学位論文

Association of dietary vitamin D intake with psychological distress during pregnancy and postpartum depressive symptoms: The Japan Environment and Children's Study

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Summary

Many recent clinical and epidemiological studies have demonstrated the effects of vitamin D on maternal depression, yet few have examined the association of dietary intake of vitamin D with maternal depression. This study examined the association of such intake with psychological distress during pregnancy and postpartum depressive symptoms at 1 month after delivery. Data obtained from 104,102 pregnant women enrolled in the longitudinal Japan Environment and Children's Study were analyzed. Dietary vitamin D intake was determined using the Food Frequency Questionnaire, psychological distress was assessed using the Kessler Psychological Distress Scale, and postpartum depressive symptoms were assessed using the Edinburgh Postnatal Depression Scale. Multivariable logistic regression for psychological distress during mid-late pregnancy revealed that odds ratios (ORs) for the second through fourth quintiles of vitamin D intake were significantly lower compared with the reference level regardless of whether intake was before or during pregnancy. At 1 month after delivery, vitamin D intake during pregnancy was associated with a reduced risk of postpartum depressive symptoms for all except the first quintile of vitamin D intake: second quintile (0.88, 95% CI 0.82-0.94), third (0.83, 95% CI 0.78-0.89), fourth (0.87, 95% CI 0.81-0.93), and fifth (0.90, 95% CI 0.83-0.97). Post-adjustment trend tests revealed a significant association between dietary vitamin D intake during pregnancy and postpartum depressive symptoms (p for trend = 0.004). Overall, dietary vitamin D intake was associated with lower risks of psychological distress during pregnancy and postpartum depressive symptoms at 1 month after delivery, suggesting the potential applicability of dietary vitamin D in reducing maternal depression.

Key words

vitamin D intake, Food Frequency Questionnaire, pregnancy, maternal depression, cohort study

Abbreviations

BMI, body mass index; CI, confidence intervals; DHQ, Diet History Questionnaire; EPDS, Edinburgh Postnatal Depression Scale; FFQ, Food Frequency Questionnaire; JECS, Japan Environment and Children's Study; JPY, Japanese yen; K6, Kessler Psychological Distress Scale; METs, metabolic equivalents; OR, odds ratio.

1. Introduction

Many recent clinical and epidemiological studies have demonstrated the effects of vitamin D on health. Vitamin D is primarily involved in bone metabolism, and its deficiency can cause osteoporosis. We obtain vitamin D from dietary intake (e.g., from fish and mushrooms) or synthesize it in the skin upon exposure to ultraviolet radiation in sunlight. Vitamin D is hydroxylated in the liver and kidneys to produce the active form of vitamin D (1,25-hydroxyvitamin D), which binds to receptors and has various biological effects [1)]. These receptors are distributed widely throughout the body [2)], including in the brain [3)]. Vitamin D is therefore believed to be associated with brain function and thus with mental health [4)].

Low blood levels of the active form of vitamin D are commonly observed in Japanese people, particularly women. One of the cited reasons is that many women, worried about skin aging, use sunblock. Applying 2 mg per 1 cm^2 of sunblock with sun protection factor-10 has been shown to reduce vitamin D synthesis in the skin by 90% [5)]. Moreover, roughly 80% of all pregnant Japanese women are reported to have a vitamin D deficiency [6)], with a mean vitamin D blood level of 16.7 ± 6.99 ng/mL. This is lower than in that of pregnant women in, for instance, Sweden (19 ng/mL) [7)] and Latvia (34.0 ng/mL) [8)]. Vitamin D deficiency in pregnant women is associated with risks that include preterm birth and gestational diabetes [9)] and should be prevented. However, in Japan, depending on the season, vitamin D deficiency can still develop even with 15 min or more exposure to sunlight daily [6)]. These findings suggest that exposure to sunlight alone is unlikely to prevent vitamin D deficiency and thus that dietary vitamin D intake is also important in prevention.

Depression is a common mental disorder, with around 300 million people worldwide thought to be living with depression [10)]. Its risk factors include being female and certain life events [11)]. Among women, the major life events of pregnancy and delivery have been found to be associated with an increased risk of maternal depression [12)]. Depression during pregnancy is a known risk factor for postpartum depression [13)], and this consequent postpartum depression can diminish mothers' quality of life, increase their suicide rate, and negatively affect their parenting [14)]. Preventing maternal depression is therefore of the utmost importance.

