A Vegetable Dietary Pattern Is Associated with Lowered Risk of Gestational Diabetes Mellitus in Chinese Women

Qiong Chen¹,², Weiwei Wu¹, Hailan Yang¹, Ping Zhang³, Yongliang Feng¹, Keke Wang³, Ying Wang², Suping Wang², Yawei Zhang²,⁴,⁵

¹Affiliated Cancer Hospital of Zhengzhou University, Henan Cancer Hospital, Zhengzhou, China, ²Department of Epidemiology, Shanxi Medical University School of Public Health, Taiyuan, China, ³Department of Obstetrics, The First Affiliated Hospital, Shanxi Medical University, Taiyuan, China, ⁴Department of Surgery, Yale University School of Medicine, New Haven, CT, USA

Background: Identification of modifiable dietary factors, which are involved in the development of gestational diabetes mellitus (GDM), could inform strategies to prevent GDM.

Methods: We examined the dietary patterns in a Chinese population and evaluated their relationship with GDM risk using a case-control study including 1,464 cases and 8,092 control subjects. Propensity score matching was used to reduce the imbalance of covariates between cases and controls. Dietary patterns were identified using factor analysis while their associations with GDM risk were evaluated using logistic regression models.

Results: A “vegetable” dietary pattern was characterized as the consumption of green leafy vegetables (Chinese little greens and bean seedling), other vegetables (cabbages, carrots, tomatoes, eggplants, potatoes, mushrooms, peppers, bamboo shoots, agarics, and garlic), and bean products (soybean milk, tofu, kidney beans, and cowpea). For every quartile increase in the vegetables factor score during 1 year prior to conception, the first trimester, and the second trimester of pregnancy, the GDM risk lowered by 6% (odds ratio [OR], 0.94; 95% confidence interval [CI], 0.89 to 0.99), 7% (OR, 0.94; 95% CI, 0.88 to 0.99), and 9% (OR, 0.91; 95% CI, 0.86 to 0.96).

Conclusion: In conclusion, our study suggests that the vegetable dietary pattern is associated with lower GDM risk; however, the interpretation of the result should with caution due to the limitations in our study, and additional studies are necessary to explore the underlying mechanism of this relationship.

Keywords: Case-control studies; Diabetes, gestational; Diet; Vegetables

INTRODUCTION

Gestational diabetes mellitus (GDM), defined as glucose intolerance first detected during pregnancy, is one of the most common pregnancy complications and has been associated with adverse health outcomes for both mothers and their offspring [1]. GDM affects approximately 5% to 17% of all pregnancies worldwide, and the prevalence has increased over the past 20 years and this upward trend is expected to continue due to a rising number of overweight and obese women of childbearing age.
Dietary components are associated with GDM development, making these modifiable factors ideal for informing GDM prevention strategies. Dietary intervention trials with probiotics or myo-inositol supplements were efficient in reducing GDM risk [3-5]. Data from observational studies reveal that distinct dietary components including energy, nutrients (total fat, cholesterol, and heme iron), and selected food items (red/processed meats and eggs) are associated with GDM risk [1,6]. Because of potential interactions among these nutrients and food items, it is difficult to single out each item's specific effect [6].

Dietary pattern analyses or dietary indexes like the Healthy Eating Index (HEI), takes into consideration interactive and cumulative effects of nutrients or foods. To date, most of the studies examining maternal dietary patterns and GDM have been conducted in Western populations [6]. Findings from the Nurses' Health Study II suggest that women who adhered to the low consumption of the prudent dietary pattern, high consumption of the Western dietary pattern, or a low-carbohydrate dietary pattern [7] were associated with an elevated risk for developing GDM, while Mediterranean diet (MD) and high HEI adherers demonstrated lower GDM risk [8]. Studies conducted in Iran [9], the Mediterranean basin [10], and Australia [11] also verified lower GDM risk among MD adherers. Furthermore, adherence to a prudent dietary pattern was associated with lower risk of GDM among Iceland women [12]. However, a study from Singapore representing multi-ethnic Asian cohort identified different dietary patterns compared to results of similar studies conducted in Western populations, and it found that the seafood-noodle-based-diet was associated with a lower risk of GDM [13].

To the best of our knowledge, only one study including 3,063 pregnant women conducted in Guangzhou, China examined dietary patterns in relation to GDM [14]. In this study, four dietary patterns vegetable, protein-rich, prudent, and sweets/seafood patterns were identified. The highest tertile of vegetable score and sweets/seafood score were associated with reduced (odds ratio [OR], 0.79; 95% confidence interval [CI], 0.64 to 0.97) and increased (OR, 1.23; 95% CI, 1.02 to 1.49) risk of GDM respectively. There are several limitations to this study. First of all, the study was conducted in Guangzhou, China. Given the vast differences in dietary habits between Northern and Southern China, the results of this study are not generalizable. Second of all, this study only used frequency of food intake to analyze dietary consumption and did not collect information on portion sizes, thus preventing the adjustment of total energy intake. Therefore, the effect of diet pattern and risk of GDM still needs to be verified in China. To examine the dietary pattern in Chinese population and evaluate its relationship with GDM risk, we conducted a case control study based on a birth cohort in Taiyuan, China.

METHODS

The study participants were recruited from the First Affiliated Hospital of Shanxi Medical University in Taiyuan, China when they came to the hospital for delivery between March 1, 2012 and December 30, 2016. Women aged 18 years or older with gestational age of 20 weeks or more and without mental illness were eligible for the study. Although 10,320 pregnant women were enrolled in the study, 91 pregnant women with previous diabetes and 94 pregnant women whose gestational age less than 20 weeks were excluded, resulting in a total sample size of 10,137 pregnant women.

All study procedures were approved by the Institutional Review Board (IRB) at the Shanxi Medical University with the approval IRB number of 2011143. Written consents were obtained from each participant. Information on demographic factors, reproductive and medical history, smoking, and alcohol were collected using standardized questionnaires [15] administered by trained interviewers. Information on birth outcomes and pregnancy complications were acquired from medical records.

