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Vegetable dietary pattern associated with low risk of preeclampsia possibly through reducing proteinuria

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ABSTRACT

Background: Evidence on the potential roles that dietary patterns play in the risk of preeclampsia remains limited.
Objective: To examine the associations between dietary patterns during pregnancy and the risk of preeclampsia.
Study Design: We analyzed data from a cluster randomized controlled trial among 987 healthy pregnant women in three rural counties in northwestern China. Maternal diet during the whole pregnancy was assessed using a 107-item food frequency questionnaire with proportion size administered before delivery. Principal component factor analysis with varimax rotation was used to identify common dietary patterns. Preeclampsia was diagnosed by trained clinicians and recorded in delivery records.
Results: Nineteen participants (1.9%) were diagnosed with preeclampsia. Gestational hypertension and proteinuria were only weakly correlated with each other (Kappa = 0.06): 10.7% participants with gestational hypertension only, 8.8% with proteinuria only, 1.9% with both, and 78.6% with neither. Five common dietary patterns were identified: vegetable, meat, fruit, snack, and wheat staple patterns. After adjusting for calories, other dietary pattern scores and baseline blood pressure, a higher vegetable pattern scores was associated with lower risk of preeclampsia (P for trend = 0.041; the highest vs lowest quartile, adjusted relative risk = 0.20 [95% confidence interval, 0.04–0.98]). A similar association was also observed for the risk of proteinuria (P for trend = 0.015): the highest vs lowest quartiles of the vegetable pattern score, adjusted relative risk = 0.44 (95% confidence interval, 0.24–0.80). The other four pattern scores were not associated with preeclampsia.
Conclusions: Adherence to vegetable dietary pattern may be associated with the lower risk of preeclampsia, possibly through reducing development of proteinuria. The original full study was registered at clinicaltrials.gov as NCT02537392.

1. Introduction

Preeclampsia is a serious multisystem disorder of pregnancy and complicates 3–5% of pregnancies globally [1]. It is an important risk factor of maternal and neonatal morbidity and mortality [2,3]. Additionally, preeclampsia is associated with a higher risk of subsequent cardiovascular disease later in life among pregnant women and their offspring [4,5]. It is important to identify modifiable protective factors that may contribute to preeclampsia prevention [6].

Some dietary factors may be associated with preeclampsia [7,8]. At the nutrient level, high intakes of dietary fiber, polyunsaturated fatty acids, calcium, potassium, and magnesium are associated with a low risk of preeclampsia [9–11]. At the food level, high consumption of fruits and vegetables is associated with lower risk of preeclampsia [12–15]. However, Analyzing single nutrients may miss information on their complex interactions. Alternatively, dietary pattern analysis, an analysis of combining foods eaten together, provides a broader view of nutrient and food consumption [16]. It can be used to comprehensively examine the effect of overall diet on risk of preeclampsia, which can inform more feasible interventions in real life [17]. However, evidence on the potential roles that dietary patterns play in the risk of preeclampsia remains limited [18].

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Furthermore, the biological mechanisms through which dietary patterns impact the development of preeclampsia remain unclear [7]. Gestational hypertension and proteinuria are the two essential diagnostic criteria of preeclampsia [19]. Although correlated with each other [20], these two distinct conditions have independent roles in the development of preeclampsia [20,21] and are potentially subject to different factors [22,23]. Gestational hypertension refers to newly developing hypertension (high blood pressure) during late pregnancy (e.g., after 20 weeks) and is characterized by peripheral vasoconstriction and decreased arterial compliance [20]. Proteinuria refers to presence of excessive protein (albumin and/or globulin) in urine and is associated with a pathognomonic renal lesion known as glomerular endotheliosis [22]. Some maternal characteristics including nulliparity, Factor V Leiden and prothrombin A20210 carrier status are risk factors of gestational hypertension with or without proteinuria [23]. Therefore, investigating the individual associations between dietary patterns and each of these two criteria of preeclampsia could help to understand the underlying biological mechanisms. In a study from Australia, high adherence to the Mediterranean-style dietary pattern was associated with a low risk of gestational hypertension [6]. Little is known of the roles of dietary patterns in the risk of proteinuria during pregnancy.

We therefore conducted the first study in this field among Chinese pregnant women to 1) examine associations between dietary patterns and risk of preeclampsia, and 2) examine associations of dietary patterns with risk of the two diagnostic criteria of preeclampsia (i.e., gestational hypertension and proteinuria).

