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Dietary Intake and Oral Glucose Tolerance Test Results in Women with Gestational Diabetes

Lucas Almeida das Chagas [1], Maria Regina Torloni [1,2], Luiz Gonzaga Ribeiro Silva-Neto [3], Patrícia Medici Dualib [4], Rosângela Maria Lopes de Sousa [5] Jalila Andréa Sampaio Bittencourt [6], Edward Araujo Júnior [1], Roberta Granese [7] and Rosiane Mattar [1]

1 Department of Obstetrics, Paulista School of Medicine, Federal University of São Paulo (EPM-UNIFESP), São Paulo 04023-062 SP, Brazil; ORCID: 0000-0002-4245-1227; ORCID: 0000-0003-4944-0720; ORCID: 0000-0002-6145-2532; ORCID: 0000-0003-1405-5371
2 Evidence Based Health Care, Department of Medicine, Paulista School of Medicine, Federal University of São Paulo (EPM-UNIFESP), São Paulo 04023-900 SP, Brazil
3 Department of Nutrition, Paulista School of Medicine, Federal University of São Paulo (EPM-UNIFESP), São Paulo 04023-062 SP, Brazil; ORCID: 0000-0002-1003-9836
4 Discipline of Endocrinology, Department of Medicine, Paulista School of Medicine, Federal University of São Paulo (EPM-UNIFESP), São Paulo 04038-001 SP, Brazil; ORCID: 0000-0003-0358-1034
5 Department of Nutrition, CEUMA University, São Luiz 65075-120 MA, Brazil; ORCID: 0000-0003-4728-9318
6 Department of Electrical Engineering, Laboratory of Biological Information Processing, Federal University of Maranhão (UFMA), São Luiz 65080-805 MA, Brazil; ORCID: 0000-0001-6294-8532
7 Department of Biomedical and Dental Sciences and Morphofunctional Imaging, "G. Martino" University Hospital, 98100 Messina, Italy; ORCID: 0000-0003-0318-9390
* Correspondence: Roberta Granese, MD, PhD, Department of Biomedical and Dental Sciences and Morphofunctional Imaging, "G. Martino" University Hospital, 98100 Messina, Italy; robertagr74@gmail.com

Abstract: Background: Diet is a risk factor for gestational diabetes mellitus (GDM). There are few studies on women´s diet and glucose tolerance test (GTT) results. **Objective:** To evaluate the relationship between previous diet and the number of abnormal values on the diagnostic GTT in women with GDM. We hypothesized there would be an inverse relation between antioxidant micronutrient consumption and the number of abnormal GTT values. **Methods:** This cross-sectional study included 60 women diagnosed with GDM (2-hours, 75g-GTT). Shortly after diagnosis, participants answered a validated food frequency questionnaire to assess food consumption in the last 6 months. Mann-Whitney´s test was used to compare the dietary intake of participants with one (group 1) versus two-three (group 2) abnormal GTT values. **Results:** Participant characteristics were similar. Median intake of total calories, carbohydrates, lipids and proteins did not differ significantly between groups. Participants in group 1 had significantly higher intakes of fiber (11.9 vs. 11.0 g/day p=0.049), vitamin D (40.6 vs. 40.4 mcg/day p=0.049) and vitamin C (180.0 vs. 151.0 mg/day p=0.008) than those in group 2. **Conclusion:** Results suggest a possible association between consumption of fiber and some antioxidant micronutrients and GDM severity at the time of diagnosis.

Keywords: Gestational diabetes mellitus; Diet; Glucose tolerance test

1. Introduction

Gestational Diabetes Mellitus (GDM) is defined as glucose intolerance of variable severity, with onset or first recognition during pregnancy, that does not meet the diagnostic criteria for pre-existing diabetes, and may or may not persist after delivery [1]. GDM is one of the most common complications of pregnancy with a worldwide prevalence of 8.4% to 30.9% [2,3]. This variation is due to differences in population characteristics (such as age and obesity) and diagnostic criteria used [2,3]. In Brazil, the prevalence of GDM is 18%, according to the International Association of Diabetes and

Pregnancy Study Groups diagnostic criterion [4]. Rates of GDM are increasing, in parallel with increasing rates of obesity, advanced maternal age, and unhealthy lifestyle habits in most populations [5–7].