Many epidemiological studies have examined the association between serum concentrations of vitamin D and maternal depression [15)-18)], but recent systematic reviews have found inconsistent evidence for the association [19)-21)]. This lack of definitive evidence might be due to differences among studies in relation to the participants' background, sample size,

timing of measurements for the assessment of depression, and methods for measuring serum vitamin D levels. Although serum vitamin D levels are the best indicator of vitamin D sufficiency in the body, the measurement results reflect sufficiency not at the time of measurement but roughly 3 weeks earlier, as the half-life of vitamin D is approximately 3 weeks [1]. Therefore, serum vitamin D may not be the optimal parameter for assessing vitamin D levels throughout a fixed period such as pregnancy.

Using dietary intake of vitamin D as an alternative parameter may enable vitamin D sufficiency to be estimated throughout pregnancy. However, only one study has examined the association between dietary intake of vitamin D and maternal depression. In that study, Miyake et al. reported that dietary intake of vitamin D during pregnancy may be associated with depressive symptoms during pregnancy [22]. However, their study included only 1,745 subjects and did not examine how dietary intake of vitamin D during pregnancy is associated with depressive symptoms after delivery.

This study therefore examined the association of dietary vitamin D intake with psychological distress during pregnancy and postpartum depressive symptoms at 1 month after delivery, using a large dataset comprising 104,102 fetal records registered in the Japan Environment and Children's Study (JECS), an ongoing national epidemiological study on children's health and environment. My *a priori* hypothesis was that dietary vitamin D intake whether before and/or during pregnancy would be associated with a lower risk of psychological distress and postpartum depressive symptoms. This thesis is based on the primary research article published for the study in 2023 [23].

2. Methods

2.1. Study population

The JECS protocol has been described in detail elsewhere [24][25]. Briefly, as a nationwide government-funded birth cohort study, the JECS aims to evaluate the impact of various environmental factors on child health and development. The pregnant women enrolled were recruited from 15 Japanese regional centers between January 2011 and March 2014. Eligibility criteria were as follows: residing in a study area at the time of recruitment and expecting to reside continuously in Japan for the foreseeable future; having an expected delivery date between 1 August 2011 and mid-2014; and being able to participate in the study without difficulty, that is, able to understand the Japanese language and complete a self-

administered questionnaire. Non-residents of the study areas were excluded from the study even if they visited cooperating healthcare providers within the study areas.

The present study analyzed the jecs-ag-20160424 dataset released in June 2016 and the allbirth_revice001_ver001 dataset released in October 2016. The full dataset comprises 104,102 fetal records. In total, I excluded 1,003 records for multiple births and 5,645 for multiple registrations as well as data for 29 pregnancies for women who withdrew from the study. After then excluding questionnaires with incomplete answers, this left the following for final analysis: data for 77,741 pregnancies in early pregnancy, 77,074 pregnancies in mid-late pregnancy, and 74,840 pregnancies in the postpartum period (Figure 1). The study protocol was approved by the Japanese Ministry of the Environment's Institutional Review Board on Epidemiological Studies (Approval No. 100910001), the ethics committees of all participating institutions, and the Ethics Committee of the University of Toyama (Approval No. R2019035). The study was performed in compliance with the principles of the Helsinki Declaration as revised in 2008. All participants provided written informed consent.

