

The Effect Of Dietary Inflammatory Index (Dii) On 50 Grams Oral Glucose Challenge Test (Ogct) In Pregnant Woman.

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ABSTRACT

Objective: To determine the effect of the Dietary Inflammatory Index (DII) on the results of 50 grams oral glucose challenge test (OGCT).

Methods: 278 patients who referred to the outpatient clinics of the University of Health Sciences, Etlik Zubeyde Hanım Women's Health Care, Training and Research Hospital between the 24th and 28th gestational weeks and had taken 50 grams OGCT were included in this study. Demographic data, health records, physical activity levels, glycosylated hemoglobin (HbA1c) and oral glucose tolerance test (OGTT) results of participants and 3- day food consumption records were collected. Patients' 3-day food consumption data was separated to food parameters using the BEBIS(Nutrition Data System) program v8.1. The DII scores of patients were calculated using the Numbers version 6.2.1(Apple Inc.) application.

Results: There were no difference between the DII scores of subjects with positive and negative 50 grams OGCT and 100 grams OGTT results. There was a statistically significant ($p < 0,001$) decrease in DII scores with multivitamin use. Overall carbohydrate consumption was higher ($p=0.03$) and fat consumption was lower ($p=0.046$) in 235 patients whose 50grams OGCT results were <140 mg/dL, but no such correlation was found in patients diagnosed with GDM.

Conclusion: There is no relationship between DII scores and the detection of GDM in 50 grams OGCT and 100 grams OGTT.

Keywords: *Gestational Diabetes Mellitus, Dietary Inflammatory Index, Oral Glucose Tolerance Test, Inflammation.*

INTRODUCTION

Inflammation

It is associated with many diseases such as cancer, cardiovascular diseases, multiple sclerosis, obesity and insulin resistance. Chronic low level inflammation; C-Reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-Alpha) is defined by circulating minimal increased concentrations of pro-inflammatory markers. Diet; has an important role in the regulation of chronic inflammation [1].

Dietary Inflammatory Index (DII)

Was developed to characterize the position of the content of a person's diet between the two extremes of maximum anti-inflammatory and maximum pro-inflammatory. It was developed using global dietary studies to assign inflammatory impact scores to common dietary nutrients based on their ability to increase or decrease pro-inflammatory and anti-inflammatory biomarkers such as the cytokines IL₁ β , IL-6, IL-4, and IL-10 [2].

In prospective and case control studies

This index; was found to be associated with the level of circulating inflammatory proteins such as CRP, IL-6 and TNF alpha. High DII scores indicate diets low in anti-inflammatory content and high in pro- inflammatory content [3].

Gestational Diabetes Mellitus (GDM)

Is defined as diabetes or glucose intolerance first detected during pregnancy and its frequency varies between 2-5%. GDM; is associated with adverse pregnancy outcomes

such as miscarriage, fetal anomaly, intrauterine growth restriction, macrosomia, primary cesarean delivery, neonatal hypoglycemia, shoulder dystocia, hypertension, preeclampsia, and long-term maternal and child-related morbidities (diabetes and childhood obesity, cardiovascular diseases) [4-6]. Advanced maternal age, family history of diabetes, history of GDM in previous pregnancy, macrosomic fetus history, obesity and smoking are among the defined risk factors of GDM [7]. Exercise habits, smoking and diet are some of the modifiable risk factors of GDM [8].

The relationship between pro-inflammatory nutrition during pregnancy and gestational hypertension, gestational diabetes, preterm birth, SGA fetus, mode of delivery, and duration of lactation was investigated and it was found that pro-inflammatory nutrition in obese patients was inversely related with the incidence of GDM, inversely related with the lactation period, and directly related with the possibility of SGA fetus [6]. In the previous studies, total fat, saturated fat, red and processed meat, high glycemic index rich diets, soft drink consumption; has been found to be a risk factor in the development of GDM and that multiple unsaturated fats, carbohydrates and fiber-rich diets, fish, poultry and nut consumption were protective [5,7,8].

Considering all this

it is thought that the diet may have a role in preventing GDM. However, the studies in literature are intended to investigate the effects of only certain micro and macro nutrients or predetermined diets such as the Mediterranean diet, the Western diet, and there are differences between the results [9].

The aim of this study is to evaluate the hypothesis that anti-inflammatory diet and therefore low DII scores will be associated with normal glucose tolerance according to OGTT results.