GDM increases the risks of obstetric and perinatal complications (e.g. gestational hypertension, neonatal hypoglycemia, macrosomia) [8], later development of type 2 diabetes in the mother, and abnormal glucose metabolism in exposed offspring[9]. However, timely and appropriate GDM treatment can decrease the risks of these complications[10,11]. Due to its high prevalence and negative impact on maternal and child health, GDM is an important public health issue.

Currently, the oral glucose tolerance test (GTT) most commonly used for the diagnosis of GDM consists in measuring serum glucose levels at three time points (fasting, 1h, and 2h after a 75g glucose load). Patients with ≥1 abnormal glucose value (≥ pre-defined thresholds) receive a diagnosis of GDM [1]. The number of GTT abnormal glucose values is associated with maternal and perinatal adverse outcomes and the need of insulin for glycemic control [12–15]. Investigators suggest that the glucose metabolism and insulin sensitivity of women with > 1 abnormal glucose value on the GTT are more compromised than those of women with only 1 abnormal value, characterizing a more severe subtype of GDM [12–15].

Evidence suggests that changing eating habits before and at the beginning of pregnancy can reduce the risk of developing GDM [16–21]. Some researchers report that the nutritional composition of the diet, especially its antioxidant and fiber content, consumed before diagnosis of GDM is related to diabetes severity and adverse maternal and perinatal outcomes [22–24]. Adopting a diet rich in dietary fiber and antioxidants, with a greater variety of fruits and vegetables, could minimize the effect of oxidative stress, helping to prevent and control GDM and its adverse effects [25,26]. We did not identify Brazilian studies that evaluated the relationship between diet and GTT results in women diagnosed with GDM.

The objective of this study was to evaluate the relationship between the type of diet consumed before GDM diagnosis and the number of abnormal glucose values on the GTT, an indicator of disease severity. Our hypothesis was that women with a larger number of abnormal glucose values on the GTT would have worse diet quality (poorer in antioxidants and fibers) than those with fewer abnormal values.

2. Methods

2.1. Study Design and Period

This is a secondary analysis of a case-control study carried out at the Federal University of São Paulo (UNIFESP), a public institution located in São Paulo, Brazil, in 2018-2019 to evaluate food consumption of women with GDM with and without hepatic steatosis [27]. The study was approved by the institutional review board (CAEE 86210318.0.0000.5505). All participants signed an informed consent form at the time of recruitment.

2.2. Participants

All pregnant women managed at UNIFESP's antenatal care clinics routinely perform a fasting blood glucose test in the first trimester of pregnancy. All those with normal fasting blood glucose (< 92 mg/dL) undergo a 75g 2-hour GTT at 24-32 weeks of gestation. Women with any of the following receive a diagnosis of GDM: fasting 92-125 mg/dL, 1-hour ≥180 mg/dL, 2-hour 153-199 mg/dL [1]. Women who are diagnosed with GDM are referred to UNIFESP's Diabetes Center, a free public outpatient clinic where they continue prenatal care with a specialized multiprofessional team which includes obstetrician-gynecologists, nurses, endocrinologists, and nutritionists. At their first visit to the Diabetes Center, before they had any contact with other healthcare professionals, all women with a recent diagnosis of GDM were approached by the first author, who invited them to participate in the study. Women 18-45 years of age, with a live singleton pregnancy between 26-34 weeks, having received a diagnosis of GDM in the last 2 weeks and not yet undergoing any GDM treatment (including nutritional counselling), were eligible to participate. Exclusion criteria were: illiteracy, having a mental, hearing or visual disability that made data collection impossible, foreigners who were not fluent in Portuguese, women with bariatric surgery, infectious diseases that can affect eating habits (such as tuberculosis), women who were on any type of diet, with a history or current alcohol consumption > 20 g/day, type 1 or 2 diabetes, ascites, history or current diagnosis of liver diseases (including hepatitis, cirrhosis, alcoholic fatty liver disease, or malignant tumors), use of medications potentially associated with hepatic steatosis (including tamoxifen , estrogen, or diltiazem) in the last six months, and women who could not remember their weight before pregnancy. We also excluded from the study women who did not complete the food frequency questionnaire for any reason, including due to inability to recall their food consumption or portion or frequency in the last six months.

