Adherence to a Dietary Approaches to Stop Hypertension (DASH)-style Diet in Relation to Preeclampsia: A Case-Control Study

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Maternal diet is an important potential factor associated with the risk of preeclampsia. However, it is unclear whether adherence to a Dietary Approaches to Stop Hypertension (DASH)-style diet can reduce the development of preeclampsia. To examine the potential association, we conducted a hospital-based case-control study at the First Affiliated Hospital of Zhengzhou University, China. A total of 449 cases with preeclampsia and 449 controls were studied. Dietary information was collected using a validated food frequency questionnaire (FFQ). DASH scores were calculated according to nutrients/food emphasised or minimised in the DASH diet. The calculated DASH scores ranged from 11 to 38 for all of the participants, and the DASH scores of the cases were significantly lower than those of the controls (23.48 ± 4.58 vs 24.51 ± 4.51; p = 0.001). Participants in the fourth quartile of the DASH score were 45% less likely to have preeclampsia than those in the first quartile in the crude model (Q4 vs Q1, odds ratio [OR]: 0.55; 95% confidence interval [CI]: 0.38, 0.80; p_trend = 0.001). The relationship remained significant in the model adjusted for multiple confounders, especially for major risk factors of preeclampsia (OR: 0.53; 95% CI: 0.36, 0.78; p_trend = 0.001). Our findings suggest an inverse relationship between adherence to a DASH-style diet and the odds of preeclampsia. Further large-scale cohort studies or randomised controlled trials are warranted to confirm these relationships.

Preeclampsia is a pregnancy-specific complication that occurs after 20 weeks of gestation and is characterised by hypertension, proteinuria and oedema, with or without multiple organ damage. It is a major cause of foetal and maternal morbidity and mortality worldwide, and affects 2–8% of all pregnancies. Currently, the only definitive treatment for preeclampsia is to terminate the pregnancy. Therefore, primary prevention of preeclampsia is vital.

Evidence indicates that maternal diet is an important potential factor affecting the incidence of preeclampsia. Studies have shown that diets rich in vegetables and fruits or various nutrients such as vitamin D, calcium and zinc are associated with lower levels of oxidative stress and inflammation, which are both recognised pathogenic factors for preeclampsia. However, individual foods or nutrients are consumed in various characteristic combinations, so nutritional epidemiologists have recommended using overall dietary patterns to find links between diet and diseases. Recent studies have used factor analysis to explore the relationship between dietary patterns and the risk of preeclampsia. However, the dietary patterns obtained in these studies were only appropriate for local residents and the results were not comparable. Universal dietary recommendations for the prevention of preeclampsia remain limited.

The Dietary Approaches to Stop Hypertension (DASH) diet is an established dietary pattern rich in whole grains, fruits, vegetables, low-fat dairy and plant proteins from nuts and legumes, but low in red/processed meat, sweets and sugar-sweetened beverages. The DASH diet was originally designed and evaluated for lowering blood pressure, but recent studies have shown its benefits for glioma, nonalcoholic fatty liver disease and other conditions.
of the DASH diet was previously found to be associated with a decreased risk of GDM19, we performed a sensitivity analysis to exclude the influence of GDM on the results.

Table 1. General characteristics and dietary intakes of participants based on patients with preeclampsia and control group. BMI: body mass index. aData are mean ± standard deviation or number (%) or M (Q1, Q3). Independent sample t-test (when satisfying a normal distribution) or Mann-Whitney U test (when not satisfying a normal distribution) for quantitative variables and chi-square test for qualitative variables.

