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Comparison of Nutritional Status with Serum Vitamin D and B12 Levels in Pregnant Women with Gestational Diabetes

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Abstract

Objective: In this study, it was aimed to evaluate the nutritional adequacy status of pregnant women with gestational diabetes and to examine the relationship between biochemical parameters such as vitamin D, vitamin B12, hemoglobin, hematocrit and fasting glucose.

Methods: In the study, serum vitamin D and B12 levels of 130 pregnant women between 24-28 weeks of gestation were examined. As a result of 75-gram oral glucose tolerance test, 70 pregnant women were diagnosed with gestational diabetes mellitus (GDM). The control group consisted of 60 healthy pregnant women. Nutritional factors were obtained through a questionnaire (anthropometric measurements, micronutrients, 3-day food consumption frequency, use of vitamin supplements) and groups were compared in terms of biochemical parameters (vitamin D, vitamin B12).

Results: Pregnant women with GDM; mean age (30.34 ± 5.28), family history of diabetes (17.1%), pre-pregnancy body mass index percentage (54.3%), rate of skipping meals were higher. The rate of use of vitamin and mineral supplements in pregnant women with GDM was low. According to the analysis of 3-day food consumption records of pregnant women with GDM, it was determined that the intake of micronutrients vitamin D and vitamin B12 was insufficient. Biochemical parameters such as vitamin D, vitamin B12, hemoglobin and hematocrit were found to be lower in pregnant women with GDM.

Conclusion: GDM is the most common endocrinological disorder in pregnancy. The study showed that inadequate nutrient intake negatively affects blood glucose levels and biochemical findings. Individuals with GDM should be referred to a nutritionist, medical nutrition therapy (TBT) appropriate for their individual characteristics should be given and monitored.

Key words: Gestational diabetes, biochemical parameters, vitamin D, vitamin B12, nutrition

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INTRODUCTION

Diabetes Mellitus (DM) is defined as a metabolic disease that has become a global epidemic worldwide, causing abnormalities in carbohydrate (CH), protein and fat metabolism, hyperglycemia, and multiorganal damage due to impaired insulin secretion, insulin action or both (1). In 2017, the number of people with diabetes worldwide was 451 million. It is estimated that by 2045, the number of people with diabetes in the world will reach 693 million (2).

Gestational diabetes mellitus (GDM) is defined as variable carbohydrate intolerance detected during pregnancy. GDM is the most common endocrinological disorder in pregnancy and is found in 7% of all pregnancies (1). Its incidence in Turkey has been reported between 1.2% and 9.2% (3). There is a 20% to 50% risk of developing Type 2 DM in 5-10 years in women with a history of GDM (4). On the other hand, children of women with GDM are also at risk of obesity and diabetes mellitus (DM) in later years.

Since the fetus is fed by the mother during pregnancy, the daily energy and nutritional needs of pregnant women increase. However, many women take insufficient nutrients during this period and cannot eat healthy. It has been reported that increasing the consumption rate of sugary foods and decreasing the consumption rate of fruits and vegetables from fibrous foods cause an increase in fasting glucose (5). Sugar from food crosses the placenta and causes insulin release from the baby's pancreas. This insulin hormone also functions as a growth hormone and leads to macrosomic birth. In addition, uncontrolled GDM causes complications such as preeclampsia, hydroamniosis, hypertension, increased risk of cesarean section in fetuses and infants.

Adequate intake of vitamin D, vitamin B12, zinc, iodine, calcium, iron, folate, and magnesium is particularly important during pregnancy (6). Vitamin D deficiency during pregnancy is associated with adverse complications such as premature birth, increased cesarean delivery, and insulin resistance (7). It has been suggested that low vitamin D levels in diabetic subjects are associated with diabetic control (8). Folic acid and vitamin B12 are involved in the division or proliferation of cells. It is effective in all cells and is a very important vitamin related to the gastrointestinal system (GIS), central nervous system (CNS). According to the data obtained from very few studies on the need for vitamin B12 during pregnancy, serum vitamin B12 values decrease in the following weeks of pregnancy (9).

The aim of this study is to compare pregnant women with gestational diabetes mellitus (GDM) and healthy control group. Anthropometric measurements of pregnant women, nutritional habits and dietary factors causing GDM were determined and the

relationship between biochemical parameters such as vitamin D, vitamin B12, hemoglobin, hematocrit and fasting glucose was tried to be examined

METHODS

The study was carried out between November 2018 and May 2019 in Turkey Ordu University Training and Research Hospital Gynecology Polyclinic, Ordu Private Sevgi Hospital Gynecology Polyclinic, Ordu General Directorate of Public Health. 130 pregnant women between 24-28 weeks diagnosed by doctor (70 gestational diabetes and 60 healthy pregnant women) were examined.