2.3. Data Collection

Immediately after recruitment, all eligible women underwent an abdominal ultrasound (US) scan at the Diabetes Center. The same physician used a portable equipment (Sanoace Pico, Medison, Seoul, Korea) to perform all exams. He classified each woman as having a normal liver, or mild, moderate or severe diffuse fatty infiltration [27,28]. The principal investigator then weighed and measured each participant using an electronic digital scale (MEA 07700, Plenna, Brazil) and a stadiometer. The investigator then interviewed women to collect sociodemographic data, family and obstetric history, and information on pre-pregnancy weight. Women were also asked about the duration and frequency of regular physical activity in the six months before getting pregnant; those who reported at least 30 minutes of regular physical activity/week were considered physically active[29]. Participants then completed a written quantitative food frequency questionnaire (FFQ) validated for pregnant women in Brazil [30].

Based on women´s pre-pregnancy weight and measured height, we classified them into one of four pre-pregnancy body mass index (BMI) category (<18.5, 18.5-24.9, 25.0-29.9, or ≥30.0 kg/m[2]) [31]. According to weight gain at the time of recruitment (weight measured by the researcher minus self-reported pre-pregnancy weight), we also classified participants into one of three gestational weight gain categories (insufficient, adequate, or excessive) according to the recommendations of the Institute of Medicine [31].

The FFQ assessed food consumption in the last six months. To facilitate quantification of portions and to reduce recall bias, we showed participants photos of standard serving tools (cups, plates, spoons), as well as photos of different food portion sizes. Using the dietary guidelines proposed for the Brazilian population, we converted portion sizes to grams or milliliters [32]. Portion sizes were categorized as small, medium, large, and extra-large using the 25th, 50th, 75th, and 100th percentiles, respectively. We then calculated the distribution of the reported food consumption of the past six months by assessing the daily, weekly, and monthly food frequency[30]. Participant´s macro and micronutrient intake were calculated using the Dietpro Clinic nutrition software (AS Systems, 2019, version 6.1). To assess the adequacy of participants´ food consumption, we followed the dietary reference intakes (DRI 2002) recommendations for pregnant women [33]. If the frequency was between the estimated average need (average reference value) and the upper tolerable limit of intake, food intake was categorized as adequate.

2.4. Sample Size

We used the first 60 eligible pregnant women with GDM (convenience sample). The 60 participants (30 with hepatic steatosis and 30 with a normal liver US) were matched for self-reported skin color (brown versus other) and pre-pregnancy BMI category (< 18.5 versus 18.5-24.9 versus $\geq$ 25 Kg/m^2), and for age (± 2 years)[27].

2.5. Statistical Analysis

For this study, we divided the original 60 participants into two groups according to the number of abnormal glucose values on the GTT. The first group (G1) consisted of all women with only 1 abnormal value (milder GDM), while the second group (G2) included all those with 2-3 abnormal values (more severe GDM). We used the Student's t test or Fisher's exact test to compare participant characteristics in the two groups. We present the median (1st - 3rd quartile) macronutrient and micronutrient intake of participants in G1 and G2. Differences in dietary intakes between the two groups were assessed using Mann-Whitney´s test. P values <0.05 were considered statistically significant. We used the software SPSS version 19.0 (IBM Corp., Armonk, NY, USA) for all analyses.

3. Results

Most (51.7%, n=31) of the participants had only 1 abnormal value on the GTT. Participant characteristics did not differ significantly between the two groups (Table 1).

Table 2 presents the participants' dietary pattern over the last six months. Participants in both groups had an average dietary intake of fiber, vitamin A, and vitamin E below the recommended level, and a higher than recommended protein intake. There were no significant differences between groups in caloric, macronutrient, and vitamin A, E, selenium, and zinc intake. The average daily consumption of fiber (11.9 vs. 11.0 g, p= 0.049), vitamin D (40.6 vs. 40.4 mcg, p=0.049) and vitamin C (180.0 vs. 151.0 mg, p=0.008) was significantly higher in the group with milder GDM (1 abnormal GTT value) than in the group with more severe GDM (2-3 abnormal GTT values).