Dietary intake assessment

Dietary intake was assessed using a 33-item semi-quantitative food frequency questionnaire (FFQ) [16]. Participants were asked to report the frequency (times per day, week, or month) and standard portion size for each food item during the year before conception alone with the first (1 to 13 weeks), second (14 to 27 weeks), and third (≥28 weeks) trimesters of pregnancy. We did not analyze the food intake for the third trimester because GDM diagnosis usually occurs before this time period. The reported frequency and portion size of each food item were converted to grams per day.

The 33 food items were classified into the following 11 food groups according to the similarity of nutrient content: cereals (rice, wheat flour, and coarse food grain), meats (pork, beef,
A vegetable dietary pattern lowered GDM risk

mutton, poultry, fresh water fish, marine fish, and shell fish), dairy (milk, milk powder, and yogurt), eggs, bean products (soybean milk, tofu, and cowpeas), green leafy vegetables, other vegetables (cabbages, carrots, tomatoes, eggplants, potatoes, mushrooms, peppers, bamboo shoots, agarics, and garlic), alga, pickles, nuts, and fruits.

**Cases and controls selection**

Blood glucose was tested using a 75 g oral glucose tolerance test during 24 to 28 weeks of gestation. Subjects were diagnosed as having GDM according to the International Association of Diabetes and Pregnancy Study Groups Recommendations in 2010 [17], if they met at least one of the following criteria: (1) fasting blood glucose >5.1 mmol/L, (2) 1-hour blood glucose >10.0 mmol/L, and/or (3) 2-hour blood glucose >8.5 mmol/L. A total of 1,523 women had GDM (cases) while 8,614 pregnant women did not (controls). Gestational hypertension was diagnosed using the criteria of systemic pressure equal to or more than 140 mm Hg or diastolic pressure equal to or more than 90 mm Hg after 20 weeks of gestations. Due to missing FFQ information, 59 cases and 522 control subjects were excluded from the study. In the end, a total of 1,464 cases and 8,092 control subjects were included in the analysis. After propensity score matching, 1,464 cases and 2,928 controls were included in the analysis.

**Statistical analysis**

A chi-square test was conducted to compare the distributions of selected characteristics between cases and controls. Dietary patterns were estimated via principal component factor analysis. The factors were rotated by an orthogonal transformation (Varimx rotation function in SAS) to achieve simpler structure with greater interpretability. The eigenvalues, the Scree test, and interpretability of factors were utilized to determine the number of factors. The factor score of each pattern was regrouped into four groups according to quartile.

Propensity score matching was used to balance the distribution of characteristics in cases and controls. It was estimated with the use of logistic regression model, with the use of GDM as dependent variable and characteristics including age, education, body mass index (BMI), gestational week, alcohol drinking, smoking, parity, gestational hypertension, preterm, weight gain, family history of GDM, and total energy intake per day as covariates. Matching was conducted with the use of 1:2 nearest neighbor matching without replacement using R package of “MatchIt” (R Foundation for Statistical Computing, Vienna, Austria). Standardized difference was estimated and used to assess the balance before and after matching, and the value less than 0.1 for a given covariate indicate a relatively small imbalance.

Unconditional logistic regression models were used to estimate the associations between dietary patterns and GDM risk after adjusting for covariates in Table 1 in pre-matched data. Conditional logistic regression models were used in matched data. Propensity score matching was performed using R package of “MatchIt,” and other statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA).

**RESULTS**

Before propensity score matching, there were difference between the case and control groups in several variables including maternal age, education, BMI, gestational week, parity, gestational hypertension, weight gain, preterm, and family history of diabetes. With the use of propensity score matching, 1,464 GDM cases were matched with 2,928 control subjects. After matching, the standardized differences were less than 0.1 for all variables, suggesting only small difference between the two groups (Table 1).

The number of factors were determined according to the Kaiser criterion (eigenvalues over 1.0), the factor analysis identified three major factors vegetables, cereals, and meats that could explain 52.67%, 52.48%, and 50.47% of the variance of the original information respectively. The factor loading of the three patterns during these periods was shown in Table 2. The three dietary patterns identified in these three periods were similar. The first factor loaded heavily with the following food or food groups: green leafy vegetables, other vegetables, and bean products. The second factor loaded heavily with cereals, pickles, alga, fruits and nuts. The third factor loaded heavily with meats, dairy, eggs, nuts, and fruits. We labeled these three factors as “vegetables,” “cereals,” and “meats,” respectively.

As shown in Table 3, the vegetable dietary pattern was associated with lower risk of GDM before and after propensity score matching. The lowered GDM risk that associated with vegetable pattern was consistent across the three time periods with a slightly stronger effect during the second trimester (P for trend=0.025, 0.018, and 0.001, respectively). When the analysis stratified by exercise status, the OR was 0.93 (95% CI, 0.87 to 0.99), 0.92 (95% CI, 0.87 to 0.98), 0.90 (95% CI, 0.84 to 0.90).
### Table 1. Subjects characteristics before and after propensity-score matching

