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Dietary vitamin D intake and prevalence of depressive symptoms during pregnancy in Japan

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ABSTRACT

Objective: Although the relationship between vitamin D levels and depressive symptoms has been explored, the results are inconsistent. Epidemiologic evidence concerning the relationship between dietary vitamin D intake and depressive symptoms in pregnancy is nonexistent. The aim of this current cross-sectional study was to examine this issue in Japan.
Methods: The study included 1745 pregnant women. Depressive symptoms were defined as present when women had a Center for Epidemiologic Studies Depression Scale score of 16 or higher. Dietary intake during the preceding month was assessed using a self-administered diet history questionnaire. Adjustment was made for age, gestation, region of residence, number of children, family structure, history of depression, family history of depression, smoking, secondhand smoke exposure at home and at work, job type, household income, education, body mass index, intake of saturated fatty acids, and intake of eicosapentaenoic acid plus docosahexaenoic acid.
Results: The prevalence of depressive symptoms during pregnancy was 19.3%. Higher dietary vitamin D intake was significantly associated with a lower prevalence of depressive symptoms during pregnancy, independent of potential dietary and nondietary confounding factors. Multivariate odds ratios (95% confidence intervals) for depressive symptoms during pregnancy in the first, second, third, and fourth quartiles of assessed intake of vitamin D were 1 (reference), 0.79 (0.55–1.11), 0.73 (0.49–1.07), and 0.52 (0.30–0.89), respectively (P for trend = 0.02).
Conclusion: The current cross-sectional study in Japan suggests that higher vitamin D intake may be associated with a lower prevalence of depressive symptoms during pregnancy.

Introduction

Vitamin D recently has attracted widespread interest not only for its importance in bone health but also for its association with reduced risk for many chronic diseases such as autoimmune diseases, type 2 diabetes, heart disease, many cancers, and infectious diseases [1]. The association between vitamin D levels and depressive symptoms has been explored: Several studies have shown a significant inverse association between serum 25-hydroxyvitamin D [25(OH)D] levels and depressive symptoms [2–6], whereas others have reported a null relationship between 25(OH)D and depressive symptoms [7–10].

Vitamin D deficiency is pandemic worldwide [1]. In Japan, vitamin D status is poorer in young women than in women of middle and advanced ages [11]. Hypovitaminosis D is common in pregnancy because of the requirements of the fetus. If a relationship exists between hypovitaminosis D and depressive symptoms, pregnant women may be more susceptible to depressive symptoms for this reason. To our knowledge, only two epidemiologic studies, one conducted in the Netherlands and the

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other in the United States, have investigated the association between serum 25(OH)D levels and depressive symptoms during pregnancy; both studies showed a significant inverse relationship between 25(OH)D and depressive symptoms [12,13].

Vitamin D is produced when ultraviolet B radiation passes through the skin into the epidermis and dermis or is acquired from animal foods. In view of the absence of epidemiologic evidence concerning the relationship between dietary vitamin D intake and depressive symptoms in pregnancy, the aim of this current cross-sectional study was to examine this issue in pregnant Japanese women using baseline data from the Kyushu Okinawa Maternal and Child Health Study (KOMCHS).