2. Materials and methods

2.1. Study design and participants

We used data from a community-based randomized controlled trial conducted in 3 rural counties (Xunyi, Bin, and Changwu) in Shaanxi Province, northwestern China. This trial was commenced in July 2015 to investigate the effect of multi-micronutrient supplementation on preventing congenital heart diseases. Pregnant women were enrolled at preconception and prenatal care visits in township health care centers. The eligibility criteria included: 1) being aged 20–40, 2) in early pregnancy (≤20 weeks) or planning to be pregnant within 3 months, 3) not smoking cigarettes or drinking alcohol, and 4) relatively healthy without history of chronic diseases, e.g., hypertension, heart disease, renal disease, diabetes or epilepsy. Community maternal and child health workers collected baseline characteristics of participants at enrollment and managed them via a web-based surveillance system. Research assistants collected data from hospital delivery records including clinical diagnoses of pregnancy complications. Additional information about this trial were published on the ISRCTN registry (https://clinicaltrials.gov/ number NCT02537392).

In the current analysis, we considered 2929 participants who delivered between December 14, 2015 and February 2, 2018. About 1460 women who delivered within the second half of each month were supposed to complete a Food Frequency Questionnaire (FFQ) through face-to-face interviews conducted by research assistants during their monthly field visits (2 weeks long). Among them, 1034 completed FFQ but 47 had missing or implausible data on food items. Therefore, a total of 987 women were included in the final analytic sample (Fig. 1). Most characteristics were comparable between the analytic and excluded samples, except that women in the analytic sample were younger, had lower educational level, tended to be farmers, and had slightly higher systolic blood pressure at enrollment (Table 1).

The ethical approval for the study protocol was obtained from the Ethical Committee of Xi'an Jiaotong University Health Science Center (Number 20120008).

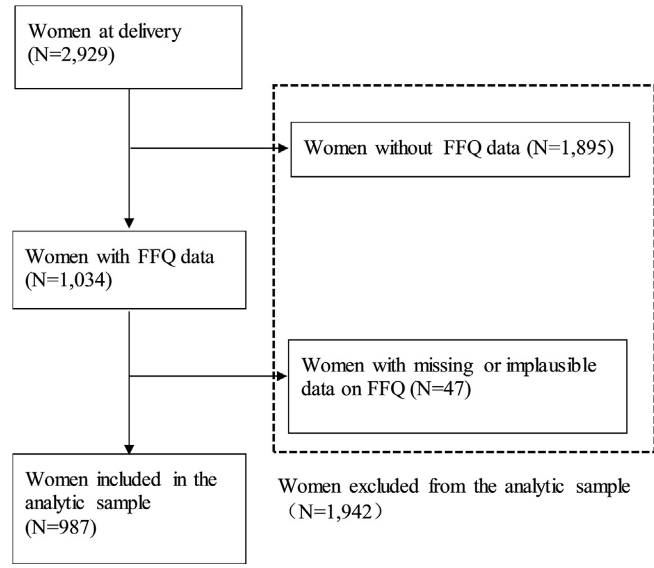

Fig. 1. Flow diagram of participants FFQ, food frequency questionnaire.

2.2. Outcome measures

Obstetricians diagnosed preeclampsia based on blood pressure measurements and urine tests from two sources: prenatal care and delivery records. Community maternal and child health workers at prenatal care visits and obstetrics nurses at the maternity hospital before delivery used a standard adult cuff along with an electric sphygmomanometer (YUYUE 660d, YUYUE Medical Equipment & Supply Co., Jiangsu, China) to measure blood pressure. To minimize variation in blood pressure measurements, each participant was comfortably seated with her back supported for at least 10 min of rest prior to the measurements. Systolic and diastolic blood pressure values were measured three times at intervals of 1 min. The average blood pressure of the three measurements was used for diagnosis of gestational hypertension. Urine protein was measured via dipstick urinalysis with a reagent strip and analyzed with a full-auto urine sediment analyzer. Urine protein results were reported on a semi-quantitative scale: negative, +/−, 1+, 2+, 3+ and 4+.

According to the Guidelines on Diagnoses and Treatments of Hypertensive Disorders in Pregnancy by Chinese Society of Obstetrics and Gynecology [24], preeclampsia was diagnosed if the pregnant woman had both gestational hypertension and proteinuria. Gestational hypertension was defined as occurrence of systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg starting at or after 20 weeks of pregnancy among women with normal blood pressure in the first 20 weeks of pregnancy. Proteinuria was defined as the protein level at 1+ or higher in a single random urine specimen in the dipstick test.