| Characteristic                  | Before matching | After matching | P value | Standardized mean difference | P value | Standardized mean difference |
|--------------------------------|----------------|---------------|---------|------------------------------|---------|------------------------------|
|                                | Cases (n=1,464) | Controls (n=8,092) |         |                              | Cases (n=1,464) | Controls (n=2,928) |
| Age, yr                        |                |               |         |                              |          |                              |
| <25                            | 31.0±4.8       | 29.3±4.5      | <0.001  | 0.339                        | 31.0±4.8 | 31.0±4.8                    | 0.489 | 0.022 |
| 25–34                          | 1,083 (74.0)   | 6,086 (75.2)  | <0.001  | 0.339                        | 1,083 (74.0) | 2,115 (72.2)               |         |       |
| ≥35                            | 303 (20.7)     | 1,051 (13.0)  | <0.001  | 0.339                        | 303 (20.7) | 620 (21.2)                 |         |       |
|                                | 1,062 (72.5)   | 5,550 (68.6)  | 0.003   | 0.089                        | 1,062 (72.5) | 2,128 (72.7)               | 0.952 | –0.003 |
| Body mass index, kg/m²         |                |               |         |                              |          |                              |
| <18.5                          | 22.9±3.7       | 21.5±3.1      | <0.001  | 0.398                        | 22.9±3.7 | 22.8±3.5                    | 0.249 | 0.043 |
| 18.5–23.9                      | 109 (7.4)      | 1,153 (14.2)  | <0.001  | 0.398                        | 109 (7.4) | 229 (7.8)                   |         |       |
| 24–27.9                        | 865 (59.1)     | 5,477 (67.7)  | <0.001  | 0.398                        | 865 (59.1) | 1,779 (60.8)               |         |       |
| ≥28                            | 342 (23.4)     | 1,175 (14.5)  | <0.001  | 0.398                        | 342 (23.4) | 676 (23.1)                 |         |       |
| Gestational week, wk           |                |               |         |                              |          |                              |
| Alcohol drinking during        |                |               |         |                              |          |                              |
| pregnancy                      | 0.10           | 0.04          | 0.510   | 0.224                        | 0.10     | 0.04                       | 0.510 | 0.224 |
| Ever exposed to smoking during  | 0.903          | 0.000         | 0.562   | 0.016                        | 0.903    | 0.000                      | 0.562 | 0.016 |
| the first trimester            | 0.500          | 0.000         | 0.562   | 0.016                        | 0.500    | 0.000                      | 0.562 | 0.016 |
| Nulliparous women              | 0.803          | 0.548         | <0.001  | 0.117                        | 0.803    | 0.548                      | 0.460 | 0.025 |
| Gestational hypertension       | 0.265          | 0.181         | <0.001  | 0.130                        | 0.265    | 0.181                      | 0.612 | –0.018 |
| Preterm                        | 0.339          | 0.232         | 0.022   | 0.064                        | 0.339    | 0.232                      | 0.970 | –0.002 |
| Weight gain, kg                | 0.152±5.8      | 15.8±5.3      | <0.001  | –0.104                       | 0.152±5.8 | 15.3±5.4                   | 0.494 | 0.021 |
| Family history                 | 0.193          | 0.132         | <0.001  | 0.232                        | 0.193    | 0.132                      | 0.199 | 0.041 |
| Total energy intake, kcal       | 1,345.6±463.3  | 1,353.2±460.8 | <0.001  | –0.016                       | 1,345.6±463.3 | 1,340.7±438.2  | 0.727 | 0.011 |

Values are presented as mean±standard deviation or number (%).

### Table 2. Foods groups factor loadings for the three dietary patterns identified during three different periods of pregnancy

| Foods group | One year before conception | The first trimester of pregnancy | The second trimester of pregnancy |
|-------------|-----------------------------|---------------------------------|---------------------------------|
|              | Vegetable | Cereal | Meat | Vegetable | Cereal | Meat | Vegetable | Cereal | Meat | Vegetable | Cereal | Meat |
| Cereal      | 0.10      | 0.77   | –0.13| 0.11      | 0.74   | –0.18| 0.17      | 0.71   | –0.19| 0.09      | 0.05   | 0.53 |
| Meat        | 0.24      | –0.16  | 0.52 | 0.23      | –0.08  | 0.53 | 0.23      | –0.10  | 0.54| 0.49      | 0.30   | 0.21 |
| Dairy       | 0.09      | 0.04   | 0.57 | 0.08      | –0.12  | 0.64 | 0.08      | –0.12  | 0.63| 0.38      | 0.22   | 0.36 |
| Egg         | 0.17      | –0.13  | 0.60 | 0.13      | –0.02  | 0.56 | 0.13      | –0.02  | 0.55| 0.59      | 0.36   | 0.56 |
| Bean products| 0.75    | 0.01   | 0.22 | 0.73      | 0.03   | 0.27 | 0.51      | –0.04  | 0.36| 0.86      | 0.08   | 0.08 |
| Green leaf vegetable | 0.84 | 0.09   | 0.04 | 0.84      | –0.10  | 0.07 | 0.86      | –0.08  | 0.07| 0.88      | 0.05   | 0.12 |
| Other vegetable| 0.88 | 0.00   | 0.08 | 0.88      | 0.00   | 0.07 | 0.87      | 0.05   | 0.12| 0.08      | 0.05   | 0.12 |
| Alga        | –0.08     | 0.67   | 0.00 | –0.05     | 0.68   | –0.05| –0.05     | 0.67   | –0.06| 0.41      | 0.04   | 0.50 |
| Pickles     | –0.03     | 0.78   | –0.08| –0.01     | 0.76   | –0.15| –0.03     | 0.77   | –0.15| 0.41      | 0.04   | 0.50 |
| Nuts        | –0.21     | 0.33   | 0.56 | –0.21     | 0.41   | 0.50 | –0.25     | 0.40   | 0.50| 0.29      | 0.58   | 0.30 |
A vegetable dietary pattern lowered GDM risk

0.95) during the three periods in exercise subjects; the OR was 1.07 (95% CI, 0.66 to 1.75), 1.01 (95% CI, 0.64 to 1.61), 1.01 (95% CI, 0.63 to 1.62) in non-exercise subjects. The cereals and meats dietary patterns were not statistically significantly asso-

