A randomized controlled clinical trial investigating the effect of DASH diet on insulin resistance, inflammation, and oxidative stress in gestational diabetes

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Objective: To our knowledge, no reports are available indicating the effects of the Dietary Approaches to Stop Hypertension (DASH) eating plan on insulin resistance, inflammation, and oxidative stress among pregnant women with gestational diabetes mellitus (GDM). This study was designed to investigate the effects of the DASH diet on insulin resistance, serum high-sensitivity C-reactive protein (hs-CRP) and biomarkers of oxidative stress among pregnant women with GDM.

Methods: This randomized controlled clinical trial was performed with 32 pregnant women diagnosed with GDM at 24 to 28 wk gestation. Participants were randomly assigned to consume either the control (n = 16) or DASH diet (n = 16) for 4 wk. The DASH diet was rich in fruits, vegetables, whole grains, and low-fat dairy products and was low in saturated fats, total fats, cholesterol, refined grains, and sweets, with a total of 2400 mg/d of sodium. The control diet contained 40% to 55% of its energy as carbohydrates, 10% to 20% as proteins, and 25% to 30% as total fats. Fasting blood samples were taken at baseline and after 4 wk of intervention to measure fasting plasma glucose (FPG), serum insulin, and hs-CRP, Homeostasis Model of Assessment—Insulin Resistance (HOMA-IR), plasma total antioxidant capacity (TAC), and total glutathione levels (GSH).

Results: Consumption of the DASH diet compared with the control diet resulted in decreased FPG (-7.62 versus 3.68 mg/dL; P = 0.02), serum insulin levels (-2.62 versus 4.32 μIU/mL, P = 0.03), and HOMA-IR score (-0.8 versus 1.1; P = 0.03). Increased concentrations of plasma TAC (45.2 versus -159.2 mmol/L; P < 0.0001) and GSH (108.1 versus -150.9 μmol/L; P < 0.0001) also were seen in the DASH group compared with control group. We failed to find a significant difference in mean changes of serum hs-CRP levels between the two diets. Within-group comparisons revealed significant reductions in plasma TAC and GSH levels in the control diet, while a significant increase in these biomarkers in the DASH diet.

Conclusion: Consumption of the DASH diet in pregnant women with GDM had beneficial effects on FPG, serum insulin levels, HOMA-IR score, plasma TAC, and total GSH levels. The effects of this dietary pattern on pregnancy outcomes need to be investigated in future studies.

Introduction

Gestational diabetes mellitus (GDM) is a condition in which pregnant women without previously diagnosed diabetes exhibit high blood glucose levels especially during the third trimester [1]. It affects 3% to 6% of all pregnancies, depending on the studied population [2]. The precise mechanisms underlying GDM remain unknown. The main hallmark of GDM is increased insulin...
with adherence to the DASH diet along with exercise and weight to investigate the effects of the DASH eating plan on insulin women with GDM. The aim of the current study, therefore, was indicating the effects of the DASH diet on insulin resistance, in-potassium, magnesium, folic acid, and other bene factors [24], features of metabolic syndrome[25], and metabolic the bene hs-CRP in patients with diabetes. These investigators also reported DASH diet for 8 wk was associated with decreased serum levels of hypertension[23]; however, its effects on cardiovascular risk (DASH) eating plan was originally suggested for patients with vitamins E and A, have resulted in a lower circulating level of been suggested for management of GDM. The use of antioxidants, vitamins E and A, and insulin injections[19], have been suggested for management of GDM. The use of antioxidants, elevated circulating levels of inflammatory factors and biomarkers of oxidative stress during pregnancy [20–22]. The Dietary Approaches to Stop Hypertension (DASH) eating plan was originally suggested for patients with hypertension [23]; however, its effects on cardiovascular risk factors [24], features of metabolic syndrome [25], and metabolic profile of diabetic patients [26] have recently been shown. Azadbakht et al. [26] have demonstrated that consumption of the DASH diet for 8 wk was associated with decreased serum levels of hs-CRP in patients with diabetes. These investigators also reported the beneficial effects of this dietary pattern on CRP, coagulation abnormalities, and hepatic function tests [26]. Improvements in insulin sensitivity and lipid profiles also have been documented with adherence to the DASH diet along with exercise and weight loss in hypertensive overweight patients [27].