2.3. Dietary measures

Anticipating a minimal change in dietary patterns from early to late pregnancy [25–27], we assessed maternal diet during the entire pregnancy using a 107-item FFQ with proportion sizes. Our team designed this FFQ for pregnant women in rural western China and validated it extensively in previous studies [28–30]. From the eight predefined categories (never, < 1 times/month, 1–3 times/month, 1 time/week, 2–4 times/week, 5–6 times/week, 1 time/day, and ≥2 times/day), participants were asked to recall consumption frequency and proportion size for 102 main food items. The other 5 food items were all ingredients (animal oils, vegetable oils, salt, sugar, and soy sauce) and were recorded as kilograms per month for the whole household. They also reported the number of household members regularly consuming

Table 1
Socio-demographic and pregnancy characteristics of women in analytic and excluded samples (N = 2929).

Characteristic	Analytic sample (N = 987)		Excluded sample (N = 1942)		P value*
	Mean ± SD	n (%)	Mean ± SD	n (%)	
Age, years	25.3 ± 4.2		25. 7 ± 5.4		**0.014**
20–24		468 (47.4)		843 (43.5)	**0.044**
25–29		384 (38.9)		772 (39.8)	
≥30		135 (13.7)		324 (16.7)	
Missing		–		3 (0.1)	
Nulliparity		468 (47.4)		955 (49.2)	0.37
Educational level, years					
≤8		149 (15.1)		229 (11.8)	< **0.001**
9–11		506 (51.3)		930 (47.9)	
≥12		332 (33.6)		783 (40.3)	
Farmer		879 (89.1)		1663 (85.6)	< **0.001**
Family history of hypertension and other vascular disease		53 (5.4)		113 (5.8)	0.62
Height, cm	159.7 ± 4.9		159.7 ± 5.3		0.94
Prepregnancy BMI, kg/m²	21.4 ± 3.2		21.3 ± 3.6		0.47
Underweight (< 18.5)		168 (17.0)		381 (19.6)	0.18
Normal (18.5–23.9)		630 (63.8)		1192 (61.4)	
Overweight (24.0–27.9)		167 (16.9)		310 (16.0)	
Obesity (≥28.0)		22 (2.2)		59 (3.0)	
Intervention group assignment					
Vitamin B complex		358 (36.3)		640 (33.0)	0.07
Iron		317 (32.1)		609 (31.4)	
Usual care		312 (31.6)		693 (35.7)	
Use of dietary vitamin/mineral					
Folic acid		951 (96.4)		–	
Multivitamin		765 (77.5)		–	
Calcium		657 (66.6)		–	
SBP at enrollment, mmHg	105.8 ± 13.4		104.5 ± 15.9		**0.023**
DBP at enrollment, mmHg	66.9 ± 9.7		66.8 ± 11.0		0.81

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; SD, standard deviation.
Bold values means the signicifance of P value less than 0.05.
* Analysis of variance or Chi-square test.

these ingredients. We calculated consumed amounts (g/d) of the 107 food items and nutrient intakes, according to the Chinese Food Composition Tables [31,32]. In addition, they reported their use of dietary supplements during this pregnancy.

2.4. Confounder measures

Based on previous studies on associations of dietary patterns with preeclampsia [6,33], the potential confounders that we considered included intervention group assignment in the trial, use of dietary vitamin/mineral, maternal age, nulliparity, educational level, occupation, pre-pregnancy BMI, baseline blood pressure, family history of hypertension and other vascular disease. The information on these potential confounders was collected during face-to-face interviews and anthropometric measurements at enrollment. Educational levels were divided into three categories: 8 years or less, 9 to 11 years, and 12 years or higher. Occupation was divided into two categories (farmer and others). The measurement of blood pressure was described in the previous section. Height was measured with a stadiometer (LD-SG01, Ningbo Land Corp., Ningbo, China) to the nearest 0.1 cm at enrollment. After removing all heavy clothing and shoes, participants were weighed on a calibrated electronic scale (Tanita HD-305, Tanita [Shanghai] Trading Co., Ltd., Shanghai, China) to the nearest 0.1 kg at enrollment and at each prenatal care visit. Accordingly, we calculated pre-pregnancy body mass index (BMI) as self-reported pre-pregnancy weight in kg divided by the square of height in meters measured at enrollment. Pre-pregnancy BMI was divided into four categories (underweight [< 18.5 kg/m^2], normal [18.5–23.9 kg/m^2], overweight [24–27.9 kg/m^2] and obesity [≥28 kg/m^2], based on the recommended cut-off points for Chinese adults [34].