Table 3. Vegetable dietary patterns identified from food frequency questionnaires and risk of gestational diabetes mellitus before and after propensity-score matching

| Vegetable dietary pattern | One year before conception | The first trimester of pregnancy | The second trimester of pregnancy |
|---------------------------|-----------------------------|---------------------------------|---------------------------------|
|                           | Cases | Controls | OR    | 95% CI | Cases | Controls | OR    | 95% CI | Cases | Controls | OR    | 95% CI |
| Before matching<sup>a</sup> |       |          |       |        |       |          |       |        |       |          |       |        |
| Q1                        | 391   | 1,999    | 1     |        | 399   | 1,990    | 1     |        | 411   | 1,978    | 1     |        |
| Q2                        | 351   | 2,037    | 0.81  | 0.69–0.95 | 343   | 2,046    | 0.80  | 0.68–0.94 | 351   | 2,038    | 0.79  | 0.68–0.94 |
| Q3                        | 395   | 1,994    | 0.93  | 0.79–1.09 | 389   | 2,000    | 0.91  | 0.78–1.07 | 369   | 2,020    | 0.81  | 0.69–0.95 |
| Q4                        | 327   | 2,062    | 0.77  | 0.65–0.91 | 333   | 2,056    | 0.78  | 0.65–0.91 | 333   | 2,056    | 0.74  | 0.63–0.87 |
| Total                     | 1,464 | 8,092    | 0.94  | 0.89–0.99 | 1,464 | 8,092    | 0.94  | 0.89–0.99 | 1,464 | 8,092    | 0.91  | 0.87–0.96 |
| P for trend               | 0.026 |          |       |        | 0.017 |          |       |        | 0.001 |          |       |        |

After matching

| Q1                        | 391   | 684     | 1     |        | 399   | 688     | 1     |        | 411   | 672     | 1     | 0.001  |
| Q2                        | 351   | 761     | 0.80  | 0.67–0.96 | 343   | 737     | 0.80  | 0.67–0.95 | 351   | 729     | 0.78  | 0.66–0.94 |
| Q3                        | 395   | 732     | 0.94  | 0.79–1.13 | 389   | 758     | 0.88  | 0.74–1.05 | 369   | 784     | 0.77  | 0.64–0.91 |
| Q4                        | 327   | 751     | 0.76  | 0.64–0.91 | 333   | 745     | 0.77  | 0.64–0.92 | 333   | 743     | 0.73  | 0.61–0.87 |
| Total                     | 1,464 | 2,928   | 0.94  | 0.89–0.99 | 1,464 | 2,928   | 0.93  | 0.88–0.99 | 1,464 | 2,928   | 0.91  | 0.86–0.96 |
| P for trend               | 0.025 |          |       |        | 0.018 |          |       |        | <0.001 |          |       |        |

OR, odds ratio; CI, confidence interval.
<sup>a</sup>Adjusted for covariates including age, education, body mass index, gestational week, alcohol drinking, smoking, parity, gestational hypertension, preterm, weight gain, family history of gestational diabetes mellitus, and total energy intake per day.

Table 4. Diet contents consumed by subjects stratified by the factor score quartile of the vegetable pattern (g/day)

| Food groups                  | Cases (n=1,464) | Controls (n=8,092) | P value |
|------------------------------|-----------------|--------------------|---------|
| One year before conception   |                 |                    |         |
| Bean products                | 55.46±21.74     | 73.06±19.16        | 87.56±25.34 | 131.50±51.32 |
| Green leaf vegetable         | 40.49±14.39     | 59.68±10.28        | 83.99±21.74 | 114.58±35.11 |
| Other vegetable              | 34.44±13.48     | 52.25±8.44         | 65.19±14.22 | 92.57±33.49 |
| Total                        | 130.39±34.56    | 184.99±18.27       | 236.74±25.25 | 338.65±87.23 |
| The first trimester of pregnancy |             |                    |         |
| Bean products                | 57.17±22.88     | 73.59±20.59        | 89.85±29.79 | 130.53±50.59 |
| Green leaf vegetable         | 40.14±14.13     | 59.63±9.99         | 84.33±21.48 | 113.40±34.51 |
| Other vegetable              | 34.93±14.32     | 52.44±9.21         | 65.17±14.57 | 92.40±33.37 |
| Total                        | 132.24±34.52    | 185.66±21.06       | 239.34±27.20 | 336.33±87.54 |
| The second trimester of pregnancy |            |                    |         |
| Bean products                | 39.97±22.94     | 48.30±26.85        | 57.69±27.87 | 85.95±45.81 |
| Green leaf vegetable         | 40.59±14.00     | 61.19±11.34        | 84.01±19.02 | 115.99±36.13 |
| Other vegetable              | 54.73±19.75     | 79.14±14.02        | 99.45±21.15 | 135.44±48.01 |
| Total                        | 135.28±36.40    | 188.62±27.14       | 241.15±26.79 | 337.37±90.84 |

Values are presented as mean ± standard deviation.

https://e-dmj.org Diabetes Metab J 2020;44:887-896
associated with GDM risk.

The contents of the main components in the “vegetables” dietary patterns were shown in Table 4. The vegetables and bean products consumed by the case and control subjects were similar throughout the three periods. The beans and vegetables consumed for the four quartiles were approximately 130, 185, 240, and 335 g/day in cases, and 135, 185, 240, and 330 g/day in controls, respectively.

Table 5. Vegetables dietary pattern and risk of gestational diabetes mellitus stratified by BMI after propensity-score matching

| Vegetable dietary pattern | One year before conception | The first trimester of pregnancy | The second trimester of pregnancy |
|---------------------------|-----------------------------|---------------------------------|----------------------------------|
|                           | Cases | Controls | OR    | 95% CI | Cases | Controls | OR    | 95% CI | Cases | Controls | OR    | 95% CI |
| BMI < 24 kg/m²             |       |          |       |        |       |          |       |        |       |          |       |        |
| Q1                        | 277   | 499      | 1     |        | 286   | 499      | 1     |        | 288   | 488      | 1     |        |
| Q2                        | 230   | 505      | 0.8   | 0.63–1.01 | 215   | 490      | 0.76  | 0.60–0.96 | 233   | 492      | 0.77  | 0.61–0.97 |
| Q3                        | 257   | 484      | 0.94  | 0.74–1.18 | 260   | 503      | 0.90  | 0.72–1.14 | 244   | 514      | 0.78  | 0.62–0.98 |
| Q4                        | 210   | 530      | 0.7   | 0.56–0.89 | 213   | 516      | 0.69  | 0.55–0.88 | 209   | 514      | 0.67  | 0.53–0.85 |
| Total                     | 974   | 2008     | 0.92  | 0.85–0.99 | 974   | 2008     | 0.91  | 0.85–0.98 | 974   | 2008     | 0.89  | 0.83–0.96 |
| P for trend               | 0.019 |          | 0.015 |        | 0.002 |          |       |        |
| BMI ≥ 24 kg/m²            |       |          |       |        |       |          |       |        |       |          |       |        |
| Q1                        | 114   | 185      | 1     |        | 113   | 189      | 1     |        | 123   | 184      | 1     |        |
| Q2                        | 121   | 256      | 0.69  | 0.46–1.04 | 128   | 247      | 0.77  | 0.51–1.16 | 118   | 237      | 0.76  | 0.52–1.13 |
| Q3                        | 138   | 248      | 0.92  | 0.62–1.35 | 129   | 255      | 0.85  | 0.57–1.26 | 125   | 270      | 0.77  | 0.52–1.14 |
| Q4                        | 117   | 231      | 0.72  | 0.48–1.08 | 120   | 229      | 0.74  | 0.49–1.11 | 124   | 229      | 0.74  | 0.50–1.09 |
| Total                     | 490   | 920      | 0.94  | 0.83–1.07 | 490   | 920      | 0.93  | 0.82–1.05 | 490   | 920      | 0.92  | 0.81–1.04 |
| P for trend               | 0.331 |          | 0.251 |        | 0.174 |          |       |        |