Methods

Study population

The KOMCHS is an ongoing prospective prebirth cohort study conducted to examine risk and preventive factors for maternal and child health problems. Eligible participants were pregnant women who lived in one of seven prefectures on Kyushu Island in southern Japan or in Okinawa Prefecture, an island chain in the southernmost area of Japan. Between April 2007 and March 2008, we requested that 131 obstetric hospitals in Fukuoka Prefecture, the largest prefecture on Kyushu Island, with a total population of ~5.04 million, provide as many pregnant women as possible with a set of leaflets explaining the KOMCHS, an application form to participate in the study, and a self-addressed, stamped return envelope. Between May 2007 and March 2008, we also requested that 40 obstetric hospitals in Okinawa Prefecture, with a total population of nearly 1.37 million, provide as many pregnant women as possible with the same documents. Between August 2007 and March 2008, pregnant women living in six prefectures on Kyushu Island other than Fukuoka Prefecture, with a total population of ~8.22 million, were also provided with the same documents at 252 obstetric hospitals. Pregnant women who were willing to participate in the study returned the application form containing a written description of their personal information to the data management center. Upon receiving this personal information, research technicians gave each participant a detailed explanation of the KOMCHS by telephone and sent them a self-administered questionnaire after obtaining their agreement. In total, 1757 women between weeks 5 and 39 of pregnancy gave their full informed consent in writing to participate in the KOMCHS and completed the baseline survey. Twelve women were excluded because of incomplete data on the variables under study, leaving data on 1745 pregnant women available for analysis. The KOMCHS was approved by the ethics committee of the Faculty of Medicine, Fukuoka University.

Measurements

In the baseline survey, each participant between weeks 5 and 39 of pregnancy filled out a two-part questionnaire and mailed it to the data management. Research technicians clarified or completed missing or unclear data by telephone.

The first part of the questionnaire elicited information on age, gestation, region of residence, number of children, family structure, personal history of doctor-diagnosed depression, family history of depression, smoking habits, secondhand smoke exposure at home and at work, employment status, household income, and educational level. A family history of depression was considered to be present if one or more parent or siblings of the study participant was diagnosed with depression by a physician. Employment status was elicited for the year in which the questionnaire was conducted and for the previous year; women were classified as unemployed if they were unemployed both in the year in which the questionnaire was completed and in the preceding year.

Depressive symptoms were assessed by means of a Japanese version [14] of the Center for Epidemiologic Studies Depression Scale (CES-D) [15], which was incorporated into the first part of the questionnaire. This scale consists of 20 questions addressing six symptoms of depression, including depressed mood, feelings of guilt or worthlessness, helplessness or hopelessness, psychomotor retardation, loss of appetite, and sleep disturbance experienced during the preceding week. Each question is scored on a scale of 0 to 3 according to the frequency of the symptoms, and the total CES-D score ranges from 0 to 60. The criterion validity of the CES-D scale has been well established in adult Western [15] and Japanese [14] populations. Following the validation study, we defined depressive symptoms as present when a participant had a CES-D score $\geq$16.

The second part of the questionnaire was a semiquantitative, comprehensive diet history questionnaire (DHQ) that assessed dietary habits during the preceding month [16,17]. Estimates of daily intake of foods (150 foods), energy, and selected nutrients were calculated using an ad hoc computer algorithm for the DHQ based on the Standard Tables of Food Composition in Japan [18]. Because only a small number of the women used supplemental multivitamins (5.5%) on at least a weekly basis, information on such supplements was not incorporated into the analysis. In a validation study of 92 Japanese women, Pearson's correlation coefficient between the DHQ and 16-d weighed dietary records was 0.54 for vitamin D (S. Sasaki, unpublished observations, 2006). Energy-adjusted intake by the residual method was used for the analyses [19]. Body weight and height were self-reported as part of the DHQ. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m).

Statistical analysis

Dietary vitamin D intake was categorized at quartile points on the basis of the distribution of all study participants. Age, gestation, region of residence, number of children, family structure, history of depression, family history of depression, smoking, secondhand smoke exposure at home and at work, job type, household income, education, BMI, intake of saturated fatty acids (SFAs), and intake of eicosapentaenoic acid (EPA) plus docosahexaenoic acid (DHA) were selected a priori as potential confounding factors. Higher intake levels of EPA and DHA were significantly associated with a lower prevalence of depressive symptoms during pregnancy, whereas higher intake of SFAs was significantly related to a higher prevalence of depressive symptoms during pregnancy in this population [20]. Age, gestation, BMI, and dietary confounding factors were used as continuous variables.

