk of postpartum depression. However, there was an inverted J-shaped relationship between intake of n-3 polyunsaturated fatty acids and docosahexaenoic acid and the risk of postpartum depression.

Conclusions. This study failed to substantiate a clear inverse relationship between fish and n-3 polyunsaturated fatty acid intake and postpartum depression. Further investigations are needed to determine whether fish and n-3 polyunsaturated fatty acid consumption is preventive against postpartum depression.

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INTRODUCTION

In a cross-national ecological analysis, Hibbeln (2002) found that higher docosahexaenoic acid content in mother's milk and greater seafood

intake were highly correlated with a lower prevalence of postpartum depression. Some studies examined the association of intake of fish and/or n-3 polyunsaturated fatty acids with depressive symptoms but the results were inconsistent. Two ecological studies showed an inverse correlation between fish consumption and prevalence of major depression (Hibbeln, 1998; Peet, 2004). A significant inverse relationship between frequent fish intake and depression was observed in two cross-sectional studies in Finland (Tanskanen *et al.* 2001*a*, *b*). A prospective cohort study in Australia showed no difference in n-3 polyunsaturated fatty acid intake between depressed and non-depressed groups (Jacka *et al.* 2004). Several studies reported reduced plasma and erythrocyte concentrations of n-3 fatty acids among depressive patients (Adams *et al.* 1996; Maes *et al.* 1996, 1999; Edwards *et al.* 1998; Peet *et al.* 1998). Two recent clinical trials revealed significant benefits of the addition of n-3 fatty acids compared with placebo in patients diagnosed with a major depressive disorder (Nemets *et al.* 2002; Su *et al.* 2003).

Docosahexaenoic acid, a n-3 polyunsaturated fatty acid of marine origin, is required for optimal neuronal function and it has been proposed that mothers who become depleted of n-3 fatty acids, in particular docosahexaenoic acid, may be at a higher risk of postpartum depression (Hibbeln & Salem, 1995). However, a controlled trial of docosahexaenoic acid monotherapy in 36 outpatients with major depression showed no significant improvement in the treatment group compared with controls (Marangell *et al.* 2003).

To assess the role of fish and n-3 polyunsaturated fatty acids in the development of postpartum depression, we investigated the relationship of consumption of selected high-fat foods and specific types of fatty acids with the subsequent risk of postpartum depression in Japan, where fish intake is high. We used data from a prospective cohort study: the Osaka Maternal and Child Health Study (OMCHS).

METHOD

Study population

The OMCHS is an ongoing prospective cohort study that investigates preventive and risk factors for maternal and child health problems such as allergic disorders and postpartum depression. The OMCHS requested that pregnant females complete a baseline survey, which was followed by several postnatal surveys. In Japan, when females become pregnant, they notify the municipality of the domicile of the conception and the municipality provides them with a maternal and child health handbook. Eligible subjects were those women who became pregnant in Neyagawa City, which is one of the 44 municipalities in Osaka Prefecture, a metropolis in Japan with a total population of approximately 8·8 million. During the period from November 2001 to March 2003, the Neyagawa City Government provided all pregnant females with a set of leaflets explaining our study, an application form, and a self-addressed and stamped return envelope together with the maternal and child health handbook. Research technicians asked all of the eligible females to take part in this study by telephone, excluding pregnant females who had already returned the application form to the data management centre. Of the 3639 eligible subjects in Neyagawa City, 627 pregnant females (17·2%) participated in the study. 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. In addition, there were 77 participants who received explanations of the OMCHS from public health nurses in six 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 three 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. Of the 1002 females, 867 mothers participated in the second survey at 2–9 months postpartum. Missing data on baby's birthweight caused the exclusion of two mothers. There were 865 participants left for analysis. The ethics committee of the Osaka City University School of Medicine approved the OMCHS.

Measurements

At baseline, each participant filled out a set of two self-administered questionnaires.

A self-administered questionnaire was also used in the second survey. Participants mailed these questionnaires to the data management centre in each survey. Research technicians completed missing or illogical data by telephone interview.