The DASH diet is a low-glycemic index, low energy-dense diet that contains higher amounts of dietary fiber, phytoestrogens, potassium, magnesium, folic acid, and other beneficial nutrients [24,25]. To the best of our knowledge, no reports are available indicating the effects of the DASH diet on insulin resistance, inflammation, and biomarkers of oxidative stress in pregnant women with GDM. The aim of the current study, therefore, was to investigate the effects of the DASH eating plan on insulin resistance, serum hs-CRP, and biomarkers of oxidative stress on pregnant women with GDM.

Materials and methods

Participants

This randomized, two-arm, parallel clinical trial was carried out in Kashan, Iran, from April 2011 to December 2013. On the basis of the sample size formula suggested for randomized clinical trials [26] and considering the type I error of 5% (α = 0.05), type II error of 20% (β = 0.2; Power = 80%), and serum hs-CRP level as a key variable, we reached the sample size of 16 women for each group. Pregnant women ages 18 to 40 y diagnosed with GDM by a 100-g oral glucose tolerance test at 24 to 28 wk gestation were recruited. Gestational age was assessed from the date of last menstrual period and concurrent clinical assess-ment [28]. Pregnant women without a previous diagnosis of glucose intolerance levels as a key variable, we reached the sample size of 16 women for each group. At baseline and after 4 wk of intervention, fasting blood samples (10 mL) were taken in the early morning at a Kashan reference laboratory. PPG levels were quantified by the use of glucose oxidase/peroxidase method with commercially available kits (Parsazmun Co, Iran). Serum insulin levels were measured using enzyme-linked immunoasay (ELISA) kits (DiaMetra, Italy). Insulin resistance was assessed using the homeostatic model assessment of insulin resistance (HOMA-IR) formula [31]. Serum hs-CRP levels were quantified by ELISA method using available kits (LDN, Nordhorn, Germany). Plasma total antioxidant capacity (TAC) was assessed by means of the fluorescence recovery after photobleaching method developed by Benzie and Strain [32]. Plasma GSH levels were measured using the method of Beutler et al [33].

Statistical analysis

To ensure the normal distribution of variables, histogram and the Kolmogrov-Smirnov test were applied. Log transformation was used for non-normally distributed variables. We used independent samples Student’s t test to identify between-group differences. Mean changes of each variable mentioned criteria). Individuals with premature preterm rupture of membrane, placenta abruptio, preeclampsia, and those who needed to commence insulin therapy were on insulin therapy, as well as those with a recommendation for complete bed rest were not included in this study. We also did not include women with hypothyroidism, those with kidney or liver diseases, or those taking estrogen therapy. After exclusion of two women, 38 pregnant women were included in the study and after stratification for body mass index (BMI; <30 and ≥30 kg/m2) and weeks of gestation (>26 or ≥26 wk), participants were randomly assigned to consume the control (n = 19) or the DASH diet (n = 19) for 4 wk. Random assignment was done by the use of computer-generated random numbers. A trained midwife at the maternity clinic performed randomization. With the exception of the study dietitian (ZA), who provided dietary education, all study personnel and participants were blinded to dietary assignment. Among individuals in the control group, three women (two with preeclampsia and one who needed to commence insulin therapy) were excluded. There were three exclusions in the DASH diet: two women with preeclampsia and one who was put on complete bed rest. Finally, 32 participants (16 on each diet) completed the trial (Fig. 1).

Data on anthropometric and biochemical measures were collected at the maternity clinic and a Kashan reference laboratory affiliated to Kashan University of Medical Sciences, respectively. The study was conducted according to the guidelines laid down in the Declaration of Helsinki. The ethical committee of the Kashan University of Medical Sciences approved the study (No. 1384-90-5-18) and informed written consent was obtained from all participants.

Study design

Participants were randomly assigned to consume the control or the DASH diet for 4 wk. They were asked not to alter their routine physical activity. All pregnant women were consuming a daily supplement of calcium and folic acid. Compliance with the consumption of diets was monitored weekly through phone interviews. The compliance was also double-checked by the use of 5-d dietary records completed throughout the study. To obtain nutrient intakes of partici-pants based on these 3-d food diaries, we used Nutritionist IV software (First Databank, San Bruno, CA) modified for Iranian foods.