Estimations of crude odds ratios (ORs) and 95% confidence intervals (CIs) of depressive symptoms during pregnancy for each quartile range of dietary vitamin D intake in comparison with the lowest quartile were made by means of logistic regression analysis. Multiple logistic regression analysis was used to adjust for potential confounding factors. Trend of association was assessed by a logistic regression model assigning consecutive integers (1–4) to the quartiles of dietary vitamin D intake. All computations were performed using the SAS software package version 9.2 (SAS Institute, Inc., Cary, NC, USA).

Results

Among the 1745 pregnant women, the prevalence of depressive symptoms during pregnancy was 19.3%. The mean age of the women and gestation at baseline were 31.2 y and 18.5 wk, respectively (Table 1). About 5% of the women had a personal history of depression and 10% had a family history of depression. Mean daily total energy consumption and mean daily energy-adjusted vitamin D intake during pregnancy were 7434.2 kJ and 5.7 μg (= 228 IU), respectively.

Table 2 presents the distributions of confounding factors according to dietary vitamin D intake. Dietary vitamin D intake was positively associated with age, clerical or related occupation, household income, educational level, and intake of EPA plus DHA and inversely with active smoking status, secondhand smoke exposure at home, and service occupation.

Table 3 shows ORs and 95% CIs for depressive symptoms during pregnancy by quartiles of dietary vitamin D intake. Compared with vitamin D intake in the lowest quartile, intake in the highest quartile was significantly associated with a lower prevalence of depressive symptoms during pregnancy; this inverse linear trend was also significant in crude analysis. Adjustment for age, gestation, region of residence, number of children, family structure, history of depression, family history of depression; smoking, secondhand smoke exposure at home and at work, job type, household income, education, BMI, intake of SFAs; and intake of EPA plus DHA did not materially alter the association: The adjusted ORs (95% CIs) for depressive symptoms during pregnancy in the first, second, third, and fourth quartiles of vitamin D intake were 1 (reference), 0.79 (0.55–1.11), 0.73 (0.49–1.07), and 0.52 (0.30–0.89), respectively (P for trend = 0.02).

Discussion

In this cross-sectional study in Japan, we found that, after adjustment for potential dietary and nondietary confounding

Table 1
Distribution of selected characteristics in 1745 pregnant women

Variable	n (%)
Age, y, mean ± SD	31.2 ± 4.3
Gestation, wk, mean ± SD	18.5 ± 5.4
Region of residence	
Fukuoka Prefecture, n (%)	971 (55.6)
Other than Fukuoka Prefecture in Kyushu, n (%)	592 (33.9)
Okinawa Prefecture, n (%)	182 (10.4)
Number of children	
0, n (%)	703 (40.3)
1, n (%)	690 (39.5)
≥2, n (%)	352 (20.2)
Nuclear family structure, n (%)	1474 (84.5)
History of depression, n (%)	84 (4.8)
Family history of depression, n (%)	175 (10.0)
Having ever smoked, n (%)	563 (32.3)
Ever experiencing secondhand smoke exposure at home, n (%)	1315 (75.4)
Ever experiencing secondhand smoke exposure at work, n (%)	1106 (63.4)
Job type*	
Unemployed, n (%)	705 (40.4)
Professional or technical, n (%)	435 (24.9)
Clerical or related occupation, n (%)	328 (18.8)
Sales, n (%)	83 (4.8)
Service, n (%)	115 (6.6)
Production, n (%)	51 (2.9)
Others, n (%)†	28 (1.6)
Household income, yen/y	
<4 million, n (%)	632 (36.2)
4 million to 5,999,999, n (%)	618 (35.4)
≥6 million, n (%)	495 (28.4)
Education, y	
<13, n (%)	428 (24.5)
13–14, n (%)	577 (33.1)
≥15, n (%)	740 (42.4)
Body mass index, kg/m^2, mean ± SD	21.4 ± 2.8
Daily nutrient intake‡	
Total energy, kJ, mean ± SD	7434.2 ± 2057.0
Vitamin D, μg, mean ± SD	5.7 ± 3.0
Saturated fatty acids, g, mean ± SD	16.8 ± 4.3
EPA plus DHA, g, mean ± SD	0.46 ± 0.29