MATERIALS AND METHOD

For this study, 23.10.2019 dated and 2019/62 numbered approval of the Ethics Committee of University of Health Sciences, Etilik Zubeyde Hanım Women's Health Care, Training and Research Hospital and 04.11.2019 dated and 180 numbered approval of University of Health Sciences is present.

24 to 28 week pregnant women who were referred to the outpatient clinics of University of Health Sciences, Etilik Zubeyde Hanım Women's Health Care, Training and Research Hospital and took 50 grams of OGCT were included in this study. Informed consent to participate in the study was obtained. Sample size was calculated as 278 patients, with 95% confidence interval and 5% margin of error.

Pregestational DM, type 1 DM, strong family history of DM

(≥ 2 first-degree relatives with DM), history of giving birth to a large for gestational age baby (≥ 4000 grams), own birth weight ≥ 4000 g, history of unexplained fetal loss, polyhydramnios, preeclampsia in previous pregnancies or history of gestational diabetes, symptomatic bacteriuria or glucosuria, frequent urinary tract infection or vulvovaginal candidiasis (≥ 3 /year), pre-pregnancy BMI < 18 and > 30 kg/m² were considered as exclusion criteria.

Data including sociodemographic characteristics, health information, and physical activity levels of the patients were collected. A 24-hour food consumption form for 3 days including 2 weekdays and 1 weekend day, in the last week, and a food consumption frequency form for 10 foods used in DII calculation were filled in, under the guidance of Turkey Nutrition Guide (TUBER) [10]. The limits set in the World Health Organization (WHO) guidelines were used to classify the level of physical activity [11].

In the calculation of DII there are 36 nutritional components (alcohol, vitamin B12, vitamin B6, beta carotene, caffeine, carbohydrates, cholesterol, energy, total fat, fiber, folic acid, Fe, Mg, polyunsaturated fatty acids, niacin, omega 3 and omega 6 fatty acids, protein, monounsaturated fatty acids, riboflavin, saturated fat, trans fat, Se, thiamine, vitamins A, C, D, E, Zn, total flavonoids) and 10 nutrients (coffee, tea, onion, garlic, ginger, saffron, turmeric, pepper, thyme, rosemary). By using 24-hour food consumption record data, only nutritional components can be obtained through the Nutrition Information System (BEBIS) program. For this reason, a food consumption frequency form was used for the 10 nutrients.

The laboratory results of the patients (blood glucose level measured at the first hour following ingestion of 50 grams of standardized oral glucose solution, complete urinalysis and HbA1c) were obtained using the database of the hospital where the samples were collected. The results of the patients whose 50 grams OGCT results were ≥ 140 mg/dL and who accepted the 100-grams OGTT diagnostic test were also obtained from the same database.

3-day 24-hour food consumption records of the patients; were separated into components using the BEBIS (Nutrition Information System) v8.1 program. DII scores of the patients; were calculated using the Numbers 6.2.1 (Apple Inc.) application with the method determined by Shivappa et al. [12]. Data analysis was done in SPSS 21.0 package program. Categorical variables were presented as numbers and percentages, numerical variables as mean, standard deviation, median, minimum and maximum values. Fisher Exact Test was used when sufficient number was not provided in pairwise comparisons of categorical variables, Pearson's Chi-square test was used when sufficient number was provided and for comparison of more than two groups. Normal distribution of continuous numerical data; visually histogram was evaluated statistically with the Shapiro Wilk

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test. Mann-Whitney U test was used for numerical comparisons between two independent groups that did not fit normal distribution. Statistically, a p value below 0.05 was considered significant.

RESULTS

The average age of 278 pregnant women who participated in the study was 28.01 ± 4.84 years and BMI 24.01 ± 3.59 kg/m². 75.2% (n=209) of the participants were multigravid, 7.2% (n=20) had a known comorbidity, the most common comorbidity was hypothyroidism (3.6%). 15.5% (n=43) of the pregnant women smoke. 58.3% (n=162) of the participants were inactive, 34.2% (n=95) active, 7.2% (n=20) overactive. While 16% (n=45) of the pregnant women did not use any supplements, 86% (n=239) used supplements in different combinations. The distribution of combinations of supplement used is summarized in Table 1. According to the results of 50 grams of OGCT; 84.5% (n=235) of the pregnant women had values <140 mg/dL, 15.5% (n=43) had ≥ 140 mg/dL. 30 of 43 pregnant women whose results were not normal accepted the application of 100 grams of OGTT and 9 women were diagnosed with GDM (3.2%). 13 pregnant women refused to have another OGTT because they could not tolerate the test.