|                  | Cases (n = 449) | Controls (n = 449) | p*b |
|------------------|-----------------|-------------------|-----|
| Age (years)      | 30.77 ± 4.94    | 30.98 ± 4.82      | 0.525 |
| Gestational age (weeks) | 34.12 ± 2.88    | 34.48 ± 2.85      | 0.063 |
| Pre-pregnancy BMI (kg/m²) | 23.66 ± 3.87    | 22.47 ± 3.43      | <0.001 |
| GDM (%)          | 60 (13.4)       | 60 (13.4)         | 1    |
| Nulliparity (%)  | 255 (56.8)      | 299 (66.7)        | 0.002 |
| Physical activity (MET (hour/day)) | 26.94 ± 3.99    | 26.44 ± 4.45      | 0.078 |
| Total energy (kcal/d) | 1849.2 ± 502.72 | 1983.06 ± 529.49  | <0.001 |
| Carbohydrate (% of total energy) | 52.95 ± 7.33    | 52.32 ± 7.06      | 0.195 |
| Protein (% of total energy) | 13.30 ± 2.37    | 14.19 ± 2.43      | <0.001 |
| Fat (% of total energy) | 35.14 ± 7.08    | 34.98 ± 6.19      | 0.713 |
| Fish (g/d)       | 4.07 (0.95, 11.37) | 7.60 (1.90, 16.29) | <0.001 |
| Eggs (g/d)       | 52.80 (22.63, 79.20) | 52.80 (30.17, 79.20) | 0.001 |
| Whole grains and mixed beans (g/d) | 6.91 (1.67, 16.48) | 7.14 (1.67, 17.51) | 0.361 |
| Fruits (g/d)     | 281.71 (173.79, 401.57) | 335.96 (226.8, 502.19) | <0.001 |
| Vegetables (g/d) | 299.40 (229.33, 413.39) | 335.73 (261.65, 460.67) | <0.001 |
| Nuts and legumes (g/d) | 21.50 (9.50, 38.41) | 25.08 (12.46, 46.01) | 0.003 |
| Dairy products (g/d) | 147.62 (53.57, 262.13) | 184.52 (83.33, 280.57) | 0.014 |
| Red/processed meat (g/d) | 27.90 (10.30, 50.35) | 42.09 (21.43, 74.58) | <0.001 |
| Soft drinks and sweets (g/d) | 13.33 (6.67, 30.00) | 11.43 (5.33, 26.67) | 0.076 |
| Sodium (mg/day)  | 4761.34 (4133.65, 5445.13) | 4555.85 (3976.99, 5135.09) | <0.001 |
| DASH score       | 23.48 ± 4.58    | 24.51 ± 4.51      | 0.001 |

metabolic disorders such as cardiovascular disease17, type 2 diabetes18 and gestational diabetes mellitus (GDM)19. However, so far, no study has assessed the association between the DASH diet and the odds of preeclampsia.

Although preeclampsia is also characterised by hypertension, its mechanism is not quite the same as that of adult hypertension. Therefore, the aim of this study was to explore the association between adherence to a DASH-style diet and the odds of preeclampsia among pregnant women in China. In addition, considering that the DASH diet was previously found to be associated with a decreased risk of GDM19, we performed a sensitivity analysis to exclude the influence of GDM on the results.

Results

Participants. Of the 708 inpatients with preeclampsia seen in the hospital, 162 (22.9%) did not meet the inclusion criteria for this study. Of the 546 eligible subjects, 34 (6.2%) cases were excluded due to incomplete surveys or extreme energy intakes (less than 800 or more than 4200 kcal/d)19, and 63 (11.5%) cases refused to participate. In the end, 449 cases were retained in the analysis, including 389 (86.7%) cases without GDM and 60 (13.3%) cases with GDM. In addition, 449 eligible controls from the same hospital, matched for age, gestation week and GDM, were enrolled.

Basic characteristics and dietary intakes of case and control group. The basic characteristics and dietary intakes of the participants according to case/control status are presented in Table 1. There was no significant difference between the two groups in mean age and gestational age. Mean pre-pregnancy BMI was significantly higher in patients with preeclampsia than in the control group (p < 0.001). Compared with the control group, the cases with preeclampsia had lower total dietary energy and protein intake, consumed significantly less fish, eggs, fruits, vegetables, nuts and legumes, dairy products and red/processed meat. The preeclampsia cases consumed significantly more sodium and were more likely to be nulliparous than the controls. The calculated DASH scores for all participants ranged from 11 to 38, and the cases had significantly lower adherence to the DASH diet than the controls (23.48 ± 4.58 vs 24.51 ± 4.51; p = 0.001).

