Original Article

Factors associated with symptoms of depression among pregnant women with gestational diabetes mellitus in Japan

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SUMMARY   The objective of this study was to explore the factors associated symptoms of depression among pregnant women with gestational diabetes mellitus (GDM) in Japan. This cross-sectional study was conducted at a hospital in Toyota, Japan, from January 2015 to June 2016. Pregnant women who visited the hospital and were diagnosed with GDM in the second trimester were enrolled. We analyzed depression symptoms using the Centers for Epidemiological Studies Depression Scale (CES-D) and considered related factors of depression symptoms, such as dietary intake and daily walking. Dietary intake during the past month was assessed using a brief self-administered diet history questionnaire, and daily walking was assessed using an accelerometer. The prevalence rate for GDM was 8.8%, and 25 pregnant women with GDM were analyzed. The CES-D was not significantly correlated with pre-pregnancy BMI, postprandial plasma glucose, hemoglobin A1c, and the number of steps walked. In contrast, a significant negative correlation was observed between the CES-D score and intake of fish with bones, simmered fish, pickles, green leaves, mushrooms, and green tea. Furthermore, a significant positive correlation was found between Coke® and CES-D scores. For nutrient intake, a significant negative correlation was found between the CES-D score and vitamin K, folate, and β-carotene levels. The present study suggests that depression symptoms among pregnant women with GDM in the second trimester may be associated with diet.

Keywords   gestational diabetes mellitus, depressive symptom, nutrition

1. Introduction

The link between diabetes and depression is well known (*1*). The position statement of routine psychosocial care for individuals with diabetes was published by the American Diabetes Association (*2*). A review indicated that the odds ratio of depression in the diabetic group was twice than that of the nondiabetic group, and the prevalence of depression in women with diabetes was significantly higher than that in men with diabetes (*3*). A recent meta-analysis also revealed that the prevalence of depression was 34% in 134,332 females with type 2 diabetes mellitus (*4*), which was 1.48 times more than what is seen in males. Although the age-matched population composition was different, we must also pay attention to depression for women with gestational diabetes mellitus (GDM).

GDM is a major perinatal complication (*5*). In 2010, the International Association of Diabetes and Pregnancy Study Groups established universal criteria based on the Hyperglycemia and Adverse Pregnancy Outcome study in 2008 (*6*). The prevalence of GDM has been reported to be approximately 8% in Japan (*7*). Diet and exercise therapy should be attempted first, with drug therapy added if diet and exercise alone cannot sufficiently correct glucose tolerance. Summary and recommendations for dietetic treatment for GDM were provided by the International Workshop Conference on GDM sponsored by the American Diabetes Association (*8*). The American College of Obstetricians and Gynecologists recommends at least 30 min of moderate intensity physical activity on most, if not all, days of the week (*9*). In a previous study, we reported that daily walking improves postprandial plasma glucose (PPG) in women with GDM (*10*). However, few studies have examined depression and pregnant women with GDM and suggest only the aforementioned relationship (*11-16*). For our second step, we analyzed factors associated with depression symptoms using the Center for Epidemiological Studies Depression (CES-D) Scale

(*17,18*) among pregnant women with GDM. It was a novel approach to focus on effective nursing care for pregnant women with GDM.

2. Materials and Methods

2.1. Setting and participants

As part of the longitudinal study (*10*), this cross-sectional study was conducted at TOYOTA Memorial Hospital in Toyota, Japan, from January 2015 to June 2016. In the present study, we focused on the symptoms of depression experienced during the second trimester. Inclusion criteria were as follows: (*i*) pregnant women who had regular prenatal checkups at the hospital and were diagnosed with GDM in the second trimester, (*ii*) pregnant women who were over 20 years old, and (*iii*) pregnant women who could complete a questionnaire. Exclusion criteria were as follows: (*i*) pregnant women with type 1 or 2 diabetes; (*ii*) pregnant women who were used steroids; (*iii*) pregnant women who were admitted to the hospital; (iv) pregnant women who had a pregnancy complicated by fetal disorders; and (*v*) pregnant women who had regular exercise with high intensity.