BMI, body mass index; OR, odds ratio; CI, confidence interval.

Table 6. Vegetables dietary pattern and risk of gestational diabetes mellitus stratified by maternal age after propensity-score matching

| Vegetable dietary pattern | One year before conception | The first trimester of pregnancy | The second trimester of pregnancy |
|---------------------------|-----------------------------|---------------------------------|----------------------------------|
|                           | Cases | Controls | OR    | 95% CI | Cases | Controls | OR    | 95% CI | Cases | Controls | OR    | 95% CI |
| Age < 35 yr               |       |          |       |        |       |          |       |        |       |          |       |        |
| Q1                        | 329   | 557      | 1     |        | 333   | 562      | 1     |        | 345   | 541      | 1     |        |
| Q2                        | 283   | 586      | 0.75  | 0.61–0.93 | 275   | 570      | 0.76  | 0.62–0.94 | 286   | 569      | 0.73  | 0.60–0.91 |
| Q3                        | 301   | 566      | 0.84  | 0.68–1.03 | 299   | 587      | 0.80  | 0.65–0.98 | 275   | 609      | 0.68  | 0.55–0.84 |
| Q4                        | 248   | 599      | 0.65  | 0.52–0.80 | 254   | 589      | 0.66  | 0.53–0.82 | 255   | 589      | 0.63  | 0.51–0.77 |
| Total                     | 1,161 | 2,308    | 0.89  | 0.83–0.95 | 1,161 | 2,308    | 0.89  | 0.83–0.95 | 1,161 | 2,308    | 0.86  | 0.80–0.92 |
| P for trend               | 0.001 |          | 0.001 |        | <0.001 |          |       |        |
| Age ≥ 35 yr               |       |          |       |        |       |          |       |        |       |          |       |        |
| Q1                        | 62    | 127      | 1     |        | 66    | 126      | 1     |        | 66    | 131      | 1     |        |
| Q2                        | 68    | 175      | 0.85  | 0.45–1.59 | 68    | 167      | 0.91  | 0.48–1.70 | 65    | 160      | 0.87  | 0.47–1.64 |
| Q3                        | 94    | 166      | 1.29  | 0.68–2.47 | 90    | 171      | 1.10  | 0.58–2.09 | 94    | 175      | 1.15  | 0.63–2.11 |
| Q4                        | 79    | 152      | 0.82  | 0.43–1.57 | 79    | 156      | 0.78  | 0.49–1.11 | 78    | 154      | 0.91  | 0.49–1.69 |
| Total                     | 303   | 620      | 0.98  | 0.81–1.20 | 303   | 620      | 0.95  | 0.78–1.15 | 303   | 620      | 1.01  | 0.83–1.22 |
| P for trend               | 0.867 |          | 0.595 |        | 0.961 |          |       |        |

OR, odds ratio; CI, confidence interval.
A vegetable dietary pattern lowered GDM risk

Among subjects who younger than 35 years old, control subjects consumed more vegetables (223.9±85.7, 223.9±87.0, 226.6±86.3 g/day) than the case subjects consumed (215.9±89.7, 217.3±89.8, 218.5±91.1 g/day) significantly during 1 year before conception (P=0.011), the first trimester (P=0.038), and the second trimester (P=0.010). Among subjects whose BMI less than 24, control subjects consumed more vegetables (221.8±84.0, 222.1±85.6, 224.5±84.7 g/day) than the case subjects consumed (214.4±86.4, 215.7±87.0, 216.4±87.0 g/day) significantly during 1 year before conception (P=0.024), the first trimester (P=0.055), and the second trimester (P=0.016). Among subjects older than or equal to 35 years old or subjects whose BMI greater than or equal to 24, there was no significant difference in vegetable intake between cases and controls during the periods.

As shown in Tables 5 and 6, analysis stratified by BMI and maternal age suggested that statistically significant associations between the vegetable pattern diet and risk of GDM were only found in women with BMIs less than 24 and who were younger than 35 years old. The lowered GDM risk was also consistent across the three time periods for the women mentioned above. As shown in Supplementary Table 1, stratified analysis by parity was also conducted, and, significant results were only found in nulliparous women during the second trimester of pregnancy.

**DISCUSSION**

In our study, women who adhered to the vegetable dietary pattern had lower GDM risk during the year before pregnancy as well as the first and second trimesters of pregnancy. The GDM risk lowered 6% to 9% for every quartile increase in the vegetable pattern score. Our results were consistent with a previous study conducted in China, which also found lowered GDM risk for women who adhered to a vegetable dietary pattern (root vegetables, beans, mushrooms, melon vegetables, seaweed, other legumes, fruits, leafy and cruciferous vegetables, processed vegetables, nuts, and cooking oil) [14]. The vegetable pattern in our study was slightly different from that in the previous study [14], as fruits, nuts, and cooking oil were excluded from our vegetable pattern. Although Chinese women are advised to follow a set of dietary customs after conception [18], the dietary pattern identified a year prior to pregnancy was the same as that identified in the first and second trimesters of pregnancy. The vegetable pattern in these three periods was all statistically significantly associated with lowered GDM risk. In a Multi-Ethnic Asian Cohort: the GUSTO study, consumption of the vegetable-fruit-rice diet was associated with lower risk of GDM in Chinese participants [13]. Unlike the GUSTO study, our vegetable based dietary pattern excluded rice and fruits.