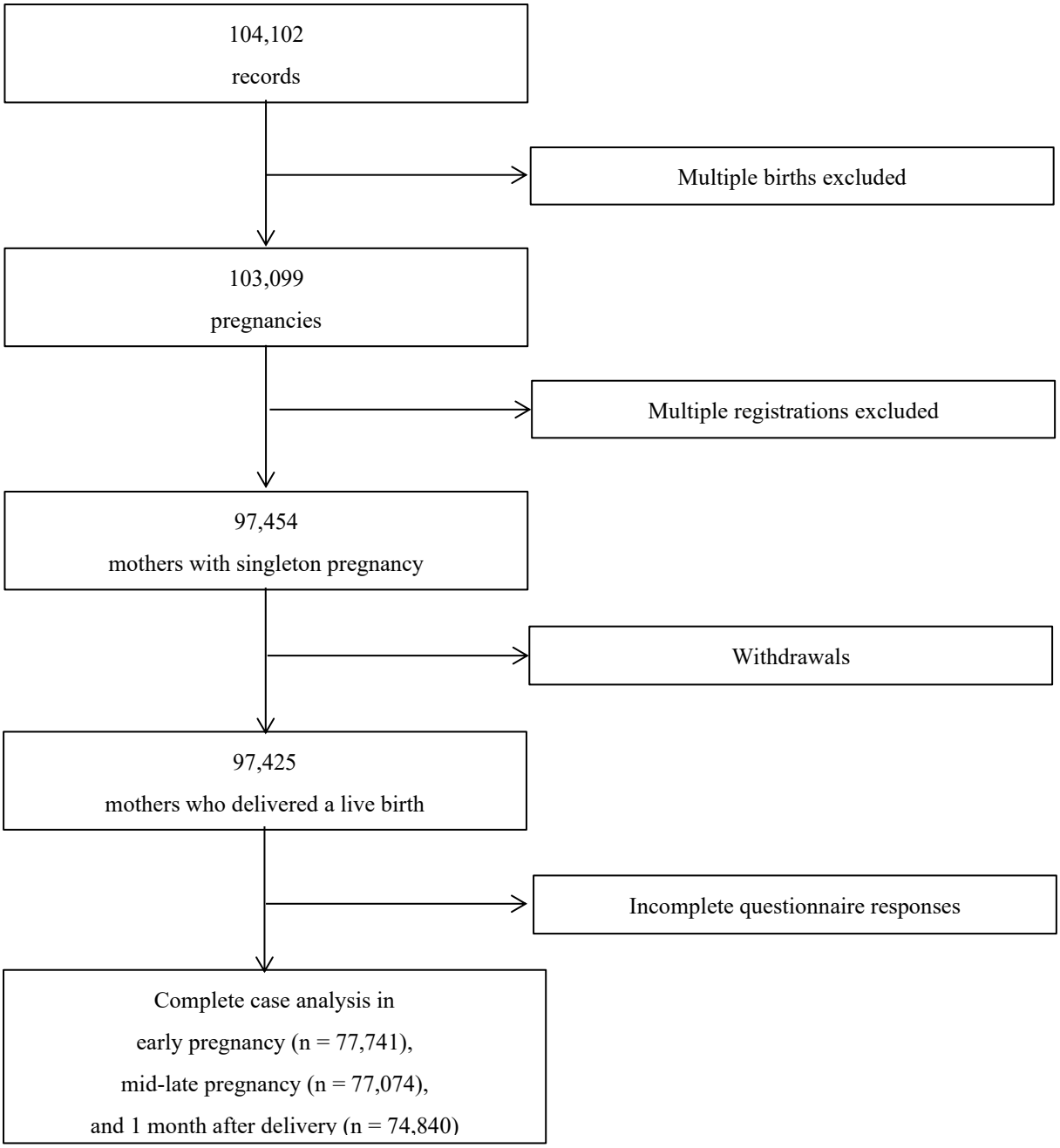

Fig. 1 Participant flow chart

2.2. Assessment of dietary vitamin D intake

Dietary intake of vitamin D was determined using the Food Frequency Questionnaire (FFQ), a semi-quantitative tool that has been validated for use in large-scale Japanese epidemiologic studies [26]. Data on vitamin D intake was collected at two time points: (1) before pregnancy (covering 1 year before learning of the pregnancy); (2) during pregnancy (covering dietary intake after learning of the pregnancy up until mid-late pregnancy). Pregnant women were asked how often they

consumed each food type. Portion size for each food type was categorized as small (50% smaller than standard), medium (same as standard), or large (50% larger than standard). Nine frequency categories for each item were used: less than 1 time/month, 1-3 times/month, 1-2 times/week, 3-4 times/week, 5-6 times/week, every day, 2-3 times/day, 4-6 times/day, and ≥ 7 times/day. I used standard tables of food composition to calculate the daily intake of vitamin D.

2.3. Assessment of psychological distress

The K6 was administrated during early pregnancy and again during mid-late pregnancy. The K6 was developed by Kessler et al. [27] and the Japanese version was validated by Furukawa et al [28]. The K6 comprises six items rated on a 5-point scale (range 0 to 4). The total score ranges from 0 to 24, with higher scores indicating a greater degree of psychological distress. I defined a K6 score ≥ 13 as indicating psychological distress as this has been suggested to be the optimal cut-off to balance false-positive and false-negative results [29].

2.4. Assessment of postpartum depressive symptoms

The Edinburgh Postnatal Depression Scale (EPDS) was used to assess postpartum depressive symptoms 1 month after delivery. The EPDS consists of 10 items rated on a 4-point scale (range 0 to 3) [30]. I defined an EPDS score ≥ 9 as indicating postpartum depressive symptoms. This value has been suggested to be the optimal cut-off for the Japanese population, and its validity and reliability have been reported [31].

