Effect of macronutrient intake on the development of glucose intolerance during pregnancy

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ABSTRACT

Background: Dietary intake influences glucose tolerance status, yet the relation between macronutrient intake and the development of glucose intolerance during pregnancy has not been adequately examined.

Objective: We examined the relation between macronutrient intake early in pregnancy and the development of glucose intolerance.

Design: Data are from 1698 women in the Pregnancy, Infection, and Nutrition Study. Dietary intake during the second trimester was assessed with a food-frequency questionnaire. Women were classified into 1 of 3 glucose categories: gestational diabetes mellitus (GDM), impaired glucose tolerance (IGT), and normal glucose tolerance. Multivariate logistic regression was used to calculate the relative risk of IGT and GDM, with adjustment for potential confounders. A series of models were specified to test alternate hypotheses about the relation of diet to risk of IGT or GDM.

Results: The overall prevalences of IGT and GDM in the cohort were 2.6% and 5.2%, respectively. The addition model showed that adding 100 kcal from carbohydrates to the diet was associated with a 12% decrease in risk of IGT and a 9% decrease in risk of GDM. The substitution model showed that substituting fat for carbohydrates (per each 1% of total calories) resulted in a significant increase in risk of both IGT and GDM [relative risk = 1.1 (95% CI: 1.02, 1.12) and 1.1 (1.02, 1.10), respectively]. Predicted probabilities of IGT and GDM were reduced by one-half with a 10% decrease in dietary fat and a 10% increase in carbohydrate.

Conclusions: This study found an association between increased fat intake and the development of glucose abnormalities in pregnancy.

INTRODUCTION

The fed state of normal pregnancy is characterized by prolonged hyperglycemia and hyperinsulinemia (1). Research has shown that insulin sensitivity in late pregnancy falls by 45–70% to values similar to those of nonpregnant individuals with type 2 diabetes (2, 3). As pregnancy progresses, there is a decrease in insulin sensitivity in the peripheral tissues (an increased insulin resistance), which reduces glucose uptake into maternal tissues and results in the hyperglycemia associated with normal pregnancy. Glucose intolerance during pregnancy is a result of the inability to produce a sufficient amount of insulin as pregnancy-related insulin sensitivity decreases.

Gestational diabetes mellitus (GDM) and impaired glucose tolerance (IGT) are serious and common concerns in pregnancy (4–9). The prevalence of GDM in the US population is estimated at 1–4% (10). In some populations, IGT has been shown to have a rate 2 times that of GDM (11). GDM has recognized consequences for poor pregnancy outcomes and for the long-term health of mother and child (4, 5, 12). Some studies have suggested that women with IGT during pregnancy may be at similar risk for poor pregnancy outcomes (6–9).

Substantial evidence exists that diet is linked to the development of glucose intolerance. Diets high in fat and low in complex carbohydrates are recognized as risk factors for the development of type 2 diabetes. Two recent clinical trials presented strong evidence that lifestyle intervention that stresses low-fat diets as part of overall lifestyle change can reduce the risk of developing type 2 diabetes (13, 14). Observational studies have linked high fat intake to the development of type 2 diabetes (15, 16) and to the progression from IGT to type 2 diabetes (17). Diets high in simple carbohydrates or low in complex carbohydrates have also been linked to the development of glucose intolerance (18–20).

Furthermore, diets high in fats have been shown to increase the risk for recurrence of GDM in future pregnancies (21).

Only one study that we know of has examined the association between diet before the diagnosis of GDM and glucose tolerance status (22). In contrast with the results of studies of type 2 diabetes, in the study by Wang et al., subjects with IGT and GDM consumed a lower percentage of their total calories from fat than did subjects with normal glucose tolerance. Further investigation of diet early in pregnancy is needed to clarify the contradiction between studies that show a detrimental effect of fat on the risk of type 2 and recurrence of GDM and this most recent study.

The results of previous research have suggested that high-fat diets may adversely influence glucose tolerance though a direct

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effect of nonesterified fatty acids on glucose metabolism, through an effect of increased energy intake on weight gain and insulin sensitivity, or simply by virtue of the fact that high-fat diets tend to be composed of lower amounts of carbohydrates (23). To distinguish among these effects, studies must attempt to separate the effect of adding individual macronutrients to the diet from the effect of changing the overall macronutrient composition of isocaloric diets. In the present study, we sought to evaluate the influence of dietary fat and carbohydrate consumption during pregnancy on the development of IGT and GDM in both isocaloric and nonisocaloric diets. If specific patterns of caloric or nutrient intake influence the development of glucose intolerance during pregnancy, dietary guidelines that incorporate these patterns would provide a low-cost and effective way to reduce risk.