DHA, docosahexaenoic acid; EPA,eicosapentaenoic acid
* Full- or part-time employment in the year when the first questionnaire was conducted or in the previous year.
† Management; protection services; farming, fishing, or forestry; transportation or communications; or construction.
‡ Nutrient intake was adjusted for total energy intake using the residual method.

factors, higher dietary vitamin D intake was independently associated with a lower prevalence of depressive symptoms during pregnancy. To our knowledge, this is the first study to examine the association between dietary vitamin D intake and depressive symptoms during pregnancy.

A cross-sectional study of 4101 Dutch women showed that, compared with women with normal vitamin D levels [25(OH)D ≥ 80 nmol/L], women with vitamin D deficiency (≤29.9 nmol/L) or insufficiency (30–49.9 nmol/L) had a significantly higher prevalence of depressive symptoms during pregnancy (CES-D score ≥16) [12]. In a cross-sectional study of 178 black women using serum 25(OH)D level as a continuous variable, a significant inverse relationship was found between 25(OH)D levels and depressive symptoms during pregnancy (CES-D score ≥16) [13]. Only one study has investigated the relationship between vitamin D status and postpartum depressive symptoms: Among 98 U.S. postpartum women attending seven monthly visits, a significant positive association was observed between serum 25(OH)D levels ≤ 32 ng/mL and high Edinburgh Postpartum Depression Scale scores [21]. With regard to dietary vitamin D intake, a cohort study of 56 366 U.S. women ages 50 to 79 y found that higher intake of vitamin D from food sources was significantly related to reduced risk for depressive symptoms (Burnam score ≥0.06) after 3 y of follow-up [22]. The current results are in partial agreement with these findings. Our results are at variance with those of a cross-sectional study of 4734 U.S. adolescents showing no association between dietary vitamin D intake and depressive symptoms based on a six-item scale previously developed [23]. Recent trials also failed to support a beneficial relationship between vitamin D supplementation and depressive symptoms [24–26].

The mechanisms underlying the observed inverse relationship between dietary vitamin D intake and depressive symptoms during pregnancy are not clear. Over the past decade, vitamin D has been thought to function as a neurosteroid [27]. The vitamin D–activating enzyme 1-α-hydroxylase (cytochrome P450 27 B1), which is responsible for the conversion of 25(OH)D to 1,25$(OH)_2D_3$, and the vitamin D receptor are widely distributed in the human brain, especially in the hypothalamus and the substantia nigra, suggesting that vitamin D may have autocrine and/or paracrine functions in the human brain [28]. In an animal study, rats born to vitamin D–deficient mothers had profound alterations in the brain at birth, increased numbers of mitotic cells, reductions in brain content of nerve growth factor and glial cell line–derived neurotrophic factor, and reduced levels of low-affinity neurotrophin receptor, suggesting a relationship between vitamin D and brain development [29]. Vitamin D is also a potent immunoregulatory agent [27], which may be relevant to this study given the hypothesis that inflammatory mechanisms may play a crucial role in the pathomechanisms of depression [30]. Finally, vitamin D may have neuroprotective effects via the regulation of proteins that decrease the levels or inhibit the toxicity of reactive oxygen species [27].

In Japan, vitamin D–fortified foods are rarely available; rather, fish and eggs are the major sources of vitamin D intake. A recent investigation found a significant inverse relationship between fish intake and depressive symptoms during pregnancy in this population [20].

Several methodologic weaknesses of the present study have to be taken into account. As the present study is cross-sectional, the temporal nature of the association between dietary vitamin D intake and depressive symptoms during pregnancy could not be assessed.