2.5. Statistical analysis

Data are expressed as the mean ± standard deviation or median unless stated otherwise. To estimate the risks of psychological distress and postpartum depressive symptoms for each level of vitamin D intake, I categorized participants according to quintile of vitamin D intake based on the findings of previous studies [32]. Then, I examined the association of the following possible combinations of factors: (1) vitamin D intake before pregnancy and psychological distress during early pregnancy; (2) vitamin D intake before pregnancy and psychological distress during mid-late pregnancy; (3) vitamin D intake during pregnancy (covering dietary intake after learning of the pregnancy up until mid-late pregnancy) and

psychological distress during mid-late pregnancy; (4) vitamin D intake before pregnancy and postpartum depressive symptoms at 1 month after delivery; and (5) vitamin D intake during mid-late pregnancy and postpartum depressive symptoms at 1 month after delivery.

I then performed logistic regression analysis to calculate odds ratios (ORs) and 95% confidence intervals (CIs). In tests for trends, categorical numbers were assigned to quintile distributions for vitamin D intake and were evaluated as continuous variables.

Confounders and covariates considered in this study were as follows: energy intake; maternal age when the first questionnaire was administered; pre-pregnancy body mass index (< 18.5, 18.5-25, or ≥ 25 kg/m^2); highest maternal educational level (1, junior high or high school; 2, technical junior college, technical/vocational college, or associate degree; or 3, bachelor's or postgraduate degree); annual household income (< 4 million, 4-6 million, or > 6 million JPY); alcohol intake in early pregnancy, which was used only for the analysis of psychological distress in early pregnancy (1, never; 2, previously drank alcohol but quit; or 3, current drinker), and alcohol intake in mid-late pregnancy, which was used for the analysis of psychological distress in mid-late pregnancy and for postpartum depressive symptoms at 1 month after delivery (1, never; 2, previously drank alcohol but quit before learning of the pregnancy; 3, previously drank alcohol but quit after learning of the pregnancy; or 4, current drinker); smoking status in early pregnancy, which was used only for the analysis of psychological distress in the early pregnancy (1, never smoked; 2, previously smoked but quit before learning of current pregnancy; 3, previously smoked but quit after learning of current pregnancy; or 4, current smoker) and the same categorization of smoking status in mid-late pregnancy, which was used for the analysis of psychological distress in the mid-late pregnancy and for postpartum depressive symptoms at 1 month after delivery; morning sickness (1, never; 2, nausea but no vomiting; 3, vomiting but able to eat; or 4, vomiting and unable to eat); physical activity during mid-late pregnancy (MET･min/day; metabolic equivalent of task multiplied by the number of minutes per day); history of anxiety disorder (yes or no); history of depression (yes or no); employment status during the mid-late pregnancy (yes or no); time spent outside during the mid-late pregnancy (hours); study area; season when the questionnaire was answered (spring, summer, fall, or winter); use of vitamin D supplementation (yes or no); and presence of neonatal physical anomaly for only the analysis of postpartum depressive symptoms at 1 month after delivery [33]. The variables were categorized

according to standard medical practice in Japan and/or the results of previous studies [34]. Two-sided P values less than 0.05 were considered to indicate statistical significance. Data were analyzed using SAS version 9.4 software (SAS Institute Inc., Cary, NC).

3. Results

3.1 Participant characteristics

Table 1 shows the characteristics of the participants divided into five groups based on their daily vitamin D intake during pregnancy. In groups with higher dietary vitamin D intake, participants were slightly older, had higher energy intake, had a smaller proportion of underweight participants, and most did not smoke, tended to have higher education and annual household income levels, and were more physically active.

Table 1. Characteristics of pregnant women according to quintile of vitamin D intake during pregnancy (n = 74,840)