In the baseline survey, we collected information on dietary habits during the previous month by using a validated self-administered diet history questionnaire. The structure and validity of the questionnaire are described in detail elsewhere (Sasaki *et al.* 1998, 2000). In this instrument, intake of 147 food items was calculated using an ad hoc computer algorithm developed to analyse the questionnaire. Fatty fish consumption included intake of eel, blue-back fish (mackerel, sardine, herring and others), 'red-meat' fish (tuna, salmon and skipjack), dried fish and small fish with bones. White fish consumption included intake of canned tuna, 'white-meat' fish (sea bream, flatfish, codfish and others), surimi (minced fish) products, shrimp or crab, squid or octopus, oysters and other shellfish. 'Other fish' was defined as intake of boiled fish in soy sauce, salted gut (fish, squid or shellfish) and fish eggs. Consumption of the three fish groups (fatty fish, white fish and 'other fish') was combined as total fish intake in the analysis. Energy-adjusted intake by the residual approach was used for the analyses (Willett & Stampfer, 1986).

Another self-administered questionnaire at baseline enquired about age, gestation, parity, smoking habits, family structure, occupation, family income, education, weight, height and changes in diet in the previous month. Body mass index was calculated by dividing self-reported body weight (kg) by the square of self-reported height (m^2).

A self-administered questionnaire in the second survey included the Japanese version of the Edinburgh Postnatal Depression Scale (EPDS). The EPDS is a 10-item self-reported scale designed to screen for postpartum depression in community samples (Cox *et al.* 1987). Each item is scored on a four-point scale (from 0 to 3) and the total score ranges from 0 to 30. The scale rates the intensity of depressive symptoms present within the previous 7 days. Although Cox *et al.* (1987) proposed a cut-off level of 10 if the test is to be used for screening purposes in the postpartum period, a cut-off score with a threshold of 8/9 was found to detect depression among Japanese women with a specificity of 93% and sensitivity of 75% (Okano *et al.* 1996). Therefore, postpartum depression was defined as present when subjects had an EPDS score of 9 or higher in the present study. The questionnaire also elicited information on medical problems in pregnancy and baby's sex, birthweight and date of birth of the infant born after the baseline survey.

Statistical analysis

Intake of selected foods rich in fat and specific types of fatty acids was categorized at quartile points based on the distribution in 865 mothers. Age was classified into three categories (<29, 29–31 and 32+ years); gestation into three (<15, 15–20 and 21+ weeks); parity into two (0 and 1+); cigarette smoking into three (never, former and current); family structure into two (nuclear and expanded); occupation into two (outside work and housewife); family income into three (JPY <4 000 000, 4 000 000–5 999 999 and 6 000 000+/year); education into three (<13, 13–14 and 15+ years); changes in diet in the previous month into three (none or seldom, slight and substantial); season when data at baseline were collected into four (spring, summer, autumn and winter); time of delivery before the second survey into two (<4 and 4+ months); medical problems in pregnancy into two (yes and no); baby's sex into two (male and female); and baby's birthweight into two (<2500 and 2500+ g). Body mass index was used as a continuous variable.

Logistic regression analysis was used to estimate crude odds ratios (ORs) and 95% confidence intervals (CIs) of postpartum depression in relation to consumption of selected dietary factors under study. Multiple logistic regression analysis was used to control for the potential confounding factors. Trend of association was assessed by a logistic regression model assigning consecutive integers (1 to 4) to the levels of the independent variable. Two-sided p values less than 0·05 were regarded as statistically significant. All computations were performed using SAS software, version 9.1 (SAS Institute, Inc., Cary, NC, USA).

Table 1. *Distribution of selected characteristics in 865 women, OMCHS, Japan*

Variable	*n* (%) or mean (S.D.)
Baseline characteristics	
Age (years)	
<29	324 (37·5)
29–31	253 (29·3)
32+	288 (33·3)
Gestation (weeks)	
<15	317 (36·7)
15–20	274 (31·7)
21+	274 (31·7)
Parity of 1 or more	440 (50·9)
Cigarette smoking	
Never	619 (71·6)
Former	102 (11·8)
Current	144 (16·7)
Nuclear family structure	755 (87·3)
Occupation	
Outside work	251 (29·0)
Housewife	614 (71·0)
Family income (JPY/year)	
<4 000 000	250 (28·9)
4 000 000–5 999 999	345 (39·9)
6 000 000+	270 (31·2)
Education (years)	
<13	257 (29·7)
13–14	367 (42·4)
15+	241 (27·9)
Body mass index (kg/m²)	21·5 (2·8)
Changes in diet in the previous month	
None or seldom	249 (28·8)
Slight	383 (44·3)
Substantial	233 (26·9)
Season when data were collected	
Spring	278 (32·1)
Summer	142 (16·4)
Autumn	190 (22·0)
Winter	255 (29·5)
Characteristics at the postnatal assessment	
Time of delivery before the assessment (months)	
<4	436 (50·4)
4+	429 (49·6)
Medical problems in pregnancy[a]	68 (7·9)
Baby's sex (male)	452 (52·3)
Baby's birthweight (g)	
<2500	54 (6·2)
2500+	811 (93·8)