Table 1. Characteristics of 60 pregnant women with gestational diabetes mellitus according to glucose tolerance test results.

	Number of abnormal glucose values on GTT*		
	1 (Group 1) (n= 31)	**2-3 (Group 2) (n=29)**	**p#**
Age, years, mean (SD)	33.0 (5.7)	34.5 (6.1)	0.337
Gestational age, weeks, mean (SD)	28.0 (2.9)	27.2 (2.6)	0.268
Skin color			0.146
Brown	11 (35.5)	10 (34.5)	
White	2 (6.5)	7 (24.1)	
Black	18 (58.1)	12 (41.4)	
Marital status			0.782
Married	10 (32.3)	8 (27.6)	
Single	21 (67.7)	21 (72.4)	
Education, years			0.140
0-7	2 (6.5)	6 (20.7)	
≥ 8	29 (93.5)	23 (79.3)	
Monthly family income			0.208
< 256 USD	17 (54.8)	11 (37.9)	
≥ 256 USD	14 (45.2)	18 (62.1)	
Religion			0.177
Catholic	18 (58.1)	22 (75.9)	
Other	13 (41.9)	7 (24.1)	
Family history of diabetes			0.800
Yes	17 (54.8)	17 (58.6)	
No	14 (45.2)	12 (41.4)	

Chronic hypertension			0.229
No	31 (100.0)	27 (93.1)	
Yes	0	2 (6.9)	
Physically active			0.783
No	22 (71.0)	19 (65.5)	
Yes	9 (29.0)	10 (34.5)	
Pre-pregnancy BMI, kg/m²			0.398
< 18.5	0	1 (3.4)	
18.5-24.9	3 (9.7)	2 (6.9)	
25.0-29.9	10 (32.3)	14 (48.3)	
≥ 30.0	18 (58.1)	12 (41.4)	
Gestational weight gain			1.000
Insufficient	14 (45.2)	13 (44.8)	
Adequate	5 (16.1)	5 (17.2)	
Excessive	12 (38.7)	11 (37.9)	
Hepatic steatosis			0.930
Absent	16 (51.6)	14 (48.3)	
Mild	12 (38.7)	13 (44.8)	
Moderate	3 (9.7)	2 (6.9)	
Abnormal glucose value in GTT*€			0.945
Fasting	19 (61.3)	21 (72.4)	
1h	5 (16.1)	19 (65.5)	
2h	7 (22.6)	27 (93.1)	

BMI: Body mass index, GTT: Glucose tolerance test, SD: Standard deviation, USD: US dollars. All values represent numbers (%) unless otherwise noted. *75g GTT cutoffs for GDM diagnosis: fasting 92-125, 1h ≥ 180, 2h 153-199 mg/dL. # Student's T test or Fisher's exact test. € The total number in G2 is > total group number (N=29) because each participant had 2 or more abnormal glucose values.

Table 2. Food consumption of 60 pregnant women with gestational diabetes according to the number of abnormal glucose values on GTT.

Variable	Nutritional recommendation*	Number of abnormal glucose values on GTT**		P#
		1 (Group 1) (n= 31)	2-3 (Group 2) (n= 29)	
Calories	1800-2500	2000.5 (1779.0-2230.0)	1905.0 (1696.0-2111.0)	0.105
Carbohydrate	45-65%	57.9 (50.0-63.5)	56.4 (53.5-63.9)	0.676
Protein	10-15%	15.8 (14.3-18.5)	16.1 (13.5-16.9)	0.245
Lipid	25-30%	27.5 (22.4-32.1)	27.1 (23.1-30.6)	0.471

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Dietary fiber	28 g	11.9 (10.8-16.2)	11.0 (9.1-14.2)	0.049
Vitamin A	550-3000 μg	144.0 (68.7-298.0)	146.0 (77.1-199.0)	0.270
Vitamin D	50 μg	40.6 (40.3-80.2)	40.4 (20.8-40.7)	0.049
Vitamin E	12-1000 mg	6.0 (4.5-8.3)	6.0 (4.6-8.1)	0.427
Vitamin C	70-2000 mg	180.0 (157.0-275.0)	151.0 (117.0-204)	0.008
Selenium	49-400 μg	43.5 (32.0-47.1)	39.0 (32.2-49.2)	0.350
Zinc	9.5-40 mg	5.6 (4.2-6.9)	5.2 (4.1-6.0)	0.185

GTT: Glucose tolerance test. All values represent median (1st-3rd quartile). * Estimated average needs to assess the adequacy of intake of pregnant women based on the recommended dietary intake and maximum tolerable intake. ** 75g GTT cutoffs for GDM diagnosis: fasting 92-125, 1h ≥ 180, 2h 153-199 mg/dL. # Mann-Whitney test.