	Quintile of vitamin D intake				
	1 (low)	2	3	4	5 (high)
Median intake of vitamin D, μg/day	1.2	2.6	3.9	5.5	9.3
Median intake of energy	1254	1461	1589	1792	2142
Maternal age, years	29.9	30.7	31.1	31.4	31.5
Pre-pregnancy BMI, n (%)					
< 18.5	2,440 (16.3)	2,394 (16.5)	2,547 (16.1)	2,278 (15.5)	2,252 (15.2)
18.5-25	10,833 (72.4)	10,624 (73.2)	11,785 (74.5)	11,008 (74.8)	10,920 (73.7)
≥ 25	1,691 (11.3)	1,504 (10.4)	1,497 (9.5)	1,425 (9.7)	1,642 (11.1)
Highest educational level, n (%)					
Junior high school or high school	6,279 (42.0)	5,181 (35.7)	5,170 (32.7)	4,376 (29.8)	4,621 (31.2)
Technical junior college, technical/vocational college, or associate degree	6,057 (40.5)	6,172 (42.5)	6,767 (42.8)	6,324 (43.0)	6,510 (43.9)
Bachelor's degree or postgraduate degree	2,628 (17.6)	3,169 (21.8)	3,892 (24.6)	4,011 (27.3)	3,683 (24.9)
Annual household income (JPY), n (%)					
< 4 million	6,976 (46.6)	5,936 (40.9)	5,960 (37.7)	5,183 (35.2)	5,363 (36.2)
4-6 million	4,623 (30.9)	4,826 (33.2)	5,463 (34.5)	4,975 (33.8)	5,068 (34.2)
> 6 million	3,365 (22.5)	3,760 (25.9)	4,406 (27.8)	4,553 (31.0)	4,383 (29.6)
Alcohol intake, n (%)					
Never	5,242 (35.0)	4,938 (34.0)	5,214 (32.9)	4,732 (32.2)	4,742 (32.0)
Quit before learning of pregnancy	2,324 (15.5)	2,293 (15.8)	2,522 (15.9)	2,469 (16.8)	2,722 (18.4)
Quit after learning of pregnancy	7,073 (47.3)	6,912 (47.6)	7,633 (48.2)	7,074 (48.1)	6,897 (46.6)
Current drinker	325 (2.2)	379 (2.6)	460 (2.9)	436 (3.0)	453 (3.1)
Smoking status, n (%)					
Never	8,095 (54.1)	8,414 (57.9)	9,506 (60.1)	8,999 (61.2)	8,849 (59.7)
Smoked previously but quit before learning of pregnancy	3,460 (23.1)	3,424 (23.6)	3,731 (23.6)	3,539 (24.1)	3,629 (24.5)
Smoked previously but quit after learning of pregnancy	2,593 (17.3)	2,058 (14.2)	1,971 (12.5)	1,675 (11.4)	1,780 (12.0)
Current smoker	816 (5.5)	626 (4.3)	621 (3.9)	498 (3.4)	556 (3.8)
Morning sickness, n (%)					
Never	2,633 (17.6)	2,508 (17.3)	2,629 (16.6)	2,440 (16.6)	2,536 (17.1)
Nausea but no vomiting	6,175 (41.3)	6,382 (44.0)	7,000 (44.2)	6,418 (43.6)	6,289 (42.5)
Vomiting but being able to eat	4,316 (28.8)	4,029 (27.7)	4,584 (29.0)	4,255 (28.9)	4,460 (30.1)
Vomiting and being unable to eat	1,840 (12.3)	1,603 (11.0)	1,616 (10.2)	1,598 (10.9)	1,529 (10.3)
Median physical activity (METs・min/day)	58.9	66.0	70.7	70.7	84.9
History of anxiety disorder, yes (%)	503 (3.4)	443 (3.1)	379 (2.4)	371 (2.5)	433 (2.9)
History of depression, yes (%)	504 (3.4)	433 (3.0)	457 (2.9)	418 (2.8)	430 (2.9)
Employed, n (%)	8,585 (57.4)	7,868 (54.2)	8,461 (53.5)	7,934 (53.9)	7,917 (53.4)
Major congenital anomaly, yes (%)	348 (2.3)	326 (2.2)	348 (2.2)	333 (2.3)	340 (2.3)
Time spent outdoors during second/third trimester, h	1.7	1.6	1.7	1.7	1.8
Season when questionnaire was answered, n (%)					
Spring	3,360 (22.5)	3,304 (22.8)	3,621 (22.9)	3,472 (23.6)	3,408 (23.0)
Summer	3,643 (24.4)	3,535 (24.3)	3,864 (24.4)	3,631 (24.7)	3,602 (24.3)
Fall	4,546 (30.4)	4,313 (29.7)	4,559 (28.8)	4,203 (28.6)	4,261 (28.8)
Winter	3,415 (22.8)	3,370 (23.2)	3,785 (23.9)	3,405 (23.2)	3,543 (23.9)
Use of vitamin D supplementation, yes (%)	15 (0.1)	24 (0.2)	21 (0.1)	29 (0.2)	23 (0.2)