2.2. Procedures

Pregnant women with GDM in the second trimester were recruited for this study while awaiting routine examination in an outpatient hospital room; questionnaires assessed depressive symptoms and dietary intake. Background information, including maternal age, gestational week, pre-pregnancy body mass index (BMI), maternal history, complications of pregnancy, and laboratory biochemical data were obtained from medical charts. Daily walking was measured using an accelerometer (Lifecorder EX; Suzuken Co Ltd, Nagoya, Japan) (*19*), as previously reported (*10*). Participants attached the accelerometer to the waistbands of their skirts or pants, as instructed at the time of recruitment by investigators. The accelerometers assessed daily walking for 8 weeks (at least > 4 weeks), excluding sleeping and bathing.

The research ethics committees of the Kyoto University School of Medicine (No. E2279) and the hospital approved the study procedures and protocol. The participants received explanations of the aim and contents in the study, the voluntary nature of their participation, the risks and benefits of their participation, and privacy considerations. Written informed consent was obtained from all participants.

2.3. Measurements

Depressive symptoms were assessed using a Japanese version (*20*) of the CES-D scale (*19*). It is a self-administered questionnaire consisting of 20 items. The participants indicated on a four-point scale how often they experienced each item in the past week from 0 (rarely) to 3 (most). The total score ranged from 0 to 60. Based on a validation study, a CES-D score of > 16 points is defined as depression.

Dietary intake during the past month was assessed using a brief self-administered diet history questionnaire (BDHQ), and the amount of daily intake for 50 foods and selected nutrients (*21,22*) was calculated from the BDHQ.

Daily walking was assessed using the accelerometer, which measured steps, PA-related intensity, and PA-related energy expenditure (PAEE), as previously reported (*10*).

2.4. Statistical analyses

The Spearman correlation coefficient was performed using Statistical Package Social Sciences version 25.0 (SPSS Inc., Chicago, IL, USA). Spearman correlation coefficients < 0.05 were considered statistically significant.

3. Results

3.1. Participants

During the 18-month recruitment period, 776 pregnant women in the first trimester had regular prenatal checkups at the hospital. Among the 716 pregnant women (92.3%) who underwent blood work, 245 pregnant women (34.2%) had PPG > 100 mg/dL in the first trimester or blood glucose > 140 mg/dL in a 50-g glucose challenge test in the second trimester. The 75-g oral glucose tolerance test (OGTT) was performed in 184 pregnant women (75.1%) to diagnose GDM based on the following standard criteria: blood glucose ≥ 92 mg/dL at fasting, ≥ 180 mg/dL at 60 min after loading, or ≥ 153 mg/dL at 120 min after loading. Clinical GDM was diagnosed in 63 patients. The prevalence rate of GDM in the hospital during the study period was 8.8%. An additional 10 pregnant women who had already been diagnosed with GDM with 75-g OGTT were referred to the hospital from nearby private clinics. Among the 73 pregnant women with GDM, 32 (43.8%) participated in the study. Seven pregnant women with GDM were excluded from the analysis due to the lack of CES-D data. Finally, we analyzed the data of 25 pregnant women with GDM. Figure 1 shows a flow diagram of the enrollment procedure.