Diet:

The control diet was designed based on the recommendations for acceptable dietary intake for GDM [30]. The macronutrient composition of the control diet was 40% to 55% of energy as carbohydrates, 10% to 20% as proteins, and 25% to 30% as total fats. The DASH diet was similar to the control diet in terms of macronutrients; however, it was rich in fruits, vegetables, whole grains, low-fat dairy products, and was low in saturated fats, cholesterol, refined grains, and sweets. The amount of sodium intake in the DASH diet was restricted to less than 2000 mg/d [25]. Both diets were planned as a 7-d menu cycle. Therefore, participants were choosing the foods from a prescribed list.

Assessment of anthropometric measures

All anthropometric measures were assessed at baseline and after 4 wk of intervention. Maternal weight was assessed by trained midwives at the maternity clinic in an overnight fasting status, without shoes, and while minimally clothed by use of a digital scale (Seca, Hamburg, Germany) and was recorded to the nearest 0.1 kg. Height was measured using a non-stretched tape measure (Seca, Hamburg, Germany) to the nearest 0.1 cm. BMI was calculated as weight in kilograms divided by height in meters squared.

Biochemical assessment

At baseline and after 4 wk of intervention, fasting blood samples (10 mL) were taken in the early morning at a Kashan reference laboratory. PPG levels were quantified by the use of glucose oxidase/peroxidase method with commercially available kits (Parsazmun Co, Iran). Serum insulin levels were measured using enzyme-linked immunoasay (ELISA) kits (DiaMetra, Italy). Insulin resistance was assessed using the homeostatic model assessment of insulin resistance (HOMA-IR) formula [31]. Serum hs-CRP levels were quantified by ELISA method using available kits (LDN, Nordhorn, Germany). Plasma total antioxidant capacity (TAC) was assessed by means of the fluorescence recovery after photobleaching method developed by Benzie and Strain [32]. Plasma GSH levels were measured using the method of Beutler et al [33].

Statistical analysis
between the two groups were compared by Student’s t test. Paired-samples t test was used to detect within-group differences. P < 0.05 was considered as statistically significant. All statistical analyses were done using the Statistical Package for Social Science version 17 (SPSS Inc., Chicago, IL, USA).

Results

Mean age, pre-pregnancy weight, and BMI were not statistically different between the two groups (Table 1). Baseline weight and BMI as well as postintervention means for these variables were not significantly different between the DASH and control groups.

Based on 3-d dietary records, no statistically significant difference was seen between the two groups in terms of energy and protein intake; however, significant differences were observed in dietary intakes of carbohydrates, fats, saturated fatty acids, polyunsaturated fatty acids, cholesterol, dietary fiber, simple sugar, fructose, arginine, sodium, potassium, magnesium, calcium, and vitamin C (P < 0.05 for all; Table 2). These findings indicated that adherence to the prescribed diets was not perfect.

Consumption of the DASH diet compared with the control diet resulted in decreased FPG (7.62 versus 3.68 mg/dL; P = 0.02), serum insulin levels (2.62 versus 4.32 μIU/mL; P = 0.03), and HOMA-IR score (0.8 versus 1.1; P = 0.03; Table 3). Increased concentrations of plasma TAC (45.2 versus 159.2 μmol/L; P < 0.0001) and GSH (108.1 versus 150.9 μmol/L; P < 0.0001) also were found in the DASH group compared with the control group. We failed to find significant differences in mean changes of serum hs-CRP levels between the two diets. Within-group changes of plasma TAC and GSH levels showed a significant reduction in the control diet, but a significant increase in the DASH diet.

<table>
<thead>
<tr>
<th>Table 1: General characteristics of the study participants*</th>
</tr>
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<tbody>
<tr>
<td>Control diet (n = 16)</td>
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<tr>
<td>-----------------------</td>
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<tr>
<td>Maternal age (y)</td>
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<tr>
<td>Height (cm)</td>
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<tr>
<td>Prepregnancy weight (kg)</td>
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<tr>
<td>Weight at study baseline (kg)</td>
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<tr>
<td>Weight at end of trial (kg)</td>
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<tr>
<td>Prepregnancy BMI (kg/m²)</td>
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<td>BMI at study baseline (kg/m²)</td>
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<tr>
<td>BMI at end of trial (kg/m²)</td>
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<tr>
<td>GTT1 h at study baseline (mg/dL)</td>
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<td>GTT2 h at study baseline (mg/dL)</td>
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<td>GTT3 h at study baseline (mg/dL)</td>
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</tbody>
</table>

BMI, body mass index; GTT, glucose tolerance test
* Data are means ± SD.
† Obtained from independent t test.