BMI, body mass index. JPY, Japanese yen. METs, metabolic equivalents

3.2. Dietary vitamin D intake and the risk of psychological distress

Table 2 shows the participants divided into 5 groups based on their daily vitamin D intake and shows the ORs and 95% CIs for psychological distress according to quintile of vitamin D intake relative to the first quintile. Multivariable logistic regression of vitamin D intake before pregnancy revealed that ORs for psychological distress during early pregnancy were significantly lower only in the second, third, and fifth quintiles (0.78, 95% CI 0.69-0.89; 0.82, 95% CI 0.72-0.93; and 0.85, 95% CI 0.74-0.97, respectively), and the trend test was not significant. As for vitamin D intake before pregnancy and during pregnancy, ORs for the second to fourth quintile were significantly lower during mid-late pregnancy. Post-adjustment trend tests revealed significant associations between vitamin D intake during pregnancy and psychological distress during mid-late pregnancy (*p* for trend = 0.03), although no significant association was observed between vitamin D intake before pregnancy and psychological distress during mid-late pregnancy.

Table 2. Odds ratios (95% confidence intervals) for psychological distress according to quintile of vitamin D intake

	Quintile of vitamin D intake					*p*-value for trend
	1 (low)	2	3	4	5 (high)	
Vitamin D intake before pregnancy and psychological distress during early pregnancy (n = 77,741)						
Median intake of vitamin D, μg/day	1.4	3.0	4.3	6.0	10.1	
K6 < 13, n	14,616	15,260	15,125	15,290	14,805	
K6 ≥ 13, n	602	458	469	523	593	
Crude odds ratio	1.00	**0.73 (0.64-0.82)**	**0.75 (0.67-0.85)**	**0.83 (0.74-0.94)**	0.97 (0.87-1.09)	0.66
Adjusted odds ratio [a]	1.00	**0.78 (0.69-0.89)**	**0.82 (0.72-0.93)**	0.89 (0.79-1.02)	**0.85 (0.74-0.97)**	0.16
Vitamin D intake before pregnancy and psychological distress during mid-late pregnancy (n = 77,068)						
Median intake of vitamin D, μg/day	1.4	3.0	4.3	6.0	10.1	
K6 < 13, n	14,623	15,051	14,997	15,198	14,772	
K6 ≥ 13, n	556	451	413	437	570	
Crude odds ratio	1.00	**0.79 (0.69-0.89)**	**0.72 (0.64-0.82)**	**0.76 (0.67-0.86)**	1.01 (0.90-1.14)	1.00
Adjusted odds ratio [a]	1.00	**0.86 (0.76-0.98)**	**0.81 (0.70-0.92)**	**0.84 (0.73-0.96)**	0.92 (0.81-1.06)	0.19
Vitamin D intake during pregnancy and psychological distress during mid-late pregnancy (n = 77,074)						
Median intake of vitamin D, μg/day	1.2	2.6	3.9	5.5	9.3	
K6 < 13, n	14,884	14,498	15,800	14,731	14,734	
K6 ≥ 13, n	601	453	430	414	529	
Crude odds ratio	1.00	**0.77 (0.68-0.88)**	**0.67 (0.59-0.76)**	**0.70 (0.61-0.79)**	0.89 (0.79-1.00)	**0.01**
Adjusted odds ratio [a]	1.00	**0.84 (0.74-0.96)**	**0.76 (0.67-0.87)**	**0.79 (0.69-0.90)**	0.89 (0.77-1.01)	**0.03**

K6, Kessler Psychological Distress Scale.
[a]Adjusted for age, energy intake, pre-pregnancy body mass index, highest maternal educational level, annual household income, alcohol intake, smoking status, morning sickness, physical activity, employment status, history of anxiety disorder, history of depression, time spent outdoors during pregnancy, study area, season when the questionnaire was answered, and use of vitamin D supplementation.
Values in bold indicate significance ($p < 0.05$).