The mean values (range) for age (years), weight before pregnancy (kg), BMI before pregnancy (kg/m²), and gestational weeks at the beginning of the study for 25 women with GDM were 36.1 (29-42), 61.8 (39-99), 24.1 (16.7-36.8), and 22.4 (14-28), respectively. One woman had a pre-pregnant BMI of < 18 kg/m²,
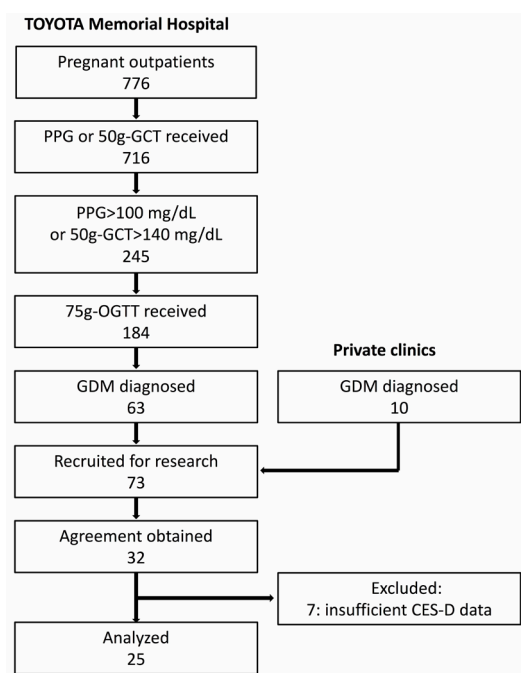
Figure 1. Flow diagram of the patients with gestational diabetes mellitus (GDM). Finally depressive condition in 25 women with GDM are analyzed.

and two had a BMI of > 30 kg/m^2. Twelve women were primiparas (Table 1). Of the 10 multiparas, one had GDM in prior pregnancies. None of the patients had symptoms of anemia. The PPG and hemoglobin A1c (HbA1c) values of the first day of walking measurement were 110 (69-173) and 5.4 (4.4-6.2), respectively. The number of steps walked/day was 6090 (2,947-10,772). The CES-D score was 9.3 (0-42), and the prevalence of depressive symptoms during the second trimester of pregnancy was 8.0%.

3.2. Relationship between CES-D score and pre-pregnant BMI, PPG, HbA1c, or walking step number

No significant correlation ($r = - 0.169$, $p = 0.452$; $r = 0.236$, $p = 0.290$; $r = - 0.356$, $p = 0.114$) was found between the CES-D score and pre-pregnant BMI, PPG, or HbA1c.

Our previous report (*10*) showed that daily walking is good for controlling PPG in pregnant women with GDM. On the other hand, no significant correlation ($r = - 0.219$, $p = 0.294$) was also observed between the CES-D score and the number of steps walked.

3.3. CES-D score relation to food intake and nutrient intake

Table 2 shows a significant negative correlation between the CES-D score and intake of fish with bone (g/day) ($r = - 0.503$, $p = 0.017$), simmered fish (g/day) ($r = - 0.464$, $p = 0.030$), pickles (green leaf) (g/day) ($r = - 0.440$, $p = 0.041$), pickles (other) (g/day) ($r = - 0.468$, $p = 0.028$),

green leaf (g/day) ($r = - 0.450$, $p = 0.036$), mushrooms (g/day) ($r = - 0.567$, $p = 0.006$), and green tea (g/day) ($r = - 0.433$, $p = 0.044$). Furthermore, a significant correlation was found ($r = 0.450$, $p = 0.036$) between CES-D score and Coke® (g/day).

Table 3 shows a significant negative correlation between the CES-D score and vitamin K (μg/day) ($r = - 0.496$, $p = 0.019$), folate (μg/day) ($r = - 0.465$, $p = 0.029$), and β-carotene (μg/day) ($r = - 0.451$, $p = 0.035$).

4. Discussion

Although little is known about the relationship between depression and pregnant women with GDM, this may be the first study that reports that the diet of pregnant women with GDM can affect the presence of depressive symptoms. One strength of this study is that it is very useful for nutrition educated for pregnant women with GDM.