Table 1. Distribution of supplement use of pregnant women participating in the study.

Supplement Usage Status	Number (n:278)	Percentage (%)
Not Using Any Supplements	39	14
Using Supplements	239	86
Only Iron	10	3.6
Only Multivitamins	19	6.8
Only Vitamin D	44	15.8
Iron + Multivitamins	35	12.6
Iron + Vitamin D	20	7.2
Multivitamins + Vitamin D	28	10.1
Iron + Multivitamins + Vitamin D	77	27.7

The mean DII score was found to be 3.15 ± 1.73 in supplement users and 4.93 ± 1.88 in non-users, and it was calculated that supplement use statistically significantly ($p < 0.001$) decreased DII scores (Table 2).

Table 2. Comparison of the DII scores of the supplement using and non-supplementation group.

	Mean	p
DII score (with supplements)	3.15 ± 1.73	<0.001
DII score (without supplements)	4.93 ± 1.88	

To determine which supplement content is causing this decrease; patients were compared as 3 groups (Table 3). The groups were defined as those who did not use any supplements, did not use multivitamins (using vitamin D and / or iron), and those using multivitamins (using only multivitamin, or vitamin D and / or iron in addition to multivitamin). The mean DII score of those who do not use supplements, do not use multivitamins, and use multivitamins were calculated as -4.37, -4.41 and -4.55, respectively. A significant difference was found between the DII scores of those who use multivitamins and those who do not use any supplements and those who do not use multivitamins ($p < 0.005$). Therefore, it has been determined that the supplement component responsible for the decrease in DII score is multivitamin.

Of the pregnant women who participated in the study; The average total energy intake is 1700.86 ± 383.09 kcal/day, with an average of 49.24% carbohydrate, 34.5% fat and 16.26% protein. No significant correlation was found between the amount of carbohydrate and fat consumption of pregnant women and DII scores.

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Table 3. Comparison of the mean DII scores of those who do not use supplements, those who do not use multivitamins, and those who use multivitamins.

Group 1	Group 2	Difference between mean values (Group 1 - Group 2)	Standard Deviation	p
Not using any supplements	Using multivitamins	0.19	0.02	p<0.005
	Not using multivitamins	0.04	0.02	0.085
Using multivitamins	Not using any supplements	-0.19	0.02	p<0.005
	Not using multivitamins	-0.15	0.02	p<0.005
Not using multivitamins	Not using any supplements	-0.04	0.02	0.085
	Using multivitamins	0.15	0.02	p<0.005

In Table 4; the distribution of DII scores, total energy intake, age, BMI and pregnancy characteristics of the women participating in the study according to the 50 grams OGCT result are given. In the total energy intake of 235 people with a 50 grams OGCT result of <140 mg/dL, the percentage of carbohydrates was statistically significantly higher (p=0.03) and the percentage of fat was significantly lower (p=0.046). There was no significant difference between DII scores (p>0.05).

When the 50 grams OGCT results of the pregnant women who participated in the study were evaluated as tertiles, there was no statistically significant difference between the supplemented DII score groups and the 50 grams OGCT results (p>0.05).

The total energy intake of the patients who were found to have GDM (n=9) and non- GDM (n=256) according to the result of 100 grams of OGTT was 1565.70±477.75 - 1715.32±382.96 kcal/day, and the percentages of diet carbohydrate, fat and protein intake were; 46-49.23%, 36.89%-34.5% and 17.11-16.26% respectively. There is no statistically significant difference between the values of the group with and without GDM. The mean DII score of patients with GDM is 3.93±1.74 and the mean DII score of patients without GDM is 3.11±1.75, and there is no statistically significant difference.

Table 4. The comparison of age, BMI, gestational week, total energy intake, percentage of carbohydrate, fat, protein consumption of diet and DII scores of the pregnant women who participated in the study, and the comparison of these data according to the 50 grams OGCT results.