3.3. Dietary vitamin D intake and risk of postpartum depressive symptoms

Table 3 shows participants divided into 5 groups based on their daily vitamin D intake and shows the ORs and 95% CIs

for postpartum depressive symptoms according to quintile of vitamin D intake relative to the first quintile. Multivariable logistic regression of vitamin D intake before pregnancy revealed that ORs for postpartum depressive symptoms at 1 month after delivery were significantly lower in the second to fifth quintiles (0.89, 95% CI 0.83-0.95; 0.84, 95% CI 0.78-0.89; 0.86, 95% CI 0.80-0.92; and 0.90, 95% CI 0.83-0.97, respectively). Post-adjustment trend tests showed significant associations (*p* for trend = 0.002). As for vitamin D intake during pregnancy, ORs for the second to fifth quintile were significantly lower at 1 month after delivery (0.88, 95% CI 0.82-0.94; 0.83, 95% CI 0.78-0.89; 0.87, 95% CI 0.81-0.93; and 0.90, 95% CI 0.83-0.97, respectively). Post-adjustment trend tests also revealed significant associations between dietary vitamin D intake during pregnancy and postpartum depressive symptoms (*p* for trend = 0.004).

Table 3. Odds ratios (95% confidence intervals) for postpartum depressive symptoms according to quintile of vitamin D intake

	Quintile of vitamin D intake					*p*-value for trend
	1 (low)	2	3	4	5 (high)	
Vitamin D intake before pregnancy and postpartum depressive symptoms at 1 month after delivery (n = 74,834)						
Median intake of vitamin D, μg/day	1.4	3.0	4.3	6.0	10.1	
EPDS < 9, n	12,432	13,037	13,110	13,208	12,593	
EPDS ≥ 9, n	2,242	2,040	1,906	2,009	2,257	
Crude odds ratio	1.00	**0.87 (0.81-0.93)**	**0.81 (0.75-0.86)**	**0.84 (0.79-0.90)**	0.99 (0.93-1.06)	0.60
Adjusted odds ratio	1.00	**0.89 (0.83-0.95)**	**0.84 (0.78-0.89)**	**0.86 (0.80-0.92)**	**0.90 (0.83-0.97)**	**0.002**
Vitamin D intake during pregnancy and postpartum depressive symptoms at 1 month after delivery (n = 74,840)						
Median intake of vitamin D, μg/day	1.2	2.6	3.9	5.5	9.3	
EPDS < 9, n	12,643	12,555	13,813	12,745	12,627	
EPDS ≥ 9, n	2,321	1,967	2,016	1,966	2,187	
Crude odds ratio	1.00	**0.85 (0.80-0.91)**	**0.80 (0.75-0.85)**	**0.84 (0.79-0.90)**	0.94 (0.89-1.01)	0.06
Adjusted odds ratio [a]	1.00	**0.88 (0.82-0.94)**	**0.83 (0.78-0.89)**	**0.87 (0.81-0.93)**	**0.90 (0.83-0.97)**	**0.004**

EPDS, Edinburgh Postnatal Depression Scale

[a]Adjusted for age, energy intake, pre-pregnancy body mass index, maternal highest educational level, annual household income, alcohol intake, smoking status, morning sickness, physical activity, employment status, history of anxiety disorder, history of depression, major congenital anomaly, time spent outdoors during pregnancy, study area, season when the questionnaire was answered, and use of vitamin D supplementation.

Values in bold indicate significance ($p < 0.05$).

4. Discussion

Using data from the JECS, I performed logistic regression analysis of the associations of dietary vitamin D intake with psychological distress and postpartum depressive symptoms. I found that dietary vitamin D intake was associated with a reduced risk of psychological distress during pregnancy and postpartum depressive symptoms at 1 month after delivery. For postpartum depressive symptoms, vitamin D intake showed a significant inverse association. To my knowledge, this is the first study to have examined the relationship between dietary vitamin D intake and postpartum depressive symptoms.

The aforementioned cross-sectional study that Miyake et al. conducted with 1,745 Japanese women found that dietary intake of vitamin D may reduce the risk of depression during pregnancy [22]. In that study, compared to the group with the lowest vitamin D intake, the group with the highest vitamin D intake (median= 8.5 μg/day) during pregnancy (5-39 weeks) had a significantly reduced risk of depressive symptoms during pregnancy (5-39 weeks) even after adjusting for covariates (0.52, 95% CI 0.30-0.89). However, in the present study, compared to the group with the lowest vitamin D intake (first quintile), even the groups with higher but not the highest vitamin D intake during pregnancy demonstrated a reduced risk of psychological distress: second quintile (0.84, 95% CI 0.74−0.96), third quintile (0.76, 95% CI 0.67−0.87), and fourth quintile (0.79, 95% CI 0.69−0.90). This discrepancy in results may involve the difference in the percentages of women with depressive symptoms in the populations. In the study by Miyake et al., 24.1% of women in the reference group (with the lowest vitamin D intake) had depressive symptoms, compared with roughly 4% of participants who exceeded the cutoff value for psychological distress in the present study. This suggests that the two populations differed in terms of health status and their abilities to metabolize and formulate active vitamin D. Furthermore, this discrepancy in results may also involve differences in the methods used for estimating vitamin D intake. In this study, I used the FFQ to estimate dietary vitamin D intake, whereas Miyake et al. used the Diet History Questionnaire (DHQ). The FFQ is a tool for estimating the amount of food intake from the frequency of food intake over a certain period, and its questions are easy for participants to answer. The FFQ is therefore considered suitable for large-scale epidemiological studies like the present study. In contrast, the DHQ includes questions not only about the frequency of food intake but also about cooking methods and seasonings [35], and as such, the DHQ is superior because it can determine vitamin D intake with greater accuracy [36]. In addition, the present study was primarily a cohort study, while that of Miyake et al. was a cross-sectional study. This difference in study design may have contributed to the difference in results.