Although dietary patterns identified in Western populations were different from that in Chinese populations [6,10,11,19], healthy diets rich in vegetables, whole grains, nuts and fish, low in red and processed meats and snacks were generally associated with lowered GDM risk. Vegetables are known to be rich in vitamins and dietary fiber. GDM risk was reported to be associated with vitamin D [20-22], vitamin C [23,24], and dietary fiber [25,26], and these nutrients were the main ingredient of vegetables. Thus, maybe fiber and ameliorated diet quality in general is associated with the lowered GDM risk. However, the lack of meat association with GDM risk is also an issue, as the increased vegetables pattern is usually associated with a reduced meats intake.

The role of vegetable dietary pattern may be related with the reduced concentrations of C-reactive protein and other inflammatory markers [27] that involved in GDM development [28], the role of dietary fiber that reducing adiposity and improve insulin sensitivity [26,29] and improving lipid homeostasis [25,30]. However, the precise pathway remains unclear, and further studies are needed to explore the mechanism behind the relationship between vegetable pattern and GDM risk.

The vegetable dietary pattern was found to be associated with lowered risk of GDM in our study and previous study [14]; however, it still needs verified by further well-designed trials before it is recommended to public. Due to the GDM risk factors include high BMI, advanced maternal age [1], so the stratified analysis was conducted, and the protective effect of vegetable dietary pattern diet was found in women who had BMIs less than 24, and were younger than 35 years old. It may due to subjects in these groups consumed more vegetables, and they focus more on life quality and exercise more during peri-conceptional periods. It was also supported by our results that the protective effect of vegetable pattern diet was only found in exercise subjects. The protective effect of vegetable pattern diet was not shown in older or obese/overweight women, and it is possible that GDM risk is much higher in these population [31]; hence, the protective effect was not shown. Vegetable dietary patterns suggest a possible way to prevent GDM with diet, but it still needs to be verified in future studies. It is imperative to find appropriate methods, frequencies, and portion sizes of vegetable dietary pattern interventions in order to effectively prevent GDM.
The association between vegetable pattern diet and GDM risk was analyzed during 1 year before conception, the first trimester and the second trimester. Although the OR of vegetable pattern diet in relation to GDM risk observed in the second trimester was slightly smaller than that observed in the first trimester and 1 year before conception; however, we thought that there is no essential difference between the effect among these periods.

There are several strengths and limitations of our study. In terms of strengths, diagnosis of GDM in our study was obtained by investigating medical records that were based upon national guidelines of GDM diagnosis. This was likely to minimize potential disease misclassification. Another strength is that information on potential confounders was collected using a standardized questionnaire, thus allowing us to control these potential confounders. A limitation may be that self-reported dietary intake could have led to measurement errors and the resulting misclassification of dietary intake may have weakened the detection of an association of specific dietary patterns with GDM. Another limitation is that the subjects were enrolled from a hospital setting, potentially limiting the generalizability of the result. The food intake data during 1 year before pregnancy and during the first and second trimesters of pregnancy were collected in our study, the recall bias maybe existed, and women may couldn't correctly refer differences in food intake between first and second trimester, and healthier women may underlines the amount of vegetables in these periods, and this may result in the over estimation of the protective effect of vegetables dietary pattern for the risk of GDM. Additionally, some characteristics of the cases and controls were not equilibrium distributed; however, they were adjusted when estimated the association between dietary patterns and risk of GDM.

In conclusion, the vegetable diet pattern characteristically abundant in green leafy vegetables, other vegetables, and bean products was associated with lowered GDM risk. Future studies, preferably consisting of appropriately designed trials, are necessary to verify the results and provide strong evidence to inform GDM prevention strategies.

SUPPLEMENTARY MATERIALS

Supplementary materials related to this article can be found online at https://doi.org/10.4093/dmj.2019.0138.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTIONS

Conception or design: Q.C., S.W., Y.Z.
Acquisition, analysis, or interpretation of data: Q.C., W.W., H.Y., P.Z., Y.F., K.W., Y.W., S.P., Y.Z.
Drafting the work or revising: Q.C., Y.Z.
Final approval of the manuscript: S.P., Y.Z.

ORCID

Qiong Chen https://orcid.org/0000-0003-2401-0046
Yawei Zhang https://orcid.org/0000-0002-9762-7752
Suping Wang https://orcid.org/0000-0002-1476-5595

ACKNOWLEDGMENTS

This work was supported by the National Institutes of Health grants (No.K02HD70324), National Natural Science Foundation of China grants (NO. 81473061), Natural Science Foundation of Shanxi Province grants (No. 2013021033-2), “100 Talent Plan” Award of Shanxi Province, Construction Project of Characteristic Key Disciplines for Universities of Shanxi Province and “10 Talent Plan” Award of Shanxi Medical University.

The authors express their appreciation to the participants in the Taiyuan Birth Cohort Study for their enthusiastic support.