Table 2 Dietary intakes of study participants throughout the study†

<table>
<thead>
<tr>
<th></th>
<th>Control diet (n = 16)</th>
<th>DASH diet (n = 16)</th>
<th>P value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kcal/d)</td>
<td>2393 ± 161</td>
<td>2410 ± 29</td>
<td>0.7</td>
</tr>
<tr>
<td>Carbohydrate (g/d)</td>
<td>318 ± 42</td>
<td>392 ± 7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Protein (g/d)</td>
<td>107 ± 10</td>
<td>106 ± 3</td>
<td>0.83</td>
</tr>
<tr>
<td>Fat (g/d)</td>
<td>74 ± 15</td>
<td>47 ± 3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SFA (g/d)</td>
<td>21 ± 4</td>
<td>9.3 ± 1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PUFA (g/d)</td>
<td>27.3 ± 9.6</td>
<td>13.9 ± 1.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cholesterol (mg/d)</td>
<td>178.2 ± 45.1</td>
<td>94.8 ± 27.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Dietary fiber (g/d)</td>
<td>15.8 ± 2.7</td>
<td>23 ± 1.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Simple sucrose (g/d)</td>
<td>19.8 ± 1.2</td>
<td>9.1 ± 0.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fructose (g/d)</td>
<td>9.0 ± 1.8</td>
<td>13.4 ± 1.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Arginine (mg/d)</td>
<td>47.5 ± 34.3</td>
<td>74.9 ± 11.9</td>
<td>0.001</td>
</tr>
<tr>
<td>Sodium (mg/d)</td>
<td>3882.8 ± 439.4</td>
<td>1394.1 ± 174.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Potassium (mg/d)</td>
<td>2594.3 ± 832.2</td>
<td>4163.6 ± 853</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Magnesium (mg/d)</td>
<td>277.2 ± 45.9</td>
<td>363.9 ± 14.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Calcium (mg/d)</td>
<td>1081.7 ± 194.2</td>
<td>1752 ± 81</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Vitamin C (mg/d)</td>
<td>140 ± 68.6</td>
<td>292.9 ± 18.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fruits (servings/d)</td>
<td>3.9 ± 0.9</td>
<td>5.9 ± 0.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Vegetables (servings/d)</td>
<td>4 ± 1</td>
<td>5.8 ± 0.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Nuts (servings/d)</td>
<td>0.4 ± 0.1</td>
<td>1.9 ± 0.2</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

DASH, Dietary Approaches to Stop Hypertension; PUFA, polyunsaturated fats; SFA, saturated fatty acids
† Data are means ± SD.
†† Obtained from independent t test.
Discussion

We found that consumption of the DASH eating pattern in pregnant women with GDM had beneficial effects on FPG, serum insulin levels, HOMA-IR score, and biomarkers of oxidative stress. Total energy intake of participants in the control and the DASH groups was the same; however, the energy density of the DASH diet was lower than the control diet. To our knowledge, this study is the first reporting the effects of the DASH diet on insulin resistance and biomarkers of oxidative stress in GDM.

Gestational diabetes is associated with fetal and maternal complications [10–12,15]. We found that consumption of the DASH diet could favorably influence the metabolic profiles of pregnant women with GDM. The effects of the DASH diet on HOMA-IR, serum hs-CRP levels, and biomarkers of oxidative stress have previously been studied in obese subjects and patients with type 2 diabetes [26,34,35]. Hindler et al. [36] showed the improvements in insulin sensitivity of overweight people following consumption of the DASH diet. Administration of the DASH diet to prehypertensive individuals for 20 wk has resulted in reduced insulin resistance [37]. The same findings also have been reported in patients with metabolic syndrome [38]. It seems that the DASH diet could be recommended as a healthy dietary pattern to all individuals, whether pregnant or not, with metabolic abnormalities.