[a] Hyperemesis, hydramnios, oligoamnios, gestosis, abruptio placentae, placenta previa or incompetent cervical os.

Table 2. *Distribution of baseline daily food and nutrient intake in 865 women, OMCHS, Japan*

Variable[a]	Mean (S.D.)
Daily intake	
Total energy (kJ)	6826·3 (1812·1)
Fish (g)	48·1 (27·9)
Fatty fish (g)	24·7 (19·0)
White fish (g)	21·8 (14·5)
Other fish (g)	1·7 (3·0)
Meat (g)	60·0 (28·6)
Eggs (g)	28·8 (20·7)
Dairy products (g)	195·0 (123·2)
Daily nutrient intake	
Total fat (g)	54·4 (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)
α-Linolenic acid (g)	1·7 (0·7)
Eicosapentaenoic acid (g)	0·2 (0·2)
Docosahexaenoic acid (g)	0·3 (0·2)
n-6 Polyunsaturated fatty acids (g)	11·0 (2·9)
Linoleic acid (g)	10·6 (2·9)
Arachidonic acid (g)	0·1 (0·04)
Cholesterol (mg)	267·9 (107·0)

[a] Food and nutrient intake were adjusted for total energy intake using the residual method.

RESULTS

The distribution of selected factors in 865 females who completed the second survey is summarized in Table 1. About 30% of subjects were from 29 to 31 years of age at baseline. About 70% of the women took part in the baseline survey by the 20th week of gestation and about half had a parity of 1 or more at baseline. Slight or substantial changes in diet in the previous month were reported by 616 females due to nausea gravidarum (509 females), maternal and foetal health (98 females), and other reasons (nine females). The second survey was conducted at 2–9 months postpartum, with 432, 339 and 63 mothers participating at 3, 4 and 5 months after delivery respectively. The remaining 31 mothers completed the survey at 2, 6, 7, 8 or 9 months postpartum. About 6% of infants were born with a birthweight less than 2500 g. There were 24 premature deliveries (24–36 weeks of gestation) and 816 babies (94·3%) were born at 37–41 weeks of gestation. Mean daily total energy was 6826 kJ, and energy-adjusted consumption of fish and n-3 polyunsaturated fatty acids was 48·1 and 2·3 g respectively (Table 2). Only two women had eaten no fish in the previous month. Subjects had eaten more fatty fish than white fish.

Of the 865 mothers, 121 (14·0%) were revealed by the second survey to have developed postpartum depression in the period from 2 to 9 months postpartum. Table 3 presents crude and adjusted ORs and 95% CIs for postpartum depression according to quartile of intake of

Table 3. *Odds ratios (ORs) and 95% confidence intervals (CIs) for postpartum depression according to quartile of intake of specific types of dietary fat in 865 women, OMCHS, Japan*[a]