All subjects included their informed consent before participating in the study. Written consent was obtained from the pregnant women for voluntary participation in the study. A questionnaire form was filled in to ask general information about pregnancy to the pregnant women in the case and control groups. Pregnant women who had a pregnancy other than their gestational week and had diabetes complications were excluded from the study.

Ethical aspect of the study

Ethics committee approval was obtained for this study by Giresun University Clinical Research Evaluation Committee with the decision dated 07/11/2018 and numbered 2018/05-06. Before starting the research, written permission was obtained from the hospitals where the research would be conducted.

Dietary evaluation

In the questionnaire applied to pregnant women, their weight, body mass indexes, whether they have chronic diseases in their families, vitamin-mineral supplements, diet program, nutritional habits (meal pattern and why they skip meals, what foods they consume, glycemic index (GI) high food consumption frequency etc.) were questioned. Food consumption was recorded for a total of 24 hours over three days, two on weekdays and one on weekends. The daily energy and nutritional values of the patient were analyzed using the nutrition information system (BEBIS) 8.2 program.

Data on energy and nutritional values obtained from the analysis were compared with the Dietary Reference Intake (DRI) (10) recommendations and ± 30-33 values of the recommended daily consumption for all nutrients were calculated. In the DRI recommendation, the content of macro and micronutrients is considered as insufficient values below 67%, sufficient values 67-133% and values above 133% as excessive consumption.

Biochemical measurements

The biochemical parameters routinely requested by the physician were recorded in the questionnaire and all data were evaluated. GDM diagnosis was made by gynecology and obstetrics clinic physicians according to biochemical blood findings. Blood samples

were taken from the pregnant women who came for routine control at 24-28 weeks of pregnancy after fasting for 10-12 hours in the biochemistry laboratory and measured by photometric method. (Roche Diagnostics GmbH, Mannheim, Germany). At the end of the measurement, 75 g OGTT was performed in patients with FPG 100- ≥126 mg/dl. Because fasting blood glucose is >92 mg/dL according to IADPSG/ADA criteria in pregnant women with GDM, a 2-hour OGTT test with 75 g glucose is recommended. A 2-hour OGTT test with 75 g glucose was performed on pregnant women with GDM (0 hours ≥92 mg/dl, 1 hour ≥180 mg/dl, 2 hours ≥153 mg/dl).

GDM was diagnosed in pregnant women if at least one glucose concentration met or exceeded the criteria as a result of the test. Hemoglobin values were measured by calorimetric method. (Sysmex Corporation, Kobe, Japan). According to the World Health Organization (WHO) criteria, hemoglobin values below 10.5 g/dl in the second trimester of pregnancy are accepted as anemia. In this study, hemoglobin values between 11.2 g/dl and 14.6 g/dL were considered normal, while those <10 g/dl were considered low. The shaped elements were precipitated by centrifugation on Sysmex Xn 1000 (Sysmex Corporation, Kobe, Japan).

The ratio of shaped elements to blood volume was calculated by the device. Hematocrit (Htc) values in women were evaluated according to the reference range of 36-46%. After fasting for 10-12 hours, venous blood samples (Cobas Hitachi E601) were measured by electrochemiluminescence method.

Vitamin B12 was defined as 191-663 pg/ml adequacy level in men and women. In our study, total vitamin D (D2-D3) was measured by electrochemiluminescence method (Cobas Hitachi E601). The lower limit of the electrochemiluminescence method is 3 µg/l and the measuring range is 3-70 µg/l. <20 µg/l vitamin deficiency was defined as 20-29 µg/l deficiency and ≥30 µg/l proficiency level (11).

Statistical Analysis

Descriptive statistics for continuous variables; Expressed as Mean, Standard Deviation, Minimum and Maximum values, while expressed as numbers and percentages for Categorical variables. Student's t-test was used to compare group means in terms of continuous variables. Chi-square test was used to determine the relationship between groups and categorical variables. As a result of the food consumption records of the patients, the data obtained using the BeBIS 8.2 program were transferred to the statistical package program and evaluated. The statistical significance level was taken as 5% in the calculations and the SPSS (ver:23) statistical package program was used for the calculations.