SUBJECTS AND METHODS

Sample and data collection

Data from the Pregnancy, Infection, and Nutrition (PIN) Study, a prospective cohort study designed to identify determinants of preterm delivery in central North Carolina, were used for this analysis. Women recruited between 24 and 29 wk of pregnancy were eligible to participate if they were having a singleton pregnancy, were >16 y of age, spoke English, had access to a phone, and planned to continue their care at one of the research sites. Several questionnaires were self-administered at the time of recruitment, including a food-frequency questionnaire. Women were then contacted via telephone within 2 wk of recruitment regarding current and pregravid health behaviors and sociodemographic characteristics. Details on the population’s characteristics and recruitment patterns were published previously (24). Preliminary analysis showed that 57% of eligible women were recruited, with a slightly higher success rate among white women (61%) than among black women (54%). The reasons for not participating were similar for both groups. The PIN Study protocols were reviewed and approved by the Institutional Review Boards of the School of Medicine at the University of North Carolina at Chapel Hill and Wake Medical Center.

The PIN Study recruited 2898 pregnant women from 1 August 1995 through 31 May 2000. We excluded 1200 women, leaving a sample of 1698 women for the present analysis. The reasons for exclusion including the following: racial group other than white or black (n = 173), second pregnancy (n = 99), preexisting diabetes (n = 28), no glucose screening data (n = 287), a high glucose screening result without an oral glucose tolerance test and thus unclassifiable (n = 57), missing dietary data (n = 236), and missing body mass index (n = 133). In addition, women with estimated total energy intake less than the 5th percentile (n = 92) or greater than the 95th percentile (n = 95) were excluded. A higher percentage of black women than of white women were excluded from the final analysis sample. A higher proportion of women in the analysis sample were married, younger, highly educated, physically active, and >350% above the poverty index.

Definition of outcome

Glucose tolerance information was obtained from hospital computer databases and medical charts. Ascertainment of the women’s glucose tolerance status involves a two-step process. The initial screening test measures the plasma glucose concentration 1 h after a 50-g glucose challenge test. This test is a random screen and thus does not require that the women be in the fasting state (25). Site-specific protocols established the cutoffs for follow-up testing. The cutoffs for each clinic were different because disagreement exists about which cutoff represents risk. Analysis of the effect of differential cutoffs showed either no effect or a slightly attenuated effect on the results. A value of ≥140 mg/dL at the University of North Carolina sites and a value ≥130 mg/dL at the Wake Medical Center sites indicated the need for a full 3-h, 100-g oral-glucose-tolerance test (OGTT). The OGTT is conducted in the fasting state with glucose analysis performed at fasting and 1, 2, and 3 h after the oral glucose load. These tests are performed on serum samples with the use of the glucose oxidase method. The Carpenter & Coustan cutoffs of 95 mg/dL for fasting, 180 mg/dL for 1-h, 155 mg/dL for 2-h, and 135 mg/dL for 3-h values were used to define abnormal values (26). IGT was defined as one abnormal value from the OGTT. Normal glucose tolerance was defined as having a normal or high result on the glucose challenge test but no high values on the OGTT. To provide further comparisons, women with GDM were included in the analysis and were defined by 2 abnormal values on the OGTT. Women with GDM received diet treatment, insulin treatment, or both at both clinics and women with IGT were not treated at either clinic.

Dietary data

Dietary intake during the second trimester was assessed by using a modified food-frequency questionnaire originally developed by Block et al (27). Modifications were made for the PIN Study population to include local foods, make the questionnaire specific to the pregnancy time period, and include more foodspecific portion sizes. The questionnaire has been validated in several populations, including the PIN Study population (28, 29). The validity of the food-frequency questionnaire in the PIN population was assessed among 99 women by comparing nutrient results from the food-frequency questionnaire with three 24-h dietary recalls collected at random on nonconsecutive days. The deattenuated Pearson correlation coefficients for total energy and macronutrient intakes between the food-frequency questionnaire and the 24-h recalls were 0.35 for total energy, 0.43 for fats, 0.44 for protein, and 0.26 for carbohydrates. These results for energy, fats, and protein are similar to a recent comparison of a food-frequency questionnaire and 10 days of food record intakes in pregnant women; the results for carbohydrates were lower (energy, r = 0.24; fats, r = 0.48; protein, r = 0.55; and carbohydrates, r = 0.49) (30).