Variable[b]	Quartile 1	2	3	4	*p* for trend
Fish					
Intake (g/day)	23·1	37·9	51·4	72·9	
No. of cases	32	37	24	28	
Crude OR (95% CI)	1·00	1·19 (0·71–2·00)	0·72 (0·40–1·26)	0·85 (0·49–1·47)	0·27
Multivariate OR (95% CI)	1·00	1·24 (0·73–2·12)	0·74 (0·41–1·33)	0·89 (0·50–1·59)	0·37
n-3 Polyunsaturated fatty acids					
Intake (g/day)	1·6	2·1	2·4	3·0	
No. of cases	36	27	24	34	
Crude OR (95% CI)	1·00	0·71 (0·41–1·22)	0·63 (0·36–1·08)	0·93 (0·56–1·55)	0·68
Multivariate OR (95% CI)	1·00	0·68 (0·39–1·18)	0·58 (0·33–1·02)	0·90 (0·53–1·53)	0·61
Eicosapentaenoic acid					
Intake (g/day)	0·08	0·15	0·21	0·32	
No. of cases	34	31	26	30	
Crude OR (95% CI)	1·00	0·90 (0·53–1·52)	0·73 (0·42–1·27)	0·86 (0·50–1·46)	0·45
Multivariate OR (95% CI)	1·00	0·93 (0·54–1·60)	0·81 (0·46–1·42)	0·89 (0·51–1·55)	0·58
Docosahexaenoic acid					
Intake (g/day)	0·16	0·26	0·34	0·50	
No. of cases	37	29	23	32	
Crude OR (95% CI)	1·00	0·75 (0·44–1·27)	0·58 (0·33–1·00)	0·84 (0·50–1·40)	0·35
Multivariate OR (95% CI)	1·00	0·76 (0·44–1·32)	0·62 (0·34–1·09)	0·85 (0·49–1·46)	0·43
n-6 Polyunsaturated fatty acids					
Intake (g/day)	8·4	10·2	11·5	13·5	
No. of cases	33	28	30	30	
Crude OR (95% CI)	1·00	0·83 (0·48–1·42)	0·89 (0·52–1·53)	0·89 (0·52–1·52)	0·75
Multivariate OR (95% CI)	1·00	0·86 (0·49–1·51)	0·85 (0·49–1·47)	0·88 (0·51–1·53)	0·65
n-3/n-6 Polyunsaturated fatty acid ratio					
Intake	0·17	0·19	0·22	0·25	
No. of cases	33	28	29	31	
Crude OR (95% CI)	1·00	0·83 (0·48–1·42)	0·86 (0·50–1·47)	0·92 (0·54–1·57)	0·81
Multivariate OR (95% CI)	1·00	0·84 (0·48–1·46)	0·88 (0·51–1·54)	0·97 (0·55–1·68)	0·95

[a] Values for intake are medians of adjusted energy intake by using the residual method for each quartile, except for the ratio of n-3 to n-6 polyunsaturated fatty acids, which were on the basis of crude intake in g/day.

[b] The multivariate models included the following: age, gestation, parity, cigarette smoking, family structure, family income, education, changes in diet in the previous month, season when data at baseline were collected, body mass index (continuous), time of delivery before the second survey, medical problems in pregnancy, baby's sex and baby's birthweight.

fish and polyunsaturated fatty acids in 865 mothers. No significant dose–response associations were observed between intake of fish, n-3 polyunsaturated fatty acids, eicosapentaenoic acid, docosahexaenoic acid and n-6 polyunsaturated fatty acids and the ratio of n-3 to n-6 polyunsaturated fatty acid consumption and the risk of postpartum depression. Adjustment for age, gestation, parity, cigarette smoking, family structure, family income, education, changes in diet in the previous month, season when data at baseline were collected, body mass index, time of delivery before the second survey, medical problems in pregnancy, baby's sex and baby's birthweight did not appreciably change these trends. We found inverted J-shaped relationships between intake of n-3 polyunsaturated fatty acids and docosahexaenoic acid and the risk of postpartum depression; adjusted ORs comparing the third with the first quartile were of borderline significance ($p=0·06$ and 0·10 respectively).

There were no statistically significant associations of intake of meat, eggs, dairy products, total fat, saturated fatty acids, monounsaturated fatty acids, cholesterol, linoleic acid, α-linolenic acid and arachidonic acid with the risk of postpartum depression in the multivariate model.

DISCUSSION

This is the first prospective study to assess the relationship of fish and n-3 polyunsaturated

fatty acid intake with the subsequent risk of postpartum depression. The study failed to substantiate a clear inverse relationship between these factors but found several suggestive relationships. Consumption of n-3 polyunsaturated fatty acids, especially docosahexaenoic acid, in the third quartile was marginally independently associated with a decreased risk of postpartum depression, although the linear trends were not statistically significant.