The DHQ could only approximate consumption and was designed to assess dietary intake for 1 mo before completing the questionnaire. The possibility of nondifferential exposure misclassification would have biased the magnitude of the observed association toward the null. Of the women in the study, 502 experienced substantial changes in diet in the previous month. Causes for changes were nausea gravidarum (n = 473), maternal and fetal health (n = 27), and other reasons (n = 2). The results of a sensitivity analysis excluding these 502 women were similar to those in the overall analysis: The adjusted OR in the highest quartile was 0.52 (95% CI, 0.24–1.10; P for trend = 0.11).

Self-reported depressive symptoms were assessed using the CES-D scale, whereas a comprehensive psychiatric assessment was not performed in the present study. The CES-D includes questions on symptoms such as fatigue and physical discomfort, which also are typical complaints of pregnancy; the consequence of this symptom overlap could have been an overestimation of depression. The prevalence of depressive symptoms in this study was, however, lower than that in a representative sample of the Japanese general population: The prevalence of depressive symptoms (CES-D score ≥16) was 30.7% in 2315 women ages 30 to 39 y [31].

Table 2
Characteristics according to Quartile (Q) of dietary vitamin D intake in 1745 pregnant women

Variable	Quartile				*P* For trend*
	1 (Lowest) (n = 436)	2 (n = 436)	3 (n = 436)	4 (Highest) (n = 437)	
Age, y, mean	30.9	30.9	31.3	31.6	0.003
Gestation, wk, mean	18.6	18.6	18.5	18.3	0.51
Region of residence, %					0.40
Fukuoka Prefecture	53.2	54.6	55.7	59.0	
Other than Fukuoka Prefecture in Kyushu	32.6	34.4	36.0	32.7	
Okinawa Prefecture	14.2	11.0	8.3	8.2	
Number of children, %					0.07
0	44.5	40.4	39.5	36.8	
1	36.9	38.8	39.7	42.8	
≥2	18.6	20.9	20.9	20.4	
Nuclear family structure, %	86.2	84.9	83.9	82.8	0.15
History of depression, %	5.3	4.1	5.3	4.6	0.84
Family history of depression, %	10.3	8.7	10.1	11.0	0.60
Having ever smoked, %	39.0	32.6	29.8	27.7	0.0003
Ever experiencing secondhand smoke exposure at home, %	78.0	76.6	74.1	72.8	0.049
Ever experiencing secondhand smoke exposure at work, %	64.9	61.0	64.2	63.4	0.90
Job type† %					0.0003
Unemployed	35.3	42.0	43.8	40.5	
Professional or technical	24.8	26.2	22.0	26.8	
Clerical or related occupation	16.7	17.2	20.2	21.1	
Sales	6.4	4.4	5.1	3.2	
Service	9.4	6.9	5.1	5.0	
Production	4.4	2.3	2.8	2.3	
Others‡	3.0	1.2	1.2	1.1	
Household income, yen/y, %					0.002
<4 million	41.7	39.7	31.4	32.0	
4 million to 5,999,999	31.7	36.0	35.3	38.7	
≥6 million	26.6	24.3	33.3	29.3	
Education, y, %					0.002
<13	30.7	21.8	24.8	20.8	
13–14	30.7	36.7	32.3	32.5	
≥15	38.5	41.5	42.9	46.7	
Body mass index, kg/m^2, mean	21.5	21.5	21.3	21.4	0.29
Saturated fatty acids, g, mean§	16.3	17.1	16.9	16.8	0.19
EPA plus DHA, g, mean§	0.22	0.36	0.49	0.79	<0.0001

DHA, docosahexaenoic acid; EPA,eicosapentaenoic acid
* For continuous variables, a linear trend test was used; for categorical variables, a Mantel-Haenszel χ^2-test was used.
† Employment status in the year when the first questionnaire was conducted or in the previous year.
‡ Management; protection services; farming, fishing, or forestry; transportation or communications; or construction.
§ Nutrient intake was adjusted for total energy intake using the residual method.