On the food-frequency questionnaire, the women were asked to report usual intake during the previous 3 mo. For each food, the women were asked how often and how much they consumed. Four frequency categories (daily, weekly, monthly, and rarely/never) and 3 serving sizes (small, medium, or large, with examples of each) were specified for most foods. The questionnaire was designed to take 20–30 min to complete and to be self-administered. The questionnaire was given to participants along with instructions at the time of enrollment.

Nutrient analysis of the food-frequency questionnaire was conducted by using the DIETSYS version 4.01 analysis program (31). DIETSYS calculates nutrient intake per day by using nutrient values based on data from the third National Health and Nutrition Examination Survey, the 1994–1996 Continuing Survey of Food Intakes by Individuals, and the US Department of...
Agriculture Nutrient Database for Standard Reference (32). The DIETSYS program included an internal edit program to flag foods and total calories considered outliers, which were routinely checked by the PIN investigators. Corrections were made on the basis of population limits of reasonable intakes.

Dietary variables of interest in this study included macronutrients and total energy. Macronutrients were assessed both as percentages of total energy and as calories from each macronutrient source. Calories from each macronutrient were calculated by multiplying grams of macronutrient by calories per gram (fat = 9 kcal/g; carbohydrate and protein = 4 kcal/g).

**Definition of covariates**

Prepregnancy BMI (in kg/m²) was classified according to guidelines established by the Institute of Medicine: underweight, <19.8; normal weight, 19.8–26; overweight, >26–29; and obese, >29 (33). Maternal height measured during clinic visits and prepregnancy weight based on the women’s recall were used for these calculations. Recalled prepregnancy weight was obtained from the medical record or the screening questionnaire. Use of recalled prepregnancy weight has been shown to be consistent with clinical records (34, 35). If recalled prepregnancy weight was not available (4.7% of subjects), then the first measured weight between 1 and 15 wk gestation was used. If the first visit was at <8 wk gestation, the weight at the first visit was used. For weights measured between 8 and 10 wk gestation, 0.45 kg (1 pound) was subtracted; for weights measured between 10 and 12 wk, 1 kg (2.2 pounds) was subtracted; and for weights measured between 12 and 15 wk, 2 kg (4.4 pounds) was subtracted (36). If the first weight measurement was after 15 wk gestation, a prepregnancy weight could not be imputed. Underweight and normal weight women were combined and used as the reference category in the analysis.

Race was self-identified by the women during the telephone interview or was taken from the medical charts. There were 18 possible categories; however, the white and black categories represented 94% of the successfully recruited population. Thus, only white and black women were included in this analysis.

Family income was represented as a percentage of the poverty index according to US Bureau of the Census 1996 poverty guidelines (37). Information was collected on cigarette smoking habits during the first 6 mo of the pregnancy. Participation in regular or strenuous physical activity was assessed 3 mo before becoming pregnant and during the first and second trimester. Physical activity variables were specified as categorical variables representing any versus none. Other variables assessed included marital status, parity, mother’s age, and mother’s education.

**Statistical analysis**

Bivariate analysis of sociodemographic characteristics and dietary variables with glucose status was performed. Chi-squared analysis was conducted to test for differences in categorical variables, and one-way analysis of variance with a Bonferroni correction for multiple comparisons was used for continuous variables. Multinomial logistic regression was used to calculate the likelihood of developing IGT or GDM compared with normal glucose tolerance while adjusting for potential confounders. Potential confounders included prepregnancy BMI, maternal age, weight gain, physical activity, height, and race. Variables that were associated with both glucose status and dietary variables and resulted in at least a 10% change in the IGT or GDM β coefficients were retained in the final models. Although weight gain has been shown to increase the risk of IGT and GDM in this population (38), we found no effect of diet on weight gain, so it was not included in the models.