2.5. Statistical analyses

Socio-demographic and pregnancy characteristics of the study participants were summarized using the mean ± SD for continuous variables, and count (proportion) for categorical variables. ANOVA and Chi-square tests were used to test differences in maternal characteristics between analytic and excluded samples.

We applied principal component analysis with varimax rotation to derive maternal dietary patterns based on consumed amounts (g/d) of the 107 food items [30]. The Kaiser–Meyer–Olkin test and Bartlett's test of sphericity were used to evaluate whether the obtained correlation matrix was suitable for factor analysis. Final derived dietary patterns were chosen based on eigenvalues ≥1.5, the scree plot, and interpretability [35]. Factor loadings represented the correlations between specific food items and a particular dietary pattern. We considered foods with factor loadings > 0.3 on a dietary pattern as substantial contributors to the dietary pattern. For each participant, factor scores were used to represent her dietary patterns. A higher factor score indicated higher adherence to a dietary pattern.

To examine the association between dietary pattern scores and the risk of preeclampsia, we used a log-binomial model to estimate relative risk (RR) with corresponding 95% confidence intervals (CIs) [36]. In a few instances, the log-binomial model did not converge and thus a log-Poisson model with robust error variance was used instead [37]. The quartiles (1st–25th, 26th–50th, 51st–75th, and 76th–100th) of dietary pattern scores were included in the model to examine the potential non-linearity associations and reduce the influence of extreme values. Among the potential confounders (i.e. intervention group assignment, use of dietary vitamin/mineral, maternal age, nulliparity, educational level, occupation, pre-pregnancy BMI, baseline blood pressure, family history of hypertension and other vascular disease) that we tested, only baseline systolic and diastolic blood pressure were significantly associated with preeclampsia and some dietary pattern scores. Three adjusted models were built: 1) model 1 adjusted for caloric intake; 2) model 2 further adjusted for other dietary patterns and 3) model 3 further adjusted for confounders, namely baseline systolic and diastolic blood pressure. P values for trend were estimated using the median score for each quartile of dietary pattern as a continuous variable in the regression model.

To explore the potential influences of maternal dietary patterns on the pathological development of preeclampsia, we used log-binomial models for further examining the associations between dietary pattern scores and each of its two diagnostic criteria (i.e. gestational hypertension and proteinuria) separately. It is worthwhile to mention that 556 participants provided urine samples for urine protein tests at the maternity hospital before delivery. The other 431 participants were not tested for urine protein before delivery because of negative urine protein test results at recent prenatal care visits and/or precipitate delivery. Most characteristics were comparable between the participants with or without protein test result at the maternity hospital before delivery except that participants with protein test result were older, had higher proportion of dietary folic acid and calcium supplements (Supplemental Table 1). Our main analysis on associations between dietary pattern scores and proteinuria included the all 987 participants, assuming those 431 women without urine protein test results before delivery to be proteinuria negative. We recognized this imputation was subject to misclassification. To assess robustness of our results, we conducted a sensitivity analysis in a subsample (N = 556) with urine protein test results before delivery.

In addition, we conducted a *post hoc* analysis [38] to calculate the power to detect a significant trend of decreasing risk of preeclampsia (binary dependent variable) with adherence of each dietary pattern score (continuous independent variable), based on the existing sample size in our study and a moderate effect size.

All statistical tests were two-sided, and P-values less than 0.05 were considered statistically significant. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, NC). Statistical power was evaluated using G * Power Software 3.1 [39].

3. Results

3.1. Participant characteristics

Among 987 participants in the analytic sample, mean age was 25.3 ± 4.2 years, 47.4% were nulliparous, 84.9% received 9 years or longer education, 89.1% were farmers, 5.4% reported a family history of hypertension and other vascular diseases, and 19.1% were overweight or obese (mean BMI, 21.4 ± 3.2 kg/m^2) (Table 1).