A review article (*23*) suggests that folate may be effective for treating depressive disorders. Patients diagnosed with major depressive disorder tend to have lower concentrations of folate in serum or red cells than healthy control subjects (*24,25*). A previous study showed that the co-administration of folic acid in female patients with depression substantially and significantly improved their response to fluoxetine (*26*). Low levels of folate and vitamin B12 have an effect on depressive symptoms (*27,28*). B-complex vitamins are coenzymes involved in homocysteine metabolism. In contrast, Watanabe *et al.* (*29*) reported no relationship between folate and homocysteine levels and depression in women in early pregnancy. Cho *et al.* (*30*) showed that the intake of multivitamins, including folic acid, was not associated with lower rates of depression during pregnancy. Our study found that CES-D scores were significantly correlated only with folate in B-complex vitamins. In food intake, green leaves and pickled green leaves were significantly correlated with CES-D scores; this was because green leaves include vitamin K and β-carotene. The association between deficiency in B-complex vitamins and depression in pregnancy is still unclear.

A previous observational study supported an association between low n-3 fatty acid intake from seafood and increased risk of high levels of depressive symptoms during pregnancy (*31*). Our study revealed that CES-D scores were significantly correlated with the intake of fish with bone and simmered fish, but no significant correlation was found with n-3 fatty acid intake. In addition to n-3 fatty acid intake, other researchers noted that zinc and iron intake, green tea intake, and intestinal environment improvement may also be useful for the alleviation of depressive symptoms (*32-35*). Our results also indicated that the CES-D scores were significantly correlated with green tea, mushroom, and pickle intake. No significant

Table 1. Participant characteristics and parameters

No.	Age (years)	Primipara(P)/ multipara(M)	History of GDM[a] at previous pregnancy	Weight when not pregnant	BMI[b] when not pregnant	Dietary intake (kcal/day)	CES-D[c]	At initiation of research					Gestational weight gain overall	Child birth		
								Gestational weeks	Body weight (kg)	PPG[d] (mg/dL)	HbA1c[e] (%)	Hb (g/dL)		Gestational weeks at delivery	Delivery mode	Birth weight (g)
1	35	M	-	62.0	25.8	2,403	0	28	67.2	108	5.4	12.9	6.0	39	NVD[g]	3,102
2	30	P		65.0	26.7	1,712	0	25	66.0	87	4.4	13.8	8.0	38	CS[i](elective)	2,950
3	40	M	-	66.0	27.5	1,520	0	27	66.0	111	6.2	ND[f]	ND[f]	ND[f]	ND[f]	ND[f]
4	42	M	-	60.0	25.3	2,057	4	18	61.0	83	5.4	12.0	5.0	38	CS[i](elective)	3,030
5	40	M	-	73.0	25.3	1,358	5	25	79.0	90	5.1	11.9	ND[f]	40	NVD[g]	3,066
6	31	M	-	48.0	18.3	1,677	5	25	56.0	81	5.6	10.3	14.4	40	NVD[g]	4,124
7	42	P		67.0	24.6	1,210	6	22	65.0	113	5.1	13.2	-0.2	35	NVD[g]	1,764
8	37	P		56.0	24.1	2,235	6	14	62.8	123	5.8	10.9	13.0	41	NVD[g]	3,658
9	37	M	-	67.0	24.1	1,814	6	19	69.0	74	5.5	12.9	5.6	40	VD[h](forceps)	3,562
10	42	M	-	49.0	18.7	1,810	7	24	53.4	102	5.3	11.2	6.8	38	NVD[g]	3,074
11	29	M		79.0	30.9	1,601	7	24	80.5	149	5.4	13.2	0.6	38	NVD[g]	2,988
12	40	P		48.0	20.5	1,552	8	19	50.0	128	5.3	14.0	9.8	41	NVD[g]	3,200
13	39	P		64.0	23.8	1,515	9	14	65.0	103	6.0	12.0	7.2	41	NVD[g]	2,946
14	38	P		71.0	29.6	1,204	9	26	77.5	173	5.2	13.0	6.8	34	CS[i](emergency)	1,554
15	40	P		54.0	19.1	1,881	9	21	56.8	90	5.1	12.5	ND[f]	ND[f]	ND[f]	ND[f]
16	32	P		66.0	26.1	1,125	10	16	60.0	156	5.4	11.6	8.6	41	NVD[g]	3,432
17	35	P		39.0	16.7	2,063	10	19	41.4	102	4.7	10.1	ND[f]	38	VD[h](forceps)	2,752
18	35	P		58.0	21.0	1,503	10	27	63.2	127	5.3	11.2	7.0	40	NVD[g]	3,144
19	29	M	+	46.0	19.9	1,938	11	23	51.2	69	5.2	11.5	ND[f]	38	NVD[g]	3,012
20	41	P		70.0	25.1	1,682	11	27	59.2	97	5.8	12.5	3.2	37	CS[i](elective)	2,218
21	37	ND[f]		ND[f]	ND[f]	1,454	12	26	58.2	ND[f]	ND[f]	ND[f]	ND[f]	ND[f]	ND[f]	ND[f]
22	36	ND[f]		ND[f]	ND[f]	ND[f]	14	26	43.0	ND[f]	ND[f]	ND[f]	ND[f]	ND[f]	ND[f]	ND[f]
23	30	P		99.0	36.8	1,319	15	24	99.2	97	5.6	11.5	14.5	40	NVD[g]	3,746
24	30	ND[f]		ND[f]	ND[f]	ND[f]	17	17	49.0	ND[f]	ND[f]	ND[f]	ND[f]	ND[f]	ND[f]	ND[f]
25	35	M	-	52.0	20.8	1,868	42	24	63.0	154	5.1	10.9	11.8	38	NVD[g]	2,966
mean	36.1			61.8	24.1	1,674	9.3	22.4	62.5	110	5.4	12.1	7.5	38.8		3,014
SD	4.3			12.8	4.6	326	7.9	4.2	12.3	28	0.4	1.1	4.1	1.9		597