General characteristics and dietary intakes of the participants by quartiles of DASH score. The general characteristics and dietary intakes of the participants in increasing quartiles of the DASH score are shown in Table 2. The participants in the highest quartiles of the DASH score had higher age and physical activity levels and lower pre-pregnancy BMI than the other quartiles. Adherence to the DASH diet was associated with greater intakes of protein, fish, fruits, vegetables, nuts and legumes, dairy products and red/processed meats. Individuals in the top quartile of the DASH diet had lower intakes of soft drinks and sweets and sodium than those in the bottom quartile. There were no significant differences in consumption of eggs or whole grains and mixed beans between quartiles of the DASH score.
The above results were consistent with our study in terms of the positive scoring and reverse scoring components of a DASH-style diet.

Furthermore, several previous studies have shown that the components of the DASH diet have different effects on preeclampsia. A meta-analysis reported that a healthy dietary pattern, rich in vegetables, fruits, legumes and whole grains, was significantly associated with lower odds of preeclampsia. These components had a large
fruits, were associated with decreased risk of preeclampsia. A possible explanation is that added sugar provides significantly associated with increased risk of preeclampsia, while foods with natural sugars, such as fresh and dried.

In Norway suggested that foods with a high content of added sugar and sugar-sweetened beverages were significantly associated with increased risk of preeclampsia, while foods with natural sugars, such as fresh and dried fruits, were associated with decreased risk of preeclampsia. A possible explanation is that added sugar provides excess energy intake while foods with a high content of natural sugars are rich in dietary fibre. Red or processed meat and sodium are reverse scoring components of the DASH diet. However, the relationship between these components and preeclampsia and its mechanism has not been reported. More research is needed in the future to uncover the specific mechanism of each component of the DASH diet and the synergistic effects among them.

The Chinese diet is characterised by high consumption of plant foods (grains, vegetables, etc.), lack of high-quality proteins (lean meat, fish, dairy products, etc.) and high oil and salt. The characteristics of high sodium, low calcium and low high-quality protein are the opposite of what the DASH diet recommends and may be important factors in the pathogenesis of preeclampsia. Therefore, for Chinese pregnant women, greater adherence to a DASH-style diet may be associated with decreased odds of preeclampsia. Further studies are also needed in other countries where the diets and foods are naturally different.

This study has many advantages. First, it is the first study to assess the association between adherence to a DASH-style diet and the odds of preeclampsia. Second, our study used a matched case-control design to control for the three major confounders, age, gestational age and GDM. In addition, the relatively large sample size of participants improved the validity, and the sensitivity analysis improved the reliability of the results.

However, some limitations must also be considered when interpreting our findings. First, although we used a validated FFQ to measure dietary intake, there were still inevitable measurement errors and recall bias. Nonetheless, the measurement accuracy benefitted from the employment of trained interviewers who used photographs of food portion sizes to administer the FFQ through face-to-face interviews. Second, considering that patients with preeclampsia have a relatively short time from onset to delivery, we only collected information on the dietary intake of the pregnant women during the final three months before delivery to reduce the recall bias of the FFQ, which may have led to a failure to account for the potential influence of early pregnancy diet on preeclampsia.