Moreover, study participants took part in the baseline survey at various points between weeks 5 and 39 of pregnancy:595 (34.1%), 1004 (57.5%), and 146 (8.4%) participants completed the baseline survey in the first (≤15 wk gestation), second (16–27 wk gestation), and third (≥28 wk gestation) trimesters, respectively. Therefore, it is difficult to accurately estimate the incidence and prevalence of depressive symptoms during pregnancy. The possibility of nondifferential outcome misclassification would have been an underestimation of values in our results. The results of a sensitivity analysis restricted to 1004 pregnant women who completed the baseline survey in the second trimester were similar to those in the overall analysis: The adjusted OR in the highest quartile was 0.38 (95% CI, 0.17–0.81; *P* for trend = 0.01).

Information on the individual pattern of affective temperaments was not available in this study. A strong association was found between a distinct pattern of affective temperaments and increased risk for suicidal behavior in patients with mood disorders [32].

We could not calculate the participation rate because we do not have exact figures for the number of pregnant women who

Table 3
Odds ratios (ORs) and 95% confidence intervals (CIs) for depressive symptoms during pregnancy by quartiles of vitamin D intake in 1745 pregnant women

Vitamin D	Quartile				*P* For trend
	1 (Lowest) (n = 436)	2 (n = 436)	3 (n = 436)	4 (Highest) (n = 437)	
Intake, μg/d*	3.1 (= 124 IU)	4.6 (= 184 IU)	5.9 (= 236 IU)	8.5 (= 340 IU)	
Depressive symptoms, %†	24.1	20.2	18.8	14.0	
Crude OR (95% CI)	1.00	0.80 (0.58–1.10)	0.73 (0.53–1.01)	0.51 (0.36–0.72)	0.0002
Adjusted OR (95% CI)‡	1.00	0.79 (0.55–1.11)	0.73 (0.49–1.07)	0.52 (0.30–0.89)	0.02

IU, International Units
* Values for intake are medians for adjusted energy intake using the residual method for each quartile.
† Prevalence of depressive symptoms during pregnancy based on the Center for Epidemiologic Studies Depression Scale for each quartile.
‡ Adjustment for age, gestation, region of residence, number of children, family structure, history of depression, family history of depression, smoking, secondhand smoke exposure at home and at work, employment; household income, education, body mass index, intake of saturated fatty acids, and intake of eicosapentaenoic acid plus docosahexaenoic acid.

were provided with a set of leaflets explaining the KOMCHS, an application form, and a self-addressed, stamped return envelope by the 423 collaborating obstetric hospitals. We were not able to assess the differences between participants and nonparticipants because information on personal characteristics such as age, socioeconomic status, and history of depression was not available for nonparticipants. Our participants were probably not representative of Japanese women in the general population, however. For example, a population census conducted in 2000 in Fukuoka Prefecture found that the percentages of women ages 30 to 34 y with <13, 13 to 14, ≥15, and an unknown number of years of education were 52%, 31.5%, 11.8%, and 4.8%, respectively [33]. The corresponding figures for this study were 24.5%, 33.1%, 42.4%, and 0, respectively. Thus, the women in this study were more educated and probably more aware of health topics than women in the general population.

Sunlight exposure status was not assessed in the study, which was conducted in southern Japan, in latitudes ranging from 26° to 33° N. Ultraviolet B radiation at this latitude is sufficient for vitamin D synthesis for about 11 mo a year [34]. Thus, seasonal variability in sunlight exposure is not as strong here as in countries at higher latitudes, where depressive symptoms have been suggested to be linked to seasonal variability in sunlight exposure [35].

Although adjustment was made for several dietary and nondietary confounding factors, residual confounding effects could not be ruled out.

In conclusion, this Japanese cross-sectional study suggests that higher vitamin D intake is independently associated with a lower prevalence of depressive symptoms during pregnancy. Increasing vitamin D intake might be an effective strategy for preventing depressive symptoms during pregnancy. We acknowledge that the current results must be confirmed by additional epidemiologic studies, and also by trials with a more rigorous assessment of dietary intake and depressive symptoms.

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