RESULTS

The average age of the groups; GDM cases in the case group were 30.34 ± 5.28 years, and the mean age of healthy individuals in the control group was 28.38 ± 4.85 years. It was determined that 80% of individuals with GDM and 93.3% of healthy individuals used vitamin-mineral supplements. There was a statistically significant difference between usage rates. Looking at the types of vitamin-mineral supplements used; It was determined that individuals with GDM used iron in 15.7%, vitamin D in 28.6%, vitamin B12 in 10%, folic acid in 21.4%, magnesium in 2.9% and probiotic supplements in 1.4%. It was determined that 21.7% of healthy individuals used iron supplements, 38.3% vitamin D, 6.5% vitamin B12, 27% folic acid and 1.4% magnesium supplements.

Healthy pregnant women consumed vitamins and mineral supplements (30.4%) during pregnancy longer than pregnant women with gestational diabetes (29.1%). There were statistically significant differences. It was found that the history of diabetes in the family of pregnant women with GDM (17.1%) was higher than that of healthy pregnant women (11.7%).

When the pre-pregnancy body mass index (BMI) of pregnant women with GDM was evaluated, it was found that the total percentage of mildly obese and obese pregnants (54.3%) was higher than the total percentage of healthy pregnants (50%). The difference between meal skipping rates of GDM and healthy individuals was statistically significant. The highest rate of skipping meals in individuals with GDM was found to be breakfast with 18.6% and lunch with 24.3%. It was determined that 3.3% of healthy pregnant women skipped breakfast and 25% skipped lunch (Table 1). The total fiber ratio of the pregnant women from the foods they consume daily was 27.9±6.6 g in pregnant women with GDM and 44.1±11.7 g in healthy pregnant women. Fiber intake of pregnant women with GDM was found to be significantly lower than the control group ($p<0.05$).

When the nutritional adequacy status of all individuals is evaluated according to DRI recommendations; It was determined that healthy pregnant women took 73.3% more, 25% normal, 1.7% insufficient vitamin D. It was determined that healthy pregnant women took 41.7% more, 45% enough, 13.3% insufficient vitamin B12. It was found that pregnant women with GDM took 7.1% more, 48.6% normal, 44.3% insufficient vitamin D. Pregnant women with GDM took 21.4% more, 55.7% adequate, 22.9% insufficient vitamin D. detected. Vitamin D and vitamin B12 were statistically significant. Vitamin D deficiency (44.3%) was found to be higher in pregnant women with GDM than in healthy pregnant women (1.7%). It was determined that vitamin B12 deficiency was higher in pregnant women

with GDM (22.9%) than in healthy pregnant women (13.3%). Dietary intake of these vitamins in pregnant women with GDM was found to be lower than in healthy pregnant women (Figure 1 and Figure 2).

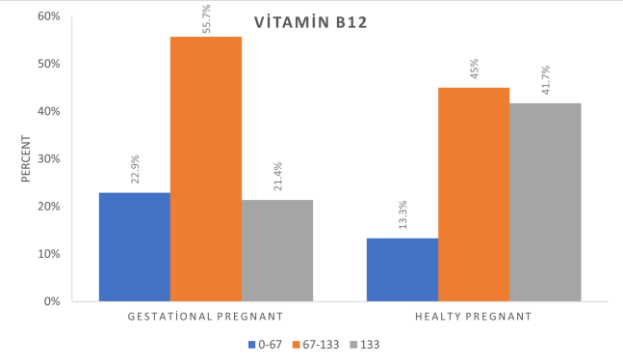

Figure 1. Distribution of adequacy status of vitamin D intakes in daily diets of pregnant women in line with DRI recommendations
(Below 0-67% insufficient, 67-133% sufficient and over 133% excessive consumption)

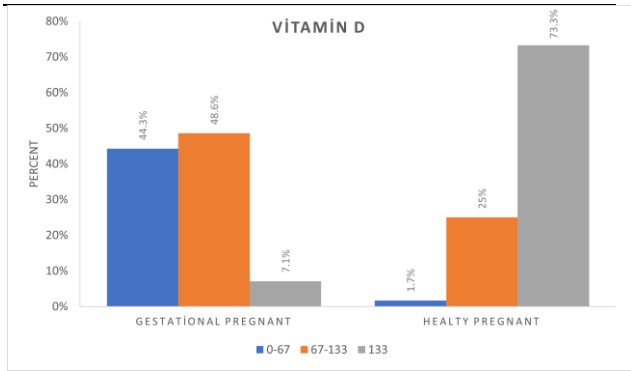

Figure 2. Distribution of adequacy status of vitamin B12 intakes in daily diets of pregnant women in line with DRI recommendations
(Below 0-67% insufficient, 67-133% sufficient and over 133% excessive consumption)