4. Discussion

We found significant differences in the food intake of women with 1 abnormal GTT value (milder GDM) compared to those with 2-3 abnormal values (more severe GDM). There were no significant differences in the consumption of macronutrients between the two groups. However, the consumption of fibers, as well as vitamins C and D, were significantly higher in women with milder GDM than in those with more severe GDM.

GDM is a disease that involves genetic factors, lifestyle and eating habits [34–36]. Several studies confirm a relationship between diet and the risk of developing GDM. Women with diets rich in ultra-processed foods, low in fibers, and rich in simple carbohydrates associated with the consumption of sugary drinks have a higher risk of developing GDM [37–41]. Our study advances knowledge in this field by showing an inverse relationship between consumption of fibers, and of vitamins C and D, and GDM severity based on the number of abnormal glucose values on the GTT.

Our finding of lower fiber intake in the group with more severe GDM is consistent with the literature. Several studies point to the role of dietary fiber in the development and glycemic control of women with GDM [42,43]. Dietary fiber plays an important role in controlling postprandial blood glucose because it delays gastric emptying, blood glucose levels, insulin resistance, and the metabolic profile of healthy and diabetic individuals [44,45].

There is evidence that a diet rich in antioxidants could reduce the incidence of GDM [46]. Normal pregnancy is characterized by increased levels of free radicals and lipid peroxides [47]. However, hyperglycemia during pregnancy is associated with increased oxidative stress, which impairs insulin-dependent glucose uptake, and increases apoptosis and placental dysfunction, factors that contribute to a greater pro-inflammatory state which, in turn, may worsen hyperglycemia and the severity of GDM [48,49].

Our findings of lower vitamin C and D values in women with more severe GDM align with those reported in the literature showing that adequate vitamin D and C intake can have a protective role in the development GDM and improve glycemic control [50–54].

This is the first study that investigated the association between usual food consumption and the number of abnormal glucose values on the GTT. This approach is innovative and aligns with the recent concept that GDM is a disease with different phenotypes [55]. Several investigators suggest the existence of different metabolic subtypes of GDM possibly associated with better or worse maternal/perinatal outcomes, that could be identified based on GTT results [13–15], [56–60]. The study has several limitations. Due to its small sample size, the study may have been underpowered to detect other associations between dietary patterns and GDM severity. Moreover, the study design and the absence of a control group (pregnant women with normal GTT) prevent inferring a causal relation. Another study limitation was that, since we used only one FFQ for the six months that preceded the diagnosis of GDM, we cannot exclude recall bias.

New studies are needed to confirm our findings. These new studies should involve a larger and more diverse number of women with GDM, and a control group of pregnant women with normal GTT.

5. Conclusion

Our results suggest a possible association between consumption of dietary fiber and some antioxidant nutrients (vitamin D and C) and the number of abnormal glucose values on the GTT at the time of GDM diagnosis. These findings contribute to the evolving field of research on the role of diet in the development of different subtypes of GDM.

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Institutional Review Board Statement: Our investigations were carried out following the rules of the Declaration of Helsinki of 1975, revised in 2013. The study was approved by the Ethics Committee of the Federal University of São Paulo (CAEE 86210318.0.0000.5505).

Informed Consent Statement: Informed consent was obtained from all participants.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Author Contributions: Conceptualization, MRT and RM; methodology, PMD; validation, LGRSN, RMLS; formal analysis, JASB; investigation, LAC; resources, RG; data curation, LAC; writing—original draft preparation, EAJ; writing—review and editing, MRT; visualization, LAC, MRT, LSRSN, RMLS, PMD, JASB, RG, EAJ, and RM; supervision, MRT; project administration, RM. All authors have read and agreed to the published version of the manuscript.

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