REFERENCES

1. Chiefari E, Arcidiacono B, Foti D, Brunetti A. Gestational diabetes mellitus: an updated overview. J Endocrinol Invest 2017; 40:899-909.
2. Zhu Y, Zhang C. Prevalence of gestational diabetes and risk of progression to type 2 diabetes: a global perspective. Curr Diab Rep 2016;16:7.
3. Agha-Jaffar R, Oliver N, Johnston D, Robinson S. Gestational diabetes mellitus: does an effective prevention strategy exist? Nat Rev Endocrinol 2016;12:533-46.
4. Matarrelli B, Vitacolonna E, D’Angelo M, Pavone G, Mattei PA, Liberati M, Celentano C. Effect of dietary myo-inositol supplementation in pregnancy on the incidence of maternal gesta-
A vegetable dietary pattern lowered GDM risk

1. Wang Y, Zhao N, Qiu J, He X, Zhou M, Cui H, Lv L, Lin X, Zhang C, Zhang H, Xu R, Zhu D, Dang Y, Han X, Zhang H, Bai H, Chen Y, Tang Z, Lin R, Yao T, Su J, Xu X, Liu X, Wang W, Ma B, Liu S, Qiu W, Huang H, Liang J, Wang S, Ehrenkrantz RA, Kim C, Liu Q, Zhang Y. Folic acid supplementation and dietary folate intake, and risk of preeclampsia. Eur J Clin Nutr 2015;69:1145-50.

2. Liu X, Lv L, Zhang H, Zhao N, Qiu J, He X, Zhou M, Xu X, Cui H, Liu S, Lerro C, Lin X, Zhang C, Zhang H, Xu R, Zhu D, Dang Y, Han X, Bai H, Chen Y, Tang Z, Lin R, Yao T, Su J, Wang W, Wang Y, Ma B, Huang H, Liang J, Qiu W, Liu Q, Zhang Y. Folic acid supplementation, dietary folate intake and risk of preterm birth in China. Eur J Clin Nutr 2016;55:1411-22.

3. International Association of Diabetes and Pregnancy Study Groups Consensus Panel, Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, Damm P, Dyer AR, Leiva Ad, Hod M, Kitzmiller JL, Lowe LP, McIntyre HD, Oats JI, Omori Y, Schmidt ML. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care 2010;33:676-82.

4. Gao H, Stiller CK, Scherbaum V, Biesalski HK, Wang Q, Homann E, Bellows AC. Dietary intake and food habits of pregnant women residing in urban and rural areas of Deyang city, Sichuan province, China. Nutrients 2013;5:2933-54.

5. Shin D, Lee KW, Song WO. Dietary patterns during pregnancy are associated with risk of gestational diabetes mellitus. Nutrients 2015;7:9369-82.

6. Burris HH, Camargo CA Jr. Vitamin D and gestational diabetes mellitus. Curr Diab Rep 2014;14:451.

7. Joergensen JS, Lamont RF, Torloni MR. Vitamin D and gestational diabetes: an update. Curr Opin Clin Nutr Metab Care 2014;17:360-7.

8. Zhang MX, Pan GT, Guo JI, Li BY, Qin LQ, Zhang ZL. Vitamin D deficiency increases the risk of gestational diabetes mellitus: a meta-analysis of observational studies. Nutrients 2015;7:8366-75.

9. Zhang C, Williams MA, Frederick IO, King IB, Sorensen TK, Kestin MM, Dashow EE, Luthy DA. Vitamin C and the risk of gestational diabetes mellitus: a case-control study. J Reprod Med 2004;49:257-66.

10. Zhang C, Williams MA, Sorensen TK, King IB, Kestin MM, Thompson ML, Leisemring WM, Dashow EE, Luthy DA. Maternal plasma ascorbic acid (vitamin C) and risk of gestational diabetes mellitus and fetal outcomes: a randomized controlled trial. J Matern Fetal Neonatal Med 2013;26:967-72.

11. Luoto R, Laitinen K, Nermes M, Isolauri E. Impact of maternal probiotic-supplemented dietary counselling on pregnancy outcome and prenatal and postnatal growth: a double-blind, placebo-controlled study. Br J Nutr 2010;103:1792-9.

12. Schoenaker DA, Mishra GD, Callaway LK, Soedamah-Muthu SS. The role of energy, nutrients, foods, and dietary patterns in the development of gestational diabetes mellitus: a systematic review of observational studies. Diabetes Care 2016;39:16-23.

13. Bao W, Bowers K, Tobias DK, Olsen SF, Chavarro J, Vaag A, Kiely M, Zhang C. Prepregnancy low-carbohydrate dietary pattern and risk of gestational diabetes mellitus: a prospective cohort study. Am J Clin Nutr 2014;99:1378-84.

14. Schoenaker DA, Mishra GD, Callaway LK, Soedamah-Muthu SS. The role of energy, nutrients, foods, and dietary patterns in the development of gestational diabetes mellitus: results from an Australian population-based prospective cohort study. J Matern Fetal Neonatal Med 2015;28:1092-6.

15. Karamanos B, Thanopoulou A, Anastasiou E, Assaad-Khalil S, Albache N, Bachaoui M, Slama CB, El Ghomari H, Jotic A, Baker P, Chong MF. Maternal dietary patterns and gestational diabetes mellitus in a multi-ethnic Asian cohort: the GUSTO Baker P, Chong MF. Maternal dietary patterns and gestational diabetes mellitus in a multi-ethnic Asian cohort: the GUSTO study. Eur J Clin Nutr 2016;70:237-42.

16. Pan YH, Qiu L, Wu YF, Xiao WQ, Liu Y, Xia HM, Qiu X, Ma B, Liu S, Qiu W, Huang H, Liang J, Wang S, Ehrenkrantz RA, Kim C, Liu Q, Zhang Y. Folic acid supplementation and dietary folate intake, and risk of preeclampsia. Eur J Clin Nutr 2016;69:1145-50.

17. Liu X, Lv L, Zhang H, Zhao N, Qiu J, He X, Zhou M, Xu X, Cui H, Liu S, Lerro C, Lin X, Zhang C, Zhang H, Xu R, Zhu D, Dang Y, Han X, Bai H, Chen Y, Tang Z, Lin R, Yao T, Su J, Wang W, Wang Y, Ma B, Huang H, Liang J, Qiu W, Liu Q, Zhang Y. Folic acid supplementation, dietary folate intake and risk of preterm birth in China. Eur J Clin Nutr 2016;55:1411-22.

18. International Association of Diabetes and Pregnancy Study Groups Consensus Panel, Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, Damm P, Dyer AR, Leiva Ad, Hod M, Kitzmiller JL, Lowe LP, McIntyre HD, Oats JI, Omori Y, Schmidt ML. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care 2010;33:676-82.