3.2. Dietary patterns

Five common dietary patterns were finally chosen and they together explained 52.5% of the total variance (Table 2). The first pattern ("Vegetable dietary pattern") explained 20.7% of the total variance and was characterized by high consumption of mushrooms, leafy and cruciferous vegetables, root vegetables, melon vegetables and legumes. The second pattern ("Meat dietary pattern") explained 10.6% of the total variance and was characterized by high consumption of beef, mutton, poultry, fish, and pork. The third pattern ("Fruit dietary pattern") explained 8.5% of the total variance and was characterized by high consumption of cantaloupes, pineapples, muskmelons, watermelons, and grapes. The fourth pattern ("Snack dietary pattern") explained 6.7% of the total variance and was characterized by high consumption of breads, cakes, biscuits and Chinese snacks. The fifth pattern ("Wheat staple dietary pattern") explained 6.0% of the total variance and was characterized by high consumption of noodles and Liangpi (cold skin noodles).

3.3. Associations between maternal dietary patterns and preeclampsia

A total of 19 preeclampsia cases were diagnosed and the risk of preeclampsia was 1.9% (19/987). The risk of preeclampsia decreased with higher adherence to "Vegetable dietary pattern": 3.7% among women within the lowest quartile (Q1), 1.6% within the 2nd quartile (Q2), 1.6% within the 3rd quartile (Q3), and 0.8% within the highest quartile (Q4). After adjusting for calories, other dietary patterns and baseline blood pressure, higher adherence to "Vegetable dietary pattern" was associated with a lower risk of preeclampsia (P for trend = 0.041). The Q4 of the vegetable dietary pattern score was associated with a lower risk of preeclampsia (adjusted RR 0.20 [95% CI, 0.04–0.98]), compared with the Q1. However, the other four dietary patterns were not significantly (P > 0.05) associated with the risk of preeclampsia (Table 3).

3.4. Associations of vegetable dietary pattern with gestational hypertension and proteinuria

The two diagnostic criteria (gestational hypertension and proteinuria) were only slightly correlated with each other (Kappa = 0.06): 10.7% with gestational hypertension only, 8.8% with proteinuria only, 1.9% with both, and 78.6% with neither (Supplemental Table 2). In the full sample (N = 987), the risk of proteinuria decreased with higher adherence to "Vegetable dietary pattern" (P for trend = 0.015) (Table 4): 14.2% among women within the Q1, 9.3% within the Q2, 11.3% within the Q3, and 7.7% among women within the Q4. The Q4 of the vegetable dietary pattern score was associated with a lower risk of proteinuria (adjusted RR 0.44 [95% CI, 0.24–0.80]), compared with the Q1. However, the vegetable dietary pattern score was not associated with risk of gestational hypertension (P for trend = 0.350).

Similar results were found in the sensitivity analysis among the subsample of 556 participants with urine protein test results before delivery. The Kappa was 0.07 for the correlation between gestational hypertension and proteinuria. As shown in Supplemental Table 3, the vegetable dietary pattern score was still associated with risk of proteinuria (P for trend = 0.005; adjusted RR for the Q4 vs the Q1: 0.39 [95% CI, 0.21–0.73]), but not associated with risk of gestational hypertension (P for trend = 0.78).

3.5. Post hoc power analysis

We assumed that the dietary pattern scores were normally distributed, the risk of preeclampsia among Chinese women was 1.8% [40], and the effect size between one unit increment in each dietary pattern adherence score and the risk of preeclampsia was moderate (OR = 0.4) [41]. With our sample size of 987 and type I error of 0.05, the estimated statistical power was 82.8% for vegetable dietary pattern, 73.4% for meat dietary pattern, 66.3% for fruit dietary pattern, 59.8% for snack dietary pattern, and 69.5% for wheat dietary staple dietary pattern (Supplemental Table 4).

4. Discussion

In the present study, we investigated the association between dietary patterns and the risk of preeclampsia among pregnant women in 3 rural counties of northwestern China. Among the 5 dietary patterns that we identified, only the vegetable dietary pattern was significantly associated with risk of preeclampsia. The seemingly association of high adherence to the vegetable dietary pattern and a lower risk of preeclampsia seemed to be explained by lowering risk of proteinuria, not through impacting risk of gestational hypertension.

The risk of preeclampsia (1.9%) in our study was similar to that (1.8%) reported in another population-based pregnancy cohort study conducted in Southern China from 2010 to 2011 (N = 6, 273) [40]. Nevertheless, it was lower than that reported in a large population-

Table 2
Maternal dietary patterns and factor loadings (N = 987).*

	