As a result of this study, while vitamin D taken through food was 31.32±7.6 mcg in healthy pregnant women, it was found as 14.1±9.9 mcg in pregnant women with GDM. When the frequency of consumption of milk, cheese and fish products from which we can get vitamin D through food is examined, the daily milk consumption of individuals with GDM is 65.7%, while that of healthy individuals is 75%; Daily cheese consumption of individuals with GDM was 74.3%, and 86.7% of healthy individuals. Percentage values of milk ($p=0.025$) and cheese ($p=0.039$) consumption of the group with GDM were statistically significantly lower than the percent values of healthy pregnant women. 22.9% of individuals with GDM and 8.3% of healthy individuals do not consume fish at all. The percentage of fish consumption of healthy individuals was statistically significantly higher than the group with GDM ($p<0.005$). In addition, iron mineral was found to be very low especially in individuals with GDM compared to healthy individuals (Table 2).

In our study, fasting glucose values of pregnant women with GDM were 99.2 ± 13 mg/dl, and 87.2 ± 9.2 mg/dl in healthy pregnant women. Pregnant women with GDM OGTT 1st hour values were 181.1 ± 2.87 mg/dl and OGTT second hour values were 153.7 ± 3.3 mg/dl. Serum 25 (OH) vitamin D levels of pregnant women with GDM (17.8 ± 10.7 ng/ml) were significantly lower than healthy pregnant women (20.6 ± 8.05 ng/ml).

The other biochemical findings of both groups were compared with those of GDM pregnant women with vitamin B12 (199.9 ± 91.5 pg / ml), hemoglobin (10.8 ± 2.9 g / dL), respectively; It was found that vitamin B12 (234 ± 114.7 pg / ml) and hemoglobin (11.9 ± 3.2 g / dL) values of healthy pregnant women

were significantly lower (p <0.05). Hematocrit values of GDM (30.3 ± 7.4%) and healthy pregnant women (33.01 ± 8%) were close to significant (p = 0.055).

Table 1. General Information About Pregnants

	GDM (n=70)		Control (n=60)	
	n	%	n	%
Age ratio				
Mean	20-44		20-40	
SD	30.34 ± 5.28		28.38 ± 4.85	
BMI				
Lightweight (BMI≥25-29,9 kg/m²)	31	44.3	26	43.3
Obese (BMI≥30,0 kg/m²)	7	10	4	6.7
Does he use vitamin-mineral supplements?				
Yes	56	80	56	93.3
Vitamins and minerals used				
Vitamin B12	7	10	7	6.5
Vitamin D	20	28.6	23	38.3
Iron	11	15.7	13	21.7
Folic acid	15	21.4	12	20
Magnesium	2	2.9	1	1.4
Probiotics	1	1.4	0	0
Vitamin-mineral consumption time				
During pregnancy	16	29.1	17	30.4
Family history of chronic disease				
Diabetes	12	17.1	7	11.7
Most skipped meal				
Breakfast	13	18.6	2	3.3
Lunch	17	24.3	15	25

GDM: gestational diabetes mellitus Control: healthy pregnant, BMI: body mass index, kg: kilogram m²: square meters

Table 2. Distribution of energy and nutrients (vitamin) according to DRI recommendations.