We specified a series of models to test alternate hypotheses about the relation of diet to risk of IGT or GDM. The first 2 models evaluated the theoretical effect of adding a specific nutrient to the diet. To evaluate the effect of adding dietary fat or carbohydrates to the diet, we used the partition method. Nutrients were partitioned into calories from fat, carbohydrates, and protein (39). Variables were scaled to represent risk per 100 kcal of the macronutrient. Because these models include all of the macronutrients simultaneously and other confounders, they do not include total energy and are not comparisons of isocaloric diets. Model 1 reports the effect of adding dietary fat to the diet, whereas model 2 reports the effect of adding carbohydrates to the diet.

Models 3 through 5 evaluated the effect of theoretically substituting one macronutrient for another, allowing us to compare isocaloric diets. To evaluate the effect of substituting dietary fat for carbohydrate (model 3), we used a nutrient density model that simultaneously included percentage of energy from fat, percentage of energy from protein, total energy intake, and other confounders (39). When protein and total energy intake are included in the model (keeping them constant), the only macronutrient that can decrease as the percentage of energy from fat increases is carbohydrate. Thus, this model can be considered the theoretical substitution of fat for carbohydrates. To evaluate the effect of substituting fat for protein (model 4), we used a nutrient density model that simultaneously included total energy intake, percentage of energy from fat, percentage of energy from carbohydrates, and other confounders. By including carbohydrates and total energy intake in the model (keeping them constant), the only macronutrient that can decrease as the percentage of energy from fat increases is protein. Thus, this model can be considered the theoretical substitution of fat for protein. Model 5 evaluated the effect of substituting carbohydrates for protein in the same manner as models 3 and 4.

To evaluate the potential for effect modification by race or weight gain on the relation between diet and glucose status, we evaluated diet-by-race and diet-byweight gain interaction terms in the models when P values were ≤1.0. These interaction terms were not significant.

To facilitate interpretation of the results, the predicted probabilities of IGT and GDM were calculated from the coefficients of the models that showed significant dietary effects (models 2 and 3). The predicted probabilities were calculated for various dietary scenarios. Separate predicted probabilities are presented for black and white women because the prevalences of IGT and GDM were significantly different by race.

**RESULTS**

The main characteristics of the analysis population are presented in Table 1. The overall prevalence of IGT in the cohort was 2.6%, and that of GDM was 5.2%. Among the women with IGT or GDM, higher proportions were white, married, or older than among the women with normal glucose tolerance. The women with GDM had a higher mean prepregnancy BMI than did the women with normal glucose tolerance or IGT. There were no
significant differences by glucose status in the other variables examined.

Distribution of total energy and macronutrient intakes by glucose status is shown in Table 2. Only the intake of carbohydrates and fat differed by glucose status. The women with IGT and GDM consumed a lower percentage of energy from carbohydrates and a higher percentage of energy from fat than did the women with normal glucose tolerance.

The relative risk ratios and 95% CIs for each of the specified models are presented in Table 3. These models examined the likelihood of developing IGT or GDM (compared with normal glucose tolerance) associated with different macronutrient intakes while controlling for BMI, maternal age, and race. Model 2 tested the hypothesis that adding a specific nutrient (carbohydrate) to the diet, with no reduction in total caloric intake, would increase the risk of IGT or GDM. Model 2 showed that adding 100 kcal carbohydrates was associated with a 12% decrease in risk of IGT and a 9% decrease in risk of GDM. Model 3 tested the hypothesis that substituting one macronutrient (fat) for another (carbohydrates), while holding calories constant, would increase the risk of IGT or GDM. Model 3 showed that substituting fat for carbohydrates resulted in a significant increase in risk of both IGT and GDM. In other words, if a woman consumes a diet with more dietary fat and less dietary carbohydrate, the risk of IGT increases 7%, whereas the risk of GDM increases by 6% for each percentage increase in fat. As expected, substituting carbohydrates for fats resulted in a 6% decrease in risk of both IGT and GDM for each percentage increase in carbohydrates (model not shown).

Shown in Figure 1 are the predicted probabilities of IGT and GDM stratified by race for different diets with decreasing percentages of dietary fat and increasing percentages of carbohydrates.