The mechanism underlying the association of dietary vitamin D intake with psychological distress during pregnancy and postpartum depressive symptoms has not been sufficiently determined. However, an increased requirement for calcium during pregnancy enhances the ability to produce active vitamin D, suggesting that serotonin secretion is enhanced and that the risk of psychological distress during pregnancy is reduced regardless of the timing of vitamin D intake [37]. This enhanced ability to produce active vitamin D during pregnancy typically reverts to normal after delivery. However, after

delivery, women require around 6−8 weeks to return to their pre-pregnancy physical status. Therefore, at 1 month after delivery, when this study was conducted, this ability may have been higher than normal, and the risk of depressive symptoms may have decreased according to the same mechanism as during pregnancy.

Interestingly, for almost all of the associations examined, participants in the third quintile of vitamin D intake had the lowest risk of psychological distress during pregnancy and postpartum depressive symptoms. As in the study by Nielsen et al [17], I found the relationship between vitamin D intake and OR to be an inverted J-shape. Nielsen et al. found that high serum concentrations of vitamin D during pregnancy were associated with a higher risk of postpartum depression, which they speculated might be caused by a reduced level of active vitamin D. Active vitamin D, which is involved in various biological functions, is hydrolyzed into inactive vitamin D (24,25-dehydroxyvitamin D) when serum concentrations of calcium are normal or high [38)39)]. In the second/third trimester, increased calcium requirements lead to reduced serum concentrations of calcium, thereby potentially enhancing the production of active vitamin D. However, in the present study, the group with the highest vitamin D intake had higher intake of calcium compared with the group that had the lowest vitamin D intake. This high intake of calcium may have elevated serum concentrations of calcium to normal or high levels and thus inhibited active vitamin D production, which may be why vitamin D intake was only weakly associated with psychological distress and postpartum depressive symptoms among the group of participants with the highest vitamin D intake. However, because the results rarely changed when adjusted for calcium intake during pregnancy (data not shown), further studies concerning calcium intake are required. Another potential explanation for this phenomenon is overweight. In the present study, analysis of BMI before pregnancy revealed that overweight (BMI≥25) was lowest in the third quintile. Overweight has been demonstrated to increase the risk of depression in women [40)]. Therefore, factors associated with unadjusted overweight may have increased the risk of depressive symptoms in groups with higher vitamin D intake.

This is the largest study to date that has investigated the association of dietary intake of vitamin D with psychological distress and postpartum depressive symptoms. Moreover, because the study was conducted in 15 regional centers across Japan, the participants can be considered representative of pregnant women in Japan, unlike in Miyake et al.'s study where they mentioned the possibility that their participants were not representative of Japanese women in the general population [22)]. However, there are several limitations to my study. First, although I employed the EPDS screening tool, which has

been validated and is widely used, the FFQ has not been validated for use with pregnant women. Second, the observational study design may have included unmeasured residual factors that might have confounded the results. Third, although the results were adjusted for season, outdoor activity time, and study area, they were not adjusted for duration of exposure to sunlight, which greatly affects vitamin D levels in the body. Finally, I cannot rule out the possibility that excluding approximately 30,000 women based on the eligibility criteria, while necessary, may have introduced some selection bias.

In conclusion, the results of this study suggest that dietary vitamin D intake might be associated with reduced risks of psychological distress and postpartum depressive symptoms. These findings can contribute to the prevention of maternal depression. Further investigations, particularly dose-response relationships and biological mechanisms are required to confirm these findings.

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