The present findings are at variance with previous epidemiological studies showing an inverse relationship between fish intake and postpartum depression or major depressive symptoms (Hibbeln, 1998, 2002; Tanskanen *et al.* 2001*a*, *b*; Peet, 2004). The Alpha-Tocopherol Beta-Carotene Cancer Prevention study found no measurable association of consumption of fish or n-3 polyunsaturated fatty acids with self-reported depressed mood and hospital treatment for major depression, although a significant positive dose–response relationship between fish intake and self-reported depressed mood was identified (Hakkarainen *et al.* 2004). Peet and Horrobin (2002) demonstrated that a dosage of 1 g/day, but not 2 or 4 g/day, of eicopentaenoic acid for 12 weeks was effective in significantly improving depressive symptoms. The current observations are partially consistent with these results.

A significant inverse association between adipose tissue docosahexaenoic acid levels and depressive symptoms was found in a cross-sectional study among 139 healthy adults from the island of Crete (Mamalakis *et al.* 2002). The current results for docosahexaenoic acid, which showed borderline significance regarding the risk of postpartum depression in comparing two quartiles, are in partial agreement with this finding. An inverse association between docosahexaenoic acid intake and postpartum depression may be attributable to the regulation of serotonergic nervous system function. Plasma docosahexaenoic acid concentrations were significantly correlated with cerebrospinal fluid concentrations of 5-hydroxyindoleacetic acid, a metabolite of serotonin, among healthy subjects (Hibbeln *et al.* 1998). Docosahexaenoic acid may inhibit signal transduction mechanisms in the human central nervous system (Stoll *et al.* 1999). A laboratory study demonstrated that dietary docosahexaenoic acid altered T-cell membrane microdomain composition and suppressed the protein kinase $C\theta$ signalling axis in mice (Fan *et al.* 2004).

The present results are incompatible with the hypothesis that a balance between n-3 and n-6 polyunsaturated fatty acid metabolism is important in the manifestation of depression (Hibbeln & Salem, 1995). The differences between Japanese and Western diets should be taken into account when interpreting our results. A clear protective association of docosahexaenoic acid and fish intake with postpartum depression may exist in populations with low fish intake. For example, in 20 Canadian pregnant women, mean intake of eicosapentaenoic and docosahexaenoic acids was estimated to be 35 and 82 mg/day respectively (Dénomme *et al.* 2005). The corresponding figures for our population were 204 and 329 mg respectively. Unknown active agents in fish might have interfered with a beneficial effect of fish or docosahexaenoic acid in the development of postpartum depression in our population. For example, methylmercury and dioxins are accumulated in fish and shellfish through the marine food web.

A case-control study in China showed no relationship between saturated, monounsaturated or n-6 polyunsaturated fatty acid levels in red bloods cells and suicide attempts, although eicosapentaenoic and docosahexaenoic acid levels were significantly inversely associated with suicide attempt risk (Huan *et al.* 2004). Mental illnesses such as depression may be an important cause of suicide. In this context, the current observations were partially consistent with these results.

The present study had several methodological strengths. The prospective design and relatively high rate of follow-up (86·3%) in this study minimized the possibility of recall bias or bias caused by loss of follow-up. Although 135 subjects did not participate in the follow-up survey, there were no material differences in the distributions of age, gestation, changes in diet in the previous month, season when data at baseline were collected and intake of total fat, monounsaturated, n-3 polyunsaturated and n-6 polyunsaturated fatty acids, fish, meat and dairy products as compared to the 867 participants (data not shown). Compared with non-participants in the follow-up, participants were

more likely to report no history of smoking, high family income, high educational level and high intake of saturated fatty acids, cholesterol and eggs and were less likely to be thin, although these differences would not be so large as to cause a serious bias. Study subjects were homogeneous in terms of having the same residential background. We incorporated extensive information on potential confounding factors and adjustments were made for these in data analysis. However, we were not able to undertake a comprehensive assessment by controlling for personal and family psychiatric history, sociocultural factors and personal and family relations.

There are several limitations in the present study that deserve recognition. The diagnosis of postpartum depression was established with the EPDS, a self-report rating scale, rather than a clinician-administered structured diagnostic interview. The EPDS was originally designed as a screening test of depressive symptoms within the previous 7 days. Moreover, the second survey was conducted at 2–9 months postpartum even though 89·2% of the subjects took part in the second survey at 3–4 months postpartum. Thus, it is difficult to estimate the incidence and prevalence of postpartum depression accurately. The disadvantage could bias the magnitude of the observed effects towards the null due to non-differential outcome misclassification.