[a]GDM, gestational diabetes mellitus; [b]BMI, body mass index; [c]CES-D, The Center for Epidemiologic Studies Depression Scale; [d]PPG, postprandial plasma glucose; [e]HbA1c, hemoglobin A1c; [f]ND, not detected; [g]NVD, normal vaginal delivery; [h]VD, vaginal delivery; [i]CS, Cesarean section.

Table 2. Food intake and spearman correlation coefficients between nutrient intake and CES-D[a] score

Food	Food intake (g/day) (mean ± SD[b])	r	p-value
Low-fat milk	75.4 ± 113.8	-0.191	0.393
Milk	52.4 ± 51.0	0.250	0.262
Chicken	33.0 ± 20.0	-0.046	0.840
Pork·Beef	37.1 ± 18.3	-0.323	0.143
Fish with bone	9.6 ± 26.5	-0.503	0.017[*]
Dried fish	14.9 ± 14.2	-0.311	0.158
Oily fish	21.0 ± 39.0	-0.030	0.895
Fish with little oile	17.0 ± 15.8	-0.331	0.132
Classification of the cooking style			
Raw fish	12.6 ± 15.3	0.035	0.879
Grilled fish	52.7 ± 62.0	-0.183	0.414
Simmered fish	35.0 ± 38.9	-0.464	0.030[*]
Fried fish	12.0 ± 17.1	-0.056	0.803
Egg	37.2 ± 25.8	-0.111	0.624
Tofu·Fried tofu	47.7 ± 32.8	-0.210	0.347
Natto	11.1 ± 10.4	-0.199	0.375
Pickles (green leaf)	4.7 ± 7.7	-0.440	0.041[*]
Pickles (other)	2.3 ± 3.9	-0.468	0.028[*]
Lettuce·Cabbage (low)	37.6 ± 24.2	-0.362	0.098
Green leaf	52.1 ± 44.7	-0.450	0.036[*]
Cabbage	41.3 ± 25.2	-0.415	0.055
Carrots·Pumpkin	24.4 ± 17.3	-0.296	0.181
Radish·Turnip	22.3 ± 21.7	-0.368	0.092
Root vegetables	44.3 ± 34.0	0.028	0.901
Tomato	39.0 ± 32.5	-0.017	0.942
Mushroom	11.2 ± 7.4	-0.567	0.006[*]
Seaweed	11.4 ± 10.2	-0.500	0.018
Green tea	65.6 ± 146.2	-0.433	0.044[*]
Tea·Oolong tea	65.6 ± 129.9	0.120	0.594
Coffee	49.6 ± 92.0	-0.197	0.379
Coke®	36.1 ± 53.0	0.450	0.036[*]