19. Gao H, Stiller CK, Scherbaum V, Biesalski HK, Wang Q, Homann E, Bellows AC. Dietary intake and food habits of pregnant women residing in urban and rural areas of Deyang city, Sichuan province, China. Nutrients 2013;5:2933-54.

20. Shin D, Lee KW, Song WO. Dietary patterns during pregnancy are associated with risk of gestational diabetes mellitus. Nutrients 2015;7:9369-82.

21. Burris HH, Camargo CA Jr. Vitamin D and gestational diabetes mellitus. Curr Diab Rep 2014;14:451.

22. Joergensen JS, Lamont RF, Torloni MR. Vitamin D and gestational diabetes: an update. Curr Opin Clin Nutr Metab Care 2014;17:360-7.

23. Zhang MX, Pan GT, Guo JI, Li BY, Qin LQ, Zhang ZL. Vitamin D deficiency increases the risk of gestational diabetes mellitus: a meta-analysis of observational studies. Nutrients 2015;7:8366-75.

24. Zhang C, Williams MA, Frederick IO, King IB, Sorensen TK, Kestin MM, Dashow EE, Luthy DA. Vitamin C and the risk of gestational diabetes mellitus: a case-control study. J Reprod Med 2004;49:257-66.

25. Zhang C, Williams MA, Sorensen TK, King IB, Kestin MM, Thompson ML, Leisemring WM, Dashow EE, Luthy DA. Maternal plasma ascorbic acid (vitamin C) and risk of gestational diabetes mellitus and fetal outcomes: a randomized controlled trial. J Matern Fetal Neonatal Med 2013;26:967-72.
diabetes mellitus. Epidemiology 2004;15:597-604.

25. Weickert MO, Pfeiffer AF. Metabolic effects of dietary fiber consumption and prevention of diabetes. J Nutr 2008;138:439-42.

26. Zhang C, Liu S, Solomon CG, Hu FB. Dietary fiber intake, dietary glycemic load, and the risk for gestational diabetes mellitus. Diabetes Care 2006;29:2223-30.

27. Oude Griep LM, Wang H, Chan Q. Empirically-derived dietary patterns, diet quality scores, and markers of inflammation and endothelial dysfunction. Curr Nutr Rep 2013;2:97-104.

28. Qiu C, Sorensen TK, Luthy DA, Williams MA. A prospective study of maternal serum C-reactive protein (CRP) concentrations and risk of gestational diabetes mellitus. Paediatr Perinat Epidemiol 2004;18:377-84.

29. McIntosh M, Miller C. A diet containing food rich in soluble and insoluble fiber improves glycemic control and reduces hyperlipidemia among patients with type 2 diabetes mellitus. Nutr Rev 2001;59:52-5.

30. Galisteo M, Duarte J, Zarzuelo A. Effects of dietary fibers on disturbances clustered in the metabolic syndrome. J Nutr Biochem 2008;19:71-84.

31. Lee KW, Ching SM, Ramachandran V, Yee A, Hoo FK, Chia YC, Wan Sulaiman WA, Suppiah S, Mohamed MH, Veettil SK. Prevalence and risk factors of gestational diabetes mellitus in Asia: a systematic review and meta-analysis. BMC Pregnancy Childbirth 2018;18:494.
**Supplementary Table 1.** Vegetables dietary pattern and risk of gestational diabetes mellitus stratified by parity after propensity-score matching

| Vegetable dietary pattern | One year before conception | The first trimester of pregnancy | The second trimester of pregnancy |
|---------------------------|----------------------------|---------------------------------|---------------------------------|
|                           | Cases | Controls | OR    | 95% CI       | Cases | Controls | OR    | 95% CI       | Cases | Controls | OR    | 95% CI       |
| Nulliparous               |       |          |       |              |       |          |       |              |       |          |       |              |
| Q1                        | 185   | 327      | 1     |              | 193   | 334      | 1     |              | 208   | 328      | 1     |              |
| Q2                        | 154   | 354      | 0.7   | 0.49–0.98    | 147   | 344      | 0.68  | 0.49–0.96    | 149   | 338      | 0.6   | 0.43–0.84    |
| Q3                        | 173   | 318      | 0.93  | 0.67–1.30    | 171   | 324      | 0.92  | 0.66–1.29    | 154   | 339      | 0.71  | 0.51–1.00    |
| Q4                        | 149   | 359      | 0.71  | 0.51–0.99    | 150   | 356      | 0.72  | 0.51–1.01    | 150   | 353      | 0.64  | 0.46–0.89    |
| Total                     | 661   | 1,358    | 0.93  | 0.84–1.03    | 661   | 1,358    | 0.94  | 0.84–1.04    | 661   | 1,358    | 0.89  | 0.80–0.98    |
| P for trend               | 0.163 |          |       |              | 0.211 |          |       |              | 0.023 |          |       |              |
| Parous                    |       |          |       |              |       |          |       |              |       |          |       |              |
| Q1                        | 206   | 357      | 1     |              | 206   | 354      | 1     |              | 203   | 344      | 1     |              |
| Q2                        | 197   | 407      | 0.75  | 0.55–1.02    | 196   | 393      | 0.74  | 0.55–1.00    | 202   | 391      | 0.78  | 0.58–1.04    |
| Q3                        | 222   | 414      | 0.94  | 0.70–1.27    | 218   | 434      | 0.87  | 0.65–1.17    | 215   | 445      | 0.82  | 0.61–1.10    |
| Q4                        | 178   | 392      | 0.79  | 0.58–1.07    | 183   | 389      | 0.80  | 0.59–1.09    | 183   | 390      | 0.8   | 0.59–1.08    |
| Total                     | 803   | 1,570    | 0.96  | 0.87–1.05    | 803   | 1,570    | 0.95  | 0.87–1.05    | 803   | 1,570    | 0.94  | 0.86–1.04    |
| P for trend               | 0.359 |          |       |              | 0.335 |          |       |              | 0.215 |          |       |              |

OR, odds ratio; CI, confidence interval.