### Table 1
Characteristics of the participants in the Pregnancy, Infection, and Nutrition Study by glucose tolerance status

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal (n = 1565)</th>
<th>IGT (n = 44)</th>
<th>GDM (n = 89)</th>
<th>P²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>60</td>
<td>73</td>
<td>76</td>
<td>0.002</td>
</tr>
<tr>
<td>Black</td>
<td>40</td>
<td>27</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Marital status (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.008</td>
</tr>
<tr>
<td>Single</td>
<td>41</td>
<td>25</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>52</td>
<td>61</td>
<td>65</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>7</td>
<td>14</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Poverty index, n = 1507 (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.78</td>
</tr>
<tr>
<td>&lt;185%</td>
<td>53</td>
<td>59</td>
<td>57</td>
<td></td>
</tr>
<tr>
<td>185–350%</td>
<td>20</td>
<td>22</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>&gt;350%</td>
<td>27</td>
<td>19</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Smoked, n = 1594 (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.97</td>
</tr>
<tr>
<td>During 3 mo before pregnancy</td>
<td>25</td>
<td>28</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>During first trimester</td>
<td>16</td>
<td>16</td>
<td>10</td>
<td>0.33</td>
</tr>
<tr>
<td>During second trimester</td>
<td>9.5</td>
<td>9.3</td>
<td>3.6</td>
<td>0.39</td>
</tr>
<tr>
<td>Pregravid BMI (kg/m²)</td>
<td>25.0 ± 6.5</td>
<td>28.4 ± 7.9</td>
<td>30.1 ± 7.7</td>
<td>0.001</td>
</tr>
<tr>
<td>BMI categories (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Underweight or normal weight (BMI &lt; 26)</td>
<td>67</td>
<td>45</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Overweight (BMI &gt; 26–29)</td>
<td>11</td>
<td>16</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Obese (BMI &gt; 29)</td>
<td>22</td>
<td>39</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Mothers’ age (y)</td>
<td>26 ± 6.2</td>
<td>29 ± 6.0</td>
<td>28 ± 5.6</td>
<td>0.001</td>
</tr>
<tr>
<td>Mothers’ education (y)</td>
<td>13.6 ± 2.9</td>
<td>13.7 ± 2.2</td>
<td>14.0 ± 2.8</td>
<td>0.54</td>
</tr>
<tr>
<td>Parity, n = 1692</td>
<td>0.8 ± 1.1</td>
<td>1.1 ± 1.1</td>
<td>0.9 ± 0.9</td>
<td>0.16</td>
</tr>
<tr>
<td>Mothers’ height (m)</td>
<td>1.65 ± 0.07</td>
<td>1.64 ± 0.07</td>
<td>1.64 ± 0.07</td>
<td>0.07</td>
</tr>
</tbody>
</table>

1 IGT, impaired glucose tolerance; GDM, gestational diabetes mellitus.
2 P values are from an overall chi-square test for categorical variables or from an ANOVA with Bonferroni correction for continuous variables.
3 x ± SD.

### Table 2
Mean dietary composition by glucose tolerance status of women in the Pregnancy, Infection, and Nutrition Study

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal</th>
<th>IGT</th>
<th>GDM</th>
<th>P²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total energy (kcal)</td>
<td>2603 ± 995</td>
<td>2431 ± 844</td>
<td>2572 ± 939</td>
<td>0.51</td>
</tr>
<tr>
<td>Protein (% of energy)</td>
<td>14 ± 2.8</td>
<td>15 ± 2.5</td>
<td>14 ± 2.7</td>
<td>0.15</td>
</tr>
<tr>
<td>Carbohydrate (% of energy)</td>
<td>53 ± 7.4</td>
<td>50 ± 6.5</td>
<td>51 ± 7.1</td>
<td>0.0004</td>
</tr>
<tr>
<td>Fat (% of energy)</td>
<td>33 ± 6.3</td>
<td>35 ± 5.9</td>
<td>35 ± 5.9</td>
<td>0.001</td>
</tr>
</tbody>
</table>

1 x ± SD. n = 1698. IGT, impaired glucose tolerance; GDM, gestational diabetes mellitus.
2 P values are from an overall chi-square test for macronutrients or from an ANOVA with Bonferroni correction for total energy.
DIET AND GLUCOSE TOLERANCE DURING PREGNANCY

TABLE 3
Relative risk ratios (RRs) of impaired glucose tolerance (IGT) and gestational diabetes mellitus (GDM)†