	50 grams OGCT result				p
	<140 mg/dL (n=235)		≥140 mg/dL (n=43)		
	Mean±SD	Median	Mean±SD	Median	
Age	27.77±4.94	28.00	29.30±4.10	30	0.053
Gestational week	25.35±1.26	25	25.21±1.42	25	0.33
BMI	23.86±3.63	23.00	24.84±3.25	24	0.104
Total energy intake	1711.20±387.44	1664.10	1644.35±357.39	1559	0.27
Carbohydrate percentage	49.57±7.61	50	47.42±6.96	48	0.03
Fat	34.19±6.97	34	36.19±6.72	37	0.046
Protein percentage	16.24±2.64	16	16.40±2.56	16	0.71
DII score (with	3.12±1.76	2.83	3.29±1.51	3.16	0.40

DISCUSSION

GDM is a common pregnancy complication with long and short term consequences for both mother and baby. For this reason, in women who are pregnant or planning to become pregnant; prevention of GDM is important [13]. Here; modifiable risk factors of GDM come into play, such as diet, physical activity, smoking, and pre-pregnancy BMI. In the study of Zhang et al.; it was found that the attributable risk of doing less than 150 minutes of mild- moderate exercise per week, unhealthy diet, smoking, and pre-pregnancy BMI for the development of GDM is 10%, 12%, 3%, and 28%, respectively [14]. Therefore, nutritional content is thought to have a role in predicting the development of GDM. In studies conducted to date, the effects of certain macro and micro nutrients or diets with a predetermined content (eg. Mediterranean diet) have been investigated [8]. There are not enough studies using DII to evaluate the relationship between individualized specific food consumption of pregnant women and GDM. In this study, the hypothesis that low DII scores would be associated with normal glucose tolerance according to OGCT results was evaluated.

In a case-control study conducted by Shivappa et al. in 2018; A total of 388 patients, 122 GDM and 266 healthy, were examined [15]. When the DII score is analyzed both as numerical data and as categorical groups (tertiles); higher DII scores (a more pro- inflammatory diet) were found to be associated with an increased incidence of GDM (OR=1.20; 95% CI=0.94-1.54 and (OR_{tertil3-1}=2.10; 95% CI=1.02-4.34). In the study of 1057 pregnant women, when DII scores were analyzed categorically, no significant difference was found between the groups in terms of the number of patients with GDM [16]. In an observational study conducted by Sen et al. , it was found that a more pro-inflammatory diet was not associated with isolated hyperglycemia or impaired glucose tolerance, but was associated with a reduced incidence of GDM (OR=0.78; 95% CI=0.65-0.95) [5]. This can be explained by the difference in the inclusion criteria of the studies. In this study, as in the study of McCullough et al., when DII scores were analyzed numerically, no statistically significant difference was found between the DII scores and 50 grams OGCT results and the detection of GDM in 100 grams OGTT. Likewise, in the categorical analysis, no significant difference was found between the 50 grams OGCT and DII scores (p= 0.84), while statistical analysis could not be performed for 100 grams OGTT results, since the number of patients per group was insufficient.

Foods that are not included as components in the BEBIS program and whose consumption frequency is examined are; coffee, tea, onion, garlic, pepper, thyme, saffron, rosemary, turmeric, ginger. More than 95% of the participants; did not consume ginger, saffron, turmeric and rosemary, therefore

they were not included in the statistical analysis. For the consumption of other nutrients; there was no statistically significant difference in patients with 50 grams OGCT results $\geq 140\text{mg/dL}$ and those with GDM detected in 100 grams OGTT compared to pregnant women whose results were within normal limits.

In our study, 86% of the patients used at least one of the iron, multivitamin and vitamin D supplements (Table 1). In the analysis made; It was determined that supplement use statistically significantly reduced DII scores (provided a more anti-inflammatory effect) ($p < 0.001$) (Table 2). It was determined that this decrease was especially associated with the use of multivitamins ($p < 0.005$) (Table 3).

In our study; there was no significant difference in terms of BMI and gestational weeks in patients with a high 50 grams OGCT result and in those with GDM detected in 100 grams OGTT compared to pregnant women whose results were within normal limits. However, in different studies, patients with GDM were found to have a higher BMI [15,17], a higher mean HbA1c level [18], a smaller gestational week [15], and less physical activity [8,15] compared to those without GDM [8,15,17,18]. This difference between BMI index results; may have been due to the inclusion of only pregnant women with a BMI of $18 \leq \text{BMI} \leq 30$ in our study, although there was no limitation in the range of BMI in other studies.