Dietary data were obtained using a self-administered semi-quantitative dietary assessment questionnaire. As we did not undertake the assessment of the dietary habits of the subjects, the possibility of misclassification should be considered. According to validation tests, 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 (Sasaki *et al.* 1998). 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 ($r=0·51$ and 0·69 in men and women respectively) (Sasaki *et al.* 2000). Subjects with postpartum depression might not be aware of the ill effects of diet. Such a hypothesis would lead to bias towards the null. Our diet history questionnaire was designed to assess recent dietary intake, that is for 1 month prior to completing the questionnaire. However, this disadvantage is likely to be alleviated after adjustment for the season when data at baseline were collected. Changes in diet in the past month were controlled for because pregnant females are likely to change their diet for reasons such as nausea gravidarum. In this study, there was no significant interaction between changes in diet in the past month and exposures under investigation in relation to postpartum depression (data not shown). Potential misclassification associated with variability across subjects with regard to the stability of diet during pregnancy is likely to be negligible. Therefore, negative findings of our study were unlikely to be ascribed to dietary assessment during pregnancy.

In the baseline survey, the participation rate was low in Neyagawa City (17·2%). We were not able to evaluate the difference between participants and non-participants in Neyagawa City because data on personal characteristics among the non-participants were not available. In addition, we were not able to calculate the participation rate of subjects from other areas, nor were data available on the non-participants in those areas. The present study 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 <13, 13–14, 15+ and unknown years of education were 49·2, 32·3, 13·6 and 4·9% respectively. The corresponding figures for the current study were 29·7, 42·4, 27·9 and 0·0% respectively. The absence of a relationship between intake of fish and n-3 polyunsaturated fatty acids in our data may be related to the fact that the current study did not have substantial statistical power.

In conclusion, the current prospective study failed to verify an inverse relationship between fish intake and the subsequent risk of postpartum depression. Larger investigations with more precise and detailed exposure and outcome measurements are needed to draw a

conclusion on whether consumption of fish and n-3 polyunsaturated fatty acids is preventive against postpartum depression.

APPENDIX

Space limitations preclude the inclusion as authors of the following members of the Osaka Maternal and Child Health Study Group: Ichiro Matsunaga and Dr Hajime Oda, Osaka Prefectural Institute of Public Health; Drs Hideharu Kanzaki and Mitsuyoshi Kitada, Department of Obstetrics and Gynaecology, Kansai Medical University; Dr Yorihiko Horikoshi, Department of Obstetrics and Gynaecology, Kansai Medical University Kori; Drs Osamu Ishiko, Yuichiro Nakai, Junko Nishio and Seiichi Yamamasu, Department of Obstetrics and Gynaecology, Osaka City University Graduate School of Medicine; Dr Jinsuke Yasuda, Department of Obstetrics and Gynaecology, Matsushita Memorial Hospital; Dr Seigo Kawai, Department of Obstetrics and Gynaecology, Hoshigaoka Koseinenkin Hospital; Dr Kazumi Yanagihara, Yanagihara Clinic; Dr Koji Wakuda, Department of Obstetrics and Gynaecology, Fujimoto Hospital; Dr Tokio Kawashima, Kyohritsu Women's Clinic; Dr Katsuhiko Narimoto, Ishida Hospital Obstetrics, Gynaecology; Dr Yoshihiko Iwasa, Iwasa Women's Clinic; Dr Katsuhiko Orino, Orino Lady's Clinic; Dr Itsuo Tsunetoh, Tsunetoh Obstetrics and Gynaecology; Dr Junichi Yoshida, Yoshida Clinic; Dr Junichi Iito, Iito Obstetrics and Gynaecology Clinic; Dr Takuzi Kaneko, Kaneko Sanfujinka; Dr Takao Kamiya, Kamiya Ladies Clinic; Dr Hiroyuki Kuribayashi, Kuribayashi Clinic; Dr Takeshi Taniguchi, Taniguchi Hospital; Dr Hideo Takemura, Kosaka Women's Hospital; Dr Yasuhiko Morimoto, Aizenbashi Hospital.

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DECLARATION OF INTEREST

None.

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