In conclusion, our findings suggest an inverse relationship between adherence to a DASH-style diet and the odds of preeclampsia. Further larger-scale cohort studies or randomised controlled trials are needed to confirm the relationship.
Methods

Participants. This hospital-based case-control study was conducted between March 2016 and June 2019 at the First Affiliated Hospital of Zhengzhou University (located in Zhengzhou, a medium-sized city in central China that has been well developed in recent years). Pregnant women of reproductive age (≥18 years) after the 28th week of pregnancy and with single pregnancy were included. The preeclampsia cases were pregnant women who had been diagnosed with preeclampsia by a physician, according to China’s ‘Diagnosis and treatment guideline of hypertensive disorders in pregnancy’ (2015). In this guideline, preeclampsia is defined as systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg after 20 weeks of gestation and accompanied by any of the following characteristics: (1) urinary protein ≥ 0.3 g/24 h, or urinary protein/creatinine ratio ≥ 0.3, or random urinary protein ≥ (+) (the test method used when urinary protein cannot be quantified); (2) no proteinuria but accompanied by damage to any of the following organs or systems: heart, lung, liver, kidney and other important organs, or abnormal changes in the blood system, digestive system, nervous system, placental foetus involved, etc. The controls were enrolled among pregnant women from the same hospital without hypertension or proteinuria and were matched with the case group based on age, gestational weeks and GDM.

The exclusion criteria for subjects in both groups were as follows: (1) patients with heart disease, malignancy, hyperthyroidism, immune system diseases, chronic renal insufficiency, and other endocrine system diseases; and (2) patients with epilepsy, depression and other mental or cognitive dysfunction.

Calculation of sample size. On the basis of earlier evidence, we assumed that approximately 30% of the people in the control group would have higher DASH scores, and the estimated OR between the higher DASH scores and preeclampsia odds was 0.6017. With 90% power (β = 0.10), type I error of 0.05 (α = 0.05) and desired CI of 0.95, the minimum required sample size in each group was calculated to be 394, that is, a total of 788 participants. Finally, 449 cases and 449 controls were enrolled in this study.

Assessment of dietary intake. The dietary intake of the study participants during the last three months before delivery was assessed through a valid and reliable semiquantitative food frequency questionnaire (FFQ)24, which included 78 items of foods commonly consumed by Chinese. For each food item, 4 possible frequencies (never, every month, every week and every day) and the amount of consumption each time in grams or millilitres were available. The daily intakes of energy (kcal/d) and key nutrients from each food were calculated according to the Chinese Food Composition Tables25.

Assessment of adherence to a dietary approaches to stop hypertension-style diet. A DASH score was calculated based on the FFQ for each participant. According to Fung’s method26, the DASH score was constructed based on the foods and nutrients emphasised or minimised in the DASH diet, focusing on eight components: high intake of whole grains; fruits; vegetables; nuts and legumes; and low-fat dairy products, and low intake of red/processed meats; sweetened beverages; and sodium26. Because we could not assess the dietary intake of whole grains and low-fat dairy products accurately, we instead calculated whole grains and mixed beans, and dairy products, respectively. Considering that pregnant women consume few sugary drinks, we added sweets to this component.

The scoring criteria and food composition of the DASH-style diet in our study are shown in Table 5. First, the energy-adjusted amounts of components of the DASH-style diet were obtained through the residual method27. Subsequently, quintile cut-off points for each component of the DASH-style diet were obtained in all participants. For the five groups of whole grains and mixed beans, fruits, vegetables, nuts and legumes, and dairy products, those in the highest quintile were given 5 points and those in the lowest quintile received 1 point. In contrast, for the remaining three components, the lowest quintile was given 5 points and the highest received 1 point. An overall DASH score ranging from 8 to 40 was obtained by summing the eight component scores. Individuals with higher DASH scores were more likely to follow the DASH diet.

Assessment of other variables. Information on sociodemographic characteristics, lifestyle habits, pre-pregnancy weight, history of disease, physical activity, menstrual and pregnancy history was obtained through a structured questionnaire. The height and weight of the participants were measured to the nearest 0.1 cm and 0.1 kg, respectively, without shoes and in light clothing. After a rest of ≥10 min, blood pressure was measured at least twice on the left arm with a sphygmomanometer; a third measurement was taken on any occasion when the first two DBP or SBP values differed by more than 3 mmHg or 4 mmHg. At least two measurements were averaged for further analysis. The participants’ physical activity during pregnancy included daily occupational, leisure-time and household-chores, and was expressed as metabolic equivalents (MET) hour/day28. Each individual’s body mass index (BMI) was calculated as weight (kg)/height (m²).