In a prospective cohort study conducted by Radesky et al. in 2008; it was observed that the average daily energy intake of the participants was 2060 ± 674 kcal, and their diets consisted of 28.2% fat, 55.5% carbohydrates and 16.3% protein [8]. GDM was detected in 5% of these participants. In our study, the average daily energy intake of the participants was 1700 ± 383 kcal, with an average of 34.5% fat, 49.24% carbohydrate and 16.26% protein consumption. GDM was detected in 3.2% of the participants. While protein consumption percentages were similar in both studies, the difference in fat and carbohydrate consumption percentages may be the reason for the different GDM incidence.

In literature, there are different results regarding the relationship between the percentage of carbohydrate and fat consumption and GDM and impaired glucose tolerance (IGT). In a study by Saldana et al. that included 1698 participants; it was observed that, participants diagnosed with GDM, met their daily energy needs less from carbohydrates and more from fat compared to healthy ones [19]. In a similar study; It has been reported that carbohydrate intake is associated with low DII scores (anti-inflammatory diet), therefore, carbohydrate consumption is found to be low in participants diagnosed with GDM [6]. In the study of Wang et al. with 171 participants, 56 of whom were GDM; decreased fat consumption was found in the GDM group [20]. On the other hand, in the study of Feng et al.; increased carbohydrate intake was found in the group with GDM compared to the

control group [21]. In the study of Radesky et al.; no significant difference was found between carbohydrate, protein, fat consumption percentages and detection of GDM [8]. In our study; The percentage of carbohydrates in the total energy intake of 235 people with a 50 grams OGCT result of <140 was statistically significantly higher ($p=0.03$), while the percentage of fat was significantly lower ($p=0.046$). There is no significant difference in carbohydrate and fat intakes of those with and without GDM as a result of 100 grams of OGTT. The reason for the discrepancy between the results of the studies in the literature may be due to differences in inclusion and exclusion criteria, differences in sample size between studies (number of patients and control group) and differences in the glycemic index of the carbohydrates ingested. As is well known, the glycemic index is influenced by a number of factors such as the variety, ripeness or processing, cooking and storage method of the food. The amount of fat, protein, organic acids, fiber and antinutrients in the meal affect the glycemic index of the food [22].

Features that increase the power of our work are; (i) the inclusion of pregnant women followed up in a single center, (ii) the fact that the food consumption records of the patients included in the study were filled by a single physician under the guidance of Turkey Nutrition Guide (TUBER) [17], and most importantly (iii) to our knowledge, it is the only study examining the relationship between DII and GDM in the Turkish society. There are also limitations related to our study. Gestational diabetes status could not be evaluated in 13 participants whose 50 grams OGCT result was ≥ 140 but who voluntarily did not take 100 grams OGTT. In the distribution of patients with GDM detected in 100 grams OGTT, categorical analysis could not be performed due to the insufficiency of the number of patients per group. In the BEBIS program, 35 of the 45 parameters used in the DII calculation were included. Due to the lack of parameters with nutrients in BEBIS, although their nutrient compositions could be examined, these 10 nutrients could not be included in the DII score calculation as a whole. During the recording phase of the foods consumed by the patients on 2 weekdays and 1 weekend day in the last 1 week, there were problems in remembering, which may have caused deficiencies in the recordings.

In our study; When DII scores were analyzed numerically and categorically; There was no statistically significant difference between the DII scores and the 50 grams OGCT results and the detection of GDM in 100 grams OGTT. It was determined that the use of multivitamins significantly decreased DII scores ($p < 0.001$). The percentage of carbohydrates in the total energy intake of 235 people with a 50 grams OGCT result of <140 was statistically significantly higher ($p=0.03$), while the percentage of fat was significantly lower ($p=0.046$). However, there is no significant difference between those with and without GDM as a result of 100 grams of OGTT in terms of carbohydrate

and fat intake. No correlation was found between DII scores and the detection of GDM in 50 grams OGCT and 100 grams OGTT.

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Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Aykan Yücel and Sezin Cansın Perçin Kafaoğlu. The first draft of the manuscript was written by Sezin Cansın Perçin Kafaoğlu and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Conflict of interest

The authors have no relevant financial or non-financial interests to disclose.

Ethics Approval

For this study, 23.10.2019 dated and 2019/62 numbered approval of the Ethics Committee of University of Health Sciences, Etlik Zubeyde Hanım Women's Health Care, Training and Research Hospital and 04.11.2019 dated and 180 numbered approval of University of Health Sciences is present.

Consent to participate

The patients provided written informed consent.

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