		GDM (n=70)						Control (n=60)						p value
Vitamins	Reference values	Insufficient (<%67)		Enough (%67-133)		Excess (%133)		Insufficient (<%67)		Enough (%67-133)		Excess (%133)		
		n	%	n	%	n	%	n	%	n	%	n	%	
Vitamin A (mcg)	700	1	1.4	2	2.9	67	95.7	-	-	1	1.7	59	98.3	0.583
Vitamin E (mg)	11	2	2.9	19	27.1	49	70	-	-	17	28.3	43	71.7	0.418
Vitamin B1 (mg)	1.4	29	41.4	40	57.1	1	1.4	-	-	47	78.3	13	21.7	0.001
Vitamin B2 (mg)	1.4	2	2.9	55	78.6	13	18.6	-	-	4	6.7	56	93.3	0.001
Vitamin B6 (mg)	1.9	36	51.4	33	47.1	1	1.4	-	-	51	85	9	15	0.001
Folate (mcg)	600	47	67.1	22	31.4	1	1.4	6	10	51	85	3	5	0.001
Vitamin C (mg)	85	3	4.3	24	34.3	43	61.4	-	-	-	-	60	100	0.001
Vitamin D (mcg)	15	31	44.3	34	48.6	5	7.1	1	1.7	15	25	44	73.3	0.001
Vitamin B12 (mcg)	4.5	16	22.9	39	55.7	15	21.4	8	13.3	27	45	25	41.7	0.037
Minerals														
Potassium (mg)	4.7	45	64.3	25	35.7	-	-	-	-	59	98.3	1	1.7	0.001
Calsiyum (mg)	1000	7	10	57	81.4	6	8.6	-	-	30	50	30	50	0.001
Magnesium (mg)	300	2	2.9	64	91.4	4	5.7	-	-	24	40	36	60	0.001
Phosphorus(mg)	550	-	-	1	1.4	69	98.6	-	-	-	-	60	100	0.353
Iron (mg)	16	45	64.3	24	34.3	1	1.4	-	-	58	96.7	2	3.3	0.001
Zinc (mg)	11	6	8.6	62	88.6	2	2.9	-	-	31	51.7	29	48.3	0.001

mcg: microgram, mg:miligram, n:number of people, p: statistical value, GDM: gestational diabetes mellitus, Control: healthy pregnant women, Dietary Reference Intake (DRI) Dietary Reference Intake

Table 3. Biochemical Findings of Pregnant Women

	GDM (n=70)		Control (n=60)		P value
	Upsıde down	x̄ ±SS	Upsıde down	x̄ ±SS	
Fasting glucose (mg/dl)	72-145	99.2 ± 1	72-112	87.2 ± 9.2	0.001
Hemoglobin (g/dl)	4.2-25	10.8 ± 2.9	7-30	11.9 ± 3.2	0.038
Hematocrit (%)	10.3-45	30.3 ± 7.4	13.9-50	33 ± 8	0.055
Vitamin D (ng/ml)	2-50	17.8 ± 10.7	8.8-52	20.6 ± 8	0.034
Vitamin B12 (pg/ml)	59-626	199.9 ± 91.5	102-627	234 ± 114.7	0.039
Ogtt 1.hour (mg/dl)	114-234	181.1 ± 2.8	-	-	0.424
Ogtt 2.hour (mg/dl)	107-100	145.1 ± 2.5	-	-	0.001

mg: miligram, dl:deciliter, g:gram, ml:millilitre, ng:nanogram, pg:picogram, p:statistic value GDM: gestational diabetes mellitus Control: healthy pregnant

DISCUSSION

Studies have shown that fasting blood sugar increases due to increased consumption of sugary foods such as cakes and pastries, and foods such as margarine and butter, which contain high saturated or trans fats, and decreased consumption of pulpy foods (12).

The ADA (1) recommends that 25 years of age and older be considered as a risk factor for GDM. Our study, along with other studies, supports that advanced gestational age is a risk factor for GDM.

The presence of diabetes in the family history of pregnant women with GDM is a risk factor. Leng et al. (13), it was concluded that 13.4% of pregnant women with GDM had a family history of diabetes and this increased the risk of GDM 1.61 times. In our study, the history of diabetes in the family of pregnant women diagnosed with GDM was found to be 17.1% higher than that of healthy pregnant women, and it was considered as a factor increasing the risk of GDM.

It becomes even more important that pregnant women take enough vitamins during the pregnancy period when their nutritional needs increase. Because the baby needs vitamins to continue its development in a healthy way. In particular, deficiencies of important micronutrients such as iron, iodine, folic acid, vitamin D and vitamin B12 cause various diseases such as megaloblastia, neural tube defects, placental and fetal defects (9). In particular, it was determined that the iron mineral was very low in individuals with GDM compared to healthy individuals. In addition, the use of vitamin and mineral supplements in pregnant women with GDM was found to be lower than in healthy pregnant women. Therefore, vitamins, minerals or both should be used during pregnancy.

BMI is the method used in the measurement of obesity, which is defined as an increase in weight above the desired level as a result of

excessive increase in the ratio of body fat mass to lean mass. Over 20% of body weight increases the risk of hypertension, chronic heart disease, hyperlipidemia, Type 2 diabetes and GDM. On this subject, Shin et al. (14) reported that GDM is 2.78 times more common in individuals with pre-pregnancy body mass index value in the obese category. In a cohort study of 226,958 women in Canada, it was reported that 9.7% of women with GDM were of normal weight before pregnancy and 51.1% were obese (15). In our study, it was determined that pregnant women with GDM started pregnancy as mildly obese and obese, and a finding supporting the literature was obtained.