<table>
<thead>
<tr>
<th>Addition models: calories of macronutrient‡</th>
<th>IGT</th>
<th>GDM</th>
<th>Substitution models: percentage of macronutrient§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1: Adding fat</td>
<td>1.1 (0.97, 1.30)</td>
<td>0.14</td>
<td>1.1 (1.0, 1.20)</td>
</tr>
<tr>
<td>Model 2: Adding carbohydrate</td>
<td>0.9 (0.79, 0.98)</td>
<td>0.02</td>
<td>0.9 (0.85, 0.98)</td>
</tr>
<tr>
<td>Substitution models: percentage of macronutrient†</td>
<td>1.1 (1.02, 1.12)</td>
<td>0.006</td>
<td>1.1 (1.02, 1.10)</td>
</tr>
<tr>
<td>Model 3: Substituting fat for carbohydrates</td>
<td>1.0 (0.93, 1.15)</td>
<td>0.58</td>
<td>1.0 (0.94, 1.10)</td>
</tr>
<tr>
<td>Model 5: Substituting carbohydrates for protein</td>
<td>0.9 (0.90, 1.06)</td>
<td>0.41</td>
<td>0.9 (0.90, 1.03)</td>
</tr>
</tbody>
</table>

† n = 1698. All models were adjusted for BMI, maternal age, and race.
‡ Addition models are per 100 kcal fat or carbohydrate.
§ Substitution models are adjusted for total calories and are per 1%.

DISCUSSION

In the present study, we isolated the effects of dietary macronutrient intake on the risk of developing IGT or GDM by constructing alternative statistical models. Our findings suggest that in an isocaloric diet, an increase in carbohydrate intake as a percentage of energy with a simultaneous decrease in fat intake as a percentage of energy significantly reduces the risk of glucose intolerance. Furthermore, increasing carbohydrates without decreasing fat and thus not controlling for total energy intake also significantly reduces the risk of both IGT and GDM. The results shown in Figures 1 and 2 present two perspectives that support the same conclusion. The diet with 30% fat achieved by adding carbohydrate shows a risk of IGT and GDM similar to that of the isocaloric diet in Figure 1 with 30% fat. The implication is that these models do not fully allow us to separate the effect of carbohydrate from fat.

The results from the other models are more insightful in understanding what is driving the change in risk. In the substitution model (model 5), when carbohydrates were substituted for protein in isocaloric diets, thus holding fat constant, although de-
creases in the risk of IGT and GDM were seen, they were not statistically significant. In the addition model (model 1), we see a marginally significant increased risk of both IGT and GDM associated with adding calories from dietary fat. These results suggest that in order for an increase in carbohydrate intake to significantly reduce the risk of developing IGT and GDM in an isocaloric diet, it must be accompanied by a decrease in fat intake.

Overall, these results support the idea that high-fat, low-carbohydrate diets result in a higher risk of developing impaired glucose tolerance during pregnancy. These findings are consistent with some previous studies of the development of type 2 diabetes, which found an increased risk of diabetes from diets high in fats (15, 16). They are also consistent with the study by Moses et al (21), which found recurrence of GDM in women consuming higher-fat diets. Women who developed GDM in a follow-up pregnancy consumed 41.4% of their diet from fat compared with 33.1% fat for the women who did not develop GDM.

Despite similarities in the prospective collection of dietary data, the results of our study are in direct contrast with those of Wang et al (22), who found a crude association between increased fat and decreased risk of IGT and GDM in 116 subjects matched for age, height, and BMI. Both genetic and cultural factors may play a role in our different results. Genetically, glucose metabolism is known to vary between ethnic groups (40, 41). The population studied by Wang et al was Chinese, whereas ours consisted of black and white women. In addition to the possibility that some populations may metabolize macronutrients slightly differently, the foods, which reflect the cultural heritage of our populations, appear to be very different. Wang et al found that the major contribution of fat was soybean oil. A previous analysis of our population’s intake showed that the top 5 sources of fat, accounting for 34% of fat intake, were mayonnaise or salad dressing, whole milk, French fries and fried potatoes, biscuits or muffins, and cheeses (42). Wang et al’s study showed that polyunsaturated fats had a strong protective effect on IGT and GDM. It may be that our population’s intake was low in polyunsaturated fat and high in saturated fat. The composition of the carbohydrate and fat intakes in the present study may thus have had different effects on glucose metabolism. We did not separate out subtypes of fat or carbohydrates.