We did not find a significant effect of the DASH diet on serum hs-CRP levels. This finding is in contrast to earlier epidemiologic evidence that have suggested an inverse association between high-fiber, low-glycemic index diets and inflammation [39,40]. Furthermore, even in healthy individuals, significant reductions in serum hs-CRP levels have been reached after consumption of the DASH diet [41]. Similar findings also have been shown in patients with diabetes [26]. Adherence to the DASH diet in normotensive adults just for 3 wk was associated with a significant decrease in serum hs-CRP levels [34]; however, these investigators failed to find a significant effect in obese individuals with hypertension. The effect of dietary intakes on serum CRP levels still remains to be understood. Findings from previous studies might be confounded by unmeasured factors or might be the result of residual confounding. Additional studies are needed to determine whether the DASH diet could affect inflammatory factors independently.

We observed that consumption of the DASH diet led to a significant increase in plasma TAC and total GSH. Increased plasma antioxidant capacity as well as decreased oxidative stress also has been reported in obese individuals with hypertension after consumption of the DASH diet for 4 wk [35]. Adherence to the DASH diet for 3 mo has led to a non-significant increase in plasma TAC in healthy individuals [42]. Al-Solaiman et al. [43] found the beneficial effects of the DASH diet on F2-isoprostane level, which is a measure of oxidative stress. Overall, as pregnancy is associated with decreased TAC and increased oxidative stress, consumption of the DASH diet by pregnant women could help them control the complications to which these conditions might lead.

Several mechanisms can explain the beneficial effects of DASH diet on human health. In the current study, the simple sugar content of the DASH diet was about half that of the control diet. Furthermore, its fiber content was 1.5 to 2 times higher than that the control diet. Earlier studies have indicated that a high-sucrose diet leads to increased plasma glucose levels, serum lipid profiles and insulin resistance [44–46]. The DASH diet contains high amounts of arginine-rich foods including fish, soy, beans, lentils, whole grains, nuts, parsley, and fresh basil. The high arginine content of the DASH diet also might explain its beneficial effects on insulin resistance. Improvements in insulin resistance following arginine intake have been attributed to increased production of nitric oxide and improved endothelial function [47]. The DASH diet is also a rich source of dietary magnesium and calcium, which could in turn affect insulin resistance [48–50]. The effect of the DASH diet on oxidative stress could be attributed to its high content of antioxidant-rich fruits and vegetables [35,51,52]. However, as the participants in the study were all pregnant women with GDM, it was unethical to reduce their consumption of fruits and vegetables. Therefore, even participants in the control diet were consuming high amounts of fruits and vegetables. When we compared individual fruits and vegetables between the two groups, we found that the dietary intakes of antioxidant-rich fruits (prunes, raisins, blackberries, strawberries, plums, oranges, and red grapes) and vegetables (kale, spinach, Brussels sprouts, broccoli, onions, and eggplant) were significantly higher in the DASH group than in the control group. Total vitamin C intake in the DASH group was nearly two times greater than that in the control group. Vitamin C, a major component of TAC, can decrease the nicotinamide adenine dinucleotide phosphate-oxidase activity, which is a major superoxide-generating enzyme [53]. The arginine content of the DASH diet might also contribute to its beneficial effects of oxidative stress. Arginine intake has been shown to reduce serum levels of angiotensin II and measures of oxidative stress. Arginine intake has been shown to reduce serum levels of angiotensin II and measures of oxidative stress. Arginine intake has been shown to reduce serum levels of angiotensin II and measures of oxidative stress.

Our findings must be interpreted in the context of some limitations. The first limitation is the relatively short duration of intervention. Long-term interventions might result in greater changes. However, it must be kept in mind that participants in the current study were pregnant women who may be concerned that dieting could have a negative effect on their babies. Second, we could not assess the effects of the DASH diet on pregnancy outcomes as well as on biochemical indicators of newborns.
Conclusion

Consumption of the DASH diet in pregnant women with GDM had beneficial effects on FPG, serum insulin levels, HOMA-IR score, plasma TAC, and total GSH levels. The effects of this dietary pattern on pregnancy outcomes need to be investigated in future studies.

Acknowledgment

The present study was supported by a grant (No. 91104) from the vice-chancellor for research, KUMS, and Iran. The authors would like to thank the staff of Naghavi and Shaheed Beheshti Clinics (Kashan, Iran) for their assistance in this project. The study was supported by a grant (No. 91104) from Kashan University of Medical Sciences.

Clinical trial registration number: IRCT201204065623N2.

Name of trial registry: Effects of the Dietary Approaches to Stop Hypertension (DASH) on metabolic profiles in gestational diabetes.


References