[a]CES-D, The Center for Epidemiologic Studies Depression Scale; [b]SD, standard deviation.

Table 3. Nutrient intake and spearman correlation coefficients between nutrient intake and CES-D[a] score

Nutrient	Nutrient intake (mean ± SD[b])	r	p-value
Protein (% of energy/day)	16.6 ± 4.2	0.079	0.721
Fat (% of energy/day)	30.8 ± 5.5	0.065	0.767
Carbohydrate (% of energy/day)	51.5 ± 8.4	0.059	0.791
Potassium (mg/day)	2,412.1 ± 811.4	-0.302	0.171
Calcium (mg/day)	542.7 ± 242.7	-0.238	0.286
Magnesium (mg/day)	227.1 ± 77.1	-0.352	0.108
Phosphorus (mg/day)	1,003.1 ± 379.4	-0.259	0.244
Iron (mg/day)	7.4 ± 2.8	-0.393	0.071
Zinc (mg/day)	7.8 ± 2.4	-0.309	0.162
Manganese (mg/day)	2.3 ± 0.9	-0.235	0.292
Vitamin D (μg/day)	13.7 ± 14.4	-0.297	0.179
Vitamin K (μg/day)	312.8 ± 169.9	-0.496	0.019[*]
Vitamin B1 (mg/day)	0.8 ± 0.2	-0.256	0.250
Vitamin B2 (mg/day)	1.2 ± 0.5	-0.222	0.321
Vitamin B6 (mg/day)	1.2 ± 0.4	-0.269	0.226
Vitamin B12 (μg/day)	9.3 ± 7.1	-0.238	0.287
Folate (μg/day)	319.4 ± 125.3	-0.465	0.029[*]
Vitamin C (mg/day)	111.0 ± 37.1	-0.382	0.080
Saturated fatty acids (g/day)	14.4 ± 5.7	0.120	0.596
cholesterol (mg/day)	368.3 ± 204.4	-0.222	0.320
n-3 fatty acid (g/day)	2.9 ± 1.6	-0.115	0.610
n-6 fatty acid (g/day)	10.8 ± 3.4	-0.069	0.762
α-carotene (μg/day)	463.3 ± 321.7	-0.303	0.170
β-carotene (μg/day)	3,876.8 ± 2191.0	-0.451	0.035[*]

[a]CES-D, The Center for Epidemiologic Studies Depression Scale; [b]SD, standard deviation.

correlation was found between zinc and iron intake. Our study also showed an association between high CES-D score and high Coke® intake. The effect of Coke® intake on depressive symptoms is unclear, and there is room for further consideration.

This study has several limitations. First, our sample size was too small and did not have adequate power. Second, since the study subjects participated on a voluntary basis, they may be healthier than the general population, causing a selection bias. Third, since the BDHQ queried diet history for the past month, recall bias was included. Fourth, we only investigated CES-D scores for depressive symptoms and could not examine the risk factors for temperament, character, and depressive episodes, including history of depression, lack of partner, lack of social support, poverty, family violence, and increased life stress (*36-38*).

In conclusion, the present study suggests that symptoms of depression in pregnant women with GDM in their second trimester may be associated with their diet. Future research should include studies with larger sample sizes. In addition, future longitudinal studies on the relationship between depressive symptoms and diet for pregnant women with GDM are required.

Acknowledgements

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