In addition to the research supporting the possibility of protective effects of some subtypes of dietary fats, there is a growing body of research looking at subtypes of carbohydrates (15, 16, 21). Researchers have recently begun to use glycemic load measurements as a tool for assessing carbohydrate types. Studies using the glycemic load have found an association between high-glycemic index diets and increased risk of type 2 diabetes (43). It has been suggested that low-glycemic index diets act similarly to low-fat diets, in that low-glycemic index foods prolong carbohydrate absorption, attenuate the insulin response, and suppress hormone-sensitive lipase, thus decreasing nonesterified fatty acids and increasing the expression of the insulin-responsive glucose transporter GLUT4 (23).

It is interesting to compare the results of the present study with those of studies of dietary treatment in GDM. Romon et al (44) used a high-carbohydrate diet to reduce macrosomia and argued that high-fat diets will increase glucose concentrations. However, Major et al (45) used carbohydrate restriction to reduce the need for insulin in GDM, and Jovanovic-Peterson et al (46) have long advocated using a carbohydrate-restricted diet containing 40% of total calories from carbohydrate, 40% from fat, and 20% from protein. The theory behind low-carbohydrate diets in the treatment of GDM is to reduce postprandial glucose concentrations, minimizing harmful effects to the fetus. Yet, controlled studies of this theory have not been conducted. More research will be needed to determine whether there is a short-term benefit of carbohydrate restriction once a diagnosis has been made, but our results suggest that the general dietary prescription to prevent glucose intolerance in pregnancy as well as in type 2 diabetes should seek to limit fats while increasing complex carbohydrates. Given that 50% of women with GDM develop type 2 diabetes, we cannot miss the chance to educate women about a healthier long-term diet (12).
Some limitations of our study are worth noting. First, as with all assessments of dietary exposure, there is the possibility of misclassification, which could result in a biased estimate of effect. Our dietary information was based on a food-frequency questionnaire administered before the diagnosis of glucose status, and thus we would not expect there to be differential reporting of dietary intake by glucose status. Second, the correlation coefficient for carbohydrates was 0.26. Validation studies have shown that correlation coefficients <0.4 can attenuate an association between an exposure and an outcome, and thus the estimates of a carbohydrate effect may be conservative (39). The values for fat and protein were between 0.4 and 0.6 and can be considered reasonable. Third, the effect of residual confounding from sources not measured could influence our estimates. Finally, the analysis population somewhat underrepresented black women, which could introduce potential bias. However, the demographic characteristics of the analysis sample and the base population were similar. Furthermore, the model estimates were based on the assumption of missing at random (MAR), which states that the probability of missing data for a given variable is unrelated to the value of the variable, with control for other variables in the analyses. Allison (47) showed that the logistic model under the MAR assumption provides consistent estimates.

In conclusion, we found an association between increased fat intake and the development of glucose abnormalities during pregnancy. The results add more information to the debate about optimum diet during pregnancy. The overall outcome is consistent with what is recommended to decrease the risk of type 2 diabetes. Pregnancy is a time period during which women are increasing their caloric intake to meet fetal needs. Our study suggests that women who maintain a diet with <30% fat and >50% carbohydrate as they increase their energy intake will reduce their risk of both IGT and GDM. Further studies are needed to discern whether the increased calories needed for a healthy pregnancy could come from an increase in carbohydrate alone or whether the goal would be a reduction in dietary fat with a concomitant increase in carbohydrate. In addition, future studies must try to separate out the composition of carbohydrate and fat that is associated with decreased risk.

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TMS conceptualized the research question for this study, conducted the statistical analysis, interpreted the results, and prepared the manuscript for publication as part of her doctoral thesis requirement. AMS-R is a co-investigator of the Pregnancy, Infection, and Nutrition Study. In this role, she contributed to the conception, design, implementation, and data collection for the cohort. For this article, she has aided in the conception of the research question, statistical analysis, interpretation of the results, and writing of the manuscript. LSA aided in the conception of the research question, statistical analysis, interpretation of the results, and writing of the manuscript. None of the authors had a conflict of interest with the funding agencies.

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