Statistical analysis. The Shapiro-Wilk test and Q-Q plots were used to check the normality of the general characteristics and dietary intake. The general characteristics of the cases and controls were compared using the chi-square test for categorical variables and independent samples t-test for continuous variables and were described by number and mean ± SD (normal distribution). Considering that the dietary intake did not show a normal distribution, we used the Mann-Whitney U test to compare the dietary intakes among cases and controls and described the results using M (p15–p85). To assess the association of a DASH-style diet with preeclampsia, the total DASH score was divided into four ascending categories on an ordinal scale. The general characteristics were also compared among quartiles of the DASH score using the chi-square test for categorical variables and one-way ANOVA for continuous variables. The dietary intakes of the participants by quartiles of the DASH score were analysed using analysis of covariance (ANCOVA) adjusted for total energy intake.
Table 5. Scoring criteria and food composition for the DASH-style diet in this case-control studya. DASH: Dietary Approaches to Stop Hypertension; FFQ: food frequency questionnaire; Q: quintile. Food intake across Q1 (Low Consumption) to Q5 (High Consumption).

| Component/Quintile | Foods | Scoring criteriaa |
|--------------------|-------|-------------------|
| Whole grains and mixed beans | Brown rice, wholemeal bread, whole grain cereal, oats, popcorn; Red beans, mung beans and other mixed beans | Positive scoring: Q1 = 1 point, Q2 = 2 points, Q3 = 3 points, Q4 = 4 points, Q5 = 5 points |
| Fruits | All fruits | |
| Vegetables | All vegetables except potatoes and legumes | Reverse scoring: Q1 = 5 points, Q2 = 4 points, Q3 = 3 points, Q4 = 2 points, Q5 = 1 point |
| Nuts and legumes | Nuts and peanut butter, soybean, tofu, soybean milk, peas | |
| Dairy | Milk, yoghurt, cottage cheese | |
| Red and processed meats | Pork, beef, lamb, deli meats, organ meats, hot dogs, sausage, bacon | |
| Beverages and sweets | Carbonated and noncarbonated sweetened beverages, cake, egg tart, pumpkin cake and other desserts | |
| Sodium | Sum of sodium content of all foods in FFQ (including salt) | |

The association of the DASH diet with preeclampsia was assessed using binary logistic regression. In addition to the original model, three different models were developed: Model 1 was adjusted for age, gestational age and GDM (yes/no). Model 2 was further adjusted for total energy intake (kcal/d), physical activity (MET) and nulliparity (yes/no). Model 3 comprised Model 2 plus an adjustment for pre-pregnancy BMI. In all models, the first quartile of the DASH score was considered as the reference group. The overall trend of OR across increasing quartiles of the DASH score was examined by considering the median score in each category as a continuous variable. All probability values below 0.05 were considered statistically significant. All of the statistical analyses were performed using SPSS (version 25.0; SPSS Inc., Chicago, IL).

Ethical approval. This study was approved by the Ethics Committee of Scientific Research and Clinical Trials of the First Affiliated Hospital of Zhengzhou University and written informed consent was obtained from all participants. All of the procedures were performed in accordance with the approved guidelines laid down in the Declaration of Helsinki.

Data availability Additional data are available from the corresponding author upon reasonable request.

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Author contributions
Y.L., X.Z. and D.D. designed the research study. Y.C., W.D., D.D. and W.F. performed the research. Y.C., Y.L. and H.C. contributed to analysis of the data. Y.C. and Y.Q. drafted the manuscript. Y.L., Y.B. and Q.L. revised the manuscript. All authors read and approved the final manuscript.

Competing interests
The authors declare no competing interests.

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