According to the guidelines, it is recommended to include four snacks in the diet of pregnant women. In countries such as Switzerland and England, the recommended number of snacks is seven (16). Snacking is more important for pregnant women with GDM. Since there is a continuous glucose transfer from mother to baby, it helps to control glucose and insulin in the prevention of hypoglycemia. Especially if the hyperglycemia is more than 15-30 g in the morning, carbohydrate (CH) should be given at breakfast (17). In this study, it was found that the highest rate of skipping meals in individuals with GDM was breakfast. It was evaluated as a risk factor for GDM.

Consumption of fibrous foods should be increased. Since fibers are given to the bloodstream very slowly, they prevent blood sugar from being absorbed by the body and balance the sugar level in the blood (13). Zhang et al. (18) showed that a low-fiber and high-glycemic index diet increased the formation of GDM by 2.15 times. In addition, consumption of simple carbohydrate foods with high sugar and sugar content in women with GDM prevents the beneficial effects of fiber. Our results showed that pregnant women with GDM consumed high glycemic index and low fiber foods in food intake, similar to the study. The reason why the fiber ratios of pregnant women with GDM are low is that they consume less vegetables.

Vitamin D has an important role in glucose balance, insulin secretion and insulin sensitivity (19). Via active oxidative groups, vitamin D has antioxidant effects that can reduce damage and apoptosis of islet β cells (20). Burris et al. (21) in a study conducted with 1314 pregnant women, it was found that a significantly low serum 25 (OH) vitamin D level increased the occurrence of GDM by 3.36 times. It has been determined that GDM is significantly more common in pregnant women with severe serum 25(OH) vitamin D deficiency. (22). In this study, dietary vitamin D levels and serum 25 (OH) vitamin D levels of pregnant women with GDM were found to be significantly lower than

healthy pregnant women. Our findings are compatible with the literature.

Vitamin B12 is a coenzyme and is necessary for protein, fat, carbohydrate metabolism, erythropoiesis. Although its effect is seen in all cells, it is important for bone marrow, gastrointestinal system (GIS), central nervous system (CNS). Krishnaveni et al. (23) found that 43% of pregnant women had low levels of vitamin B12. It shows that vitamin B12 deficiency is associated with increased adiposity, insulin resistance and GDM. Serum B12 and hemoglobin levels of pregnant women with GDM were found to be significantly lower than controls. When the hematocrit levels of GDM and healthy pregnant women were evaluated, the hematocrit levels of the pregnant women with GDM were found to be lower than the healthy pregnant women.

In this study, the effects of foods and high glycemic index distribution on meals were investigated in order to provide glycemic level in pregnant women. Individuals with GDM had high blood sugar levels. It was determined that pregnant women with GDM were undernourished in terms of vitamins, minerals and macronutrients compared to healthy pregnant women.

CONCLUSION

As a result of the study, when the daily food intakes of the individuals were examined in detail, it was determined that the intake of vitamins, minerals and macronutrients was insufficient in pregnant women with gestational diabetes compared to healthy pregnant women. The study showed that insufficient food intake negatively affects blood sugar levels and biochemical parameters, especially vitamin D and B12 values. In order to meet the nutritional needs of the mother and the fetus developing in the mother's womb, it is thought that individual-specific diet should be planned and training should be given.

Considering all the studies in the literature on this subject, well-designed prospective randomized controlled studies with large participation are needed to evaluate the relationship between biochemical parameters and GDM.

Working limitations

This study had some limitations, such as the use of the food consumption frequency questionnaire (BTSA) to assess the possible relationship between food intake and biochemical parameters, based on the assumption that mothers answered all questions and scales correctly. The study relied on participants' ability to recall memories to complete BTSA questions. In line with these limitations, the results obtained from the study can be generalized to this research group.

Ethics Committee Approval: Ethics committee approval was obtained by Giresun University Clinical Research Evaluation Committee with the decision number 2018/05-06 dated

07/11/2018. Written informed consent was obtained from all subjects before participating in the study. The study protocol complies with international agreements.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept: T.C, Design: T.C, Literature search: T.C, Data Collection and Processing: H.A, M.A, Analysis or Interpretation: T.C, Writing: T.C, A.C,

Conflict of Interest: No conflict of interest was declared by the authors.

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