

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

YOSHIHIRO MIYAKE^{1*}, SATOSHI SASAKI², TETSUJI YOKOYAMA³,
KEIKO TANAKA¹, YUKIHIRO OHYA⁴, WAKABA FUKUSHIMA⁵,
KYOKO SAITO^{3,6}, SATOKO OHFUJI⁵, CHIKAKO KIYOHARA⁷,
YOSHIO HIROTA⁵ and the Osaka Maternal and Child Health Study Group†

¹ *Department of Public Health, Faculty of Medicine, Fukuoka University, Fukuoka, Japan;*

² *Nutritional Epidemiology Programme, National Institute of Health and Nutrition, Tokyo, Japan;*

³ *Department of Technology Assessment and Biostatistics, National Institute of Public Health, Wako, Japan;*

⁴ *Division of Allergy, Department of Medical Specialties, National Centre for Child Health and Development, Tokyo, Japan;* ⁵ *Department of Public Health, Osaka City University School of Medicine, Osaka, Japan;*

⁶ *Centre for Collaboration and Partnership, National Institute of Health and Nutrition, Tokyo, Japan;*

⁷ *Department of Preventive Medicine, Division of Social Medicine, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan*

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.

* Address for correspondence: Dr Yoshihiro Miyake, Department of Public Health, Faculty of Medicine, Fukuoka University, Fukuoka 814-0180, Japan.
(Email: miyake-y@fukuoka-u.ac.jp)

† The other members of the Study Group are listed in the Appendix.

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 (m²).

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/m ²)	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.

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

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.

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				<i>p</i> for trend
	1	2	3	4	
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 eicosapentaenoic 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 θ 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 (Denomme *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 blood 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 Yorihiro 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.

ACKNOWLEDGEMENTS

We thank the Neyagawa City Government, Hirakata City Government, Katano City Government, Shijonawate City Government, Kaizuka City Government, Takaishi City Government, Hannan City Government, Neyagawa City Medical Association, Hirakata City Medical Association and Kadoma City Medical Association for their valuable support;

Kumiko Shirata, Osaka City University School of Nursing for helpful discussions; and Tomoko Shibazaki, Nahoko Nishimura and Naomi Takaoka for their assistance. This study was supported by a Grant-in-Aid (13770206, 16790351) for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology, Health and Labour Sciences Research Grants, Research on Allergic Disease and Immunology from the Ministry of Health, Labour and Welfare and the Uehara Memorial Foundation, Japan.

DECLARATION OF INTEREST

None.

REFERENCES

- Adams, P. B., Lawson, S., Sanigorski, A. & Sinclair, A. J. (1996). Arachidonic acid to eicosapentaenoic acid ratio in blood correlates positively with clinical symptoms of depression. *Lipids* **31**, S157–S161.
- Cox, J. L., Holden, J. M. & Sagovsky, R. (1987). Detection of post-natal depression. Development of the 10-item Edinburgh Post-natal Depression Scale. *British Journal of Psychiatry* **150**, 782–786.
- Denomme, J., Stark, K. D. & Holub, B. J. (2005). Directly quantitated dietary (n-3) fatty acid intakes of pregnant Canadian women are lower than current dietary recommendations. *Journal of Nutrition* **135**, 206–211.
- Edwards, R., Peet, M., Shay, J. & Horrobin, D. (1998). Omega-3 polyunsaturated fatty acid levels in the diet and in red blood cell membranes of depressed patients. *Journal of Affective Disorders* **48**, 149–155.
- Fan, Y. Y., Ly, L. H., Barhoumi, R., McMurray, D. N. & Chapkin, R. S. (2004). Dietary docosahexaenoic acid suppresses T cell protein kinase C theta lipid raft recruitment and IL-2 production. *Journal of Immunology* **173**, 6151–6160.
- Hakkarainen, R., Partonen, T., Haukka, J., Virtamo, J., Albanes, D. & Lönnqvist, J. (2004). Is low dietary intake of omega-3 fatty acids associated with depression? *American Journal of Psychiatry* **161**, 567–569.
- Hibbeln, J. R. (1998). Fish consumption and major depression. *Lancet* **351**, 1213.
- Hibbeln, J. R. (2002). Seafood consumption, the DHA content of mothers' milk and prevalence rates of postpartum depression: a cross-national, ecological analysis. *Journal of Affective Disorders* **69**, 15–29.
- Hibbeln, J. R., Linnoila, M., Umhau, J. C., Rawlings, R., George, D. T. & Salem Jr., N. (1998). Essential fatty acids predict metabolites of serotonin and dopamine in cerebrospinal fluid among healthy control subjects, and early- and late-onset alcoholics. *Biological Psychiatry* **44**, 235–242.
- Hibbeln, J. R. & Salem Jr., N. (1995). Dietary polyunsaturated fatty acids and depression: when cholesterol does not satisfy. *American Journal of Clinical Nutrition* **62**, 1–9.
- Huan, M., Hamazaki, K., Sun, Y., Itomura, M., Liu, H., Kang, W., Watanabe, S., Terasawa, K. & Hamazaki, T. (2004). Suicide attempt and n-3 fatty acid levels in red blood cells: a case control study in China. *Biological Psychiatry* **56**, 490–496.
- Jacka, F. N., Pasco, J. A., Henry, M. J., Kotowicz, M. A., Nicholson, G. C. & Berk, M. (2004). Dietary omega-3 fatty acids and depression in a community sample. *Nutritional Neuroscience* **7**, 101–106.

- Maes, M., Christophe, A., Delanghe, J., Altamura, C., Neels, H. & Meltzer, H. Y. (1999). Lowered omega3 polyunsaturated fatty acids in serum phospholipids and cholesteryl esters of depressed patients. *Psychiatry Research* **85**, 275–291.
- Maes, M., Smith, R., Christophe, A., Cosyns, P., Desnyder, R. & Meltzer, H. (1996). Fatty acid composition in major depression: decreased omega 3 fractions in cholesteryl esters and increased C20:4 omega 6/C20:5 omega 3 ratio in cholesteryl esters and phospholipids. *Journal of Affective Disorders* **38**, 35–46.
- Mamalakis, G., Tornaritis, M. & Kafatos, A. (2002). Depression and adipose essential polyunsaturated fatty acids. *Prostaglandins, Leukotrienes, and Essential Fatty Acids* **67**, 311–318.
- Marangell, L. B., Martínez, J. M., Zboyan, H. A., Kertz, B., Kim, H. F. S. & Puryear, L. J. (2003). A double-blind, placebo-controlled study of the omega-3 fatty acid docosahexaenoic acid in the treatment of major depression. *American Journal of Psychiatry* **160**, 996–998.
- Nemets, B., Stahl, Z. & Belmaker, R. H. (2002). Addition of omega-3 fatty acid to maintenance medication treatment for recurrent unipolar depressive disorder. *American Journal of Psychiatry* **159**, 477–479.
- Okano, T., Murata, M., Masuji, F., Tamaki, R., Nomura, J., Miyaoka, H. & Kitamura, T. (1996). Validation and reliability of Japanese version of the EPDS. *Archives of Psychiatric Diagnostics and Clinical Evaluation* **7**, 525–533.
- Peet, M. (2004). International variations in the outcome of schizophrenia and the prevalence of depression in relation to national dietary practices: an ecological analysis. *British Journal of Psychiatry* **184**, 404–408.
- Peet, M. & Horrobin, D. F. (2002). A dose-ranging study of the effects of ethyl-eicosapentaenoate in patients with ongoing depression despite apparently adequate treatment with standard drugs. *Archives of General Psychiatry* **59**, 913–919.
- Peet, M., Murphy, B., Shay, J. & Horrobin, D. (1998). Depletion of omega-3 fatty acid levels in red blood cell membranes of depressive patients. *Biological Psychiatry* **43**, 315–319.
- Sasaki, S., Ushio, F., Amano, K., Morihara, M., Todoriki, T., Uehara, Y. & Toyooka, T. (2000). Serum biomarker-based validation of a self-administered diet history questionnaire for Japanese subjects. *Journal of Nutritional Science and Vitaminology* **46**, 285–296.
- Sasaki, S., Yanagibori, R. & Amano, K. (1998). Self-administered diet history questionnaire developed for health education: a relative validation of the test-version by comparison with 3-day diet record in women. *Journal of Epidemiology* **8**, 203–215.
- Stoll, A. L., Severus, W. E., Freeman, M. P., Rueter, S., Zboyan, H. A., Diamond, E., Cress, K. K. & Marangell, L. B. (1999). Omega 3 fatty acids in bipolar disorder: a preliminary double-blind, placebo-controlled trial. *Archives of General Psychiatry* **56**, 407–412.
- Su, K. P., Huang, S. Y., Chiu, C. C. & Shen, W. W. (2003). Omega-3 fatty acids in major depressive disorder. A preliminary double-blind, placebo-controlled trial. *European Neuropsychopharmacology* **13**, 267–271.
- Tanskanen, A., Hibbeln, J. R., Hintikka, J., Haatainen, K., Honkalampi, K. & Viinamäki, H. (2001a). Fish consumption, depression, and suicidality in a general population. *Archives of General Psychiatry* **58**, 512–513.
- Tanskanen, A., Hibbeln, J. R., Tuomilehto, J., Uutela, A., Haukkala, A., Viinamäki, H., Lehtonen, J. & Vartiainen, E. (2001b). Fish consumption and depressive symptoms in the general population in Finland. *Psychiatric Services* **52**, 529–531.
- Willett, W. & Stampfer, M. J. (1986). Total energy intake: implications for epidemiologic analyses. *American Journal of Epidemiology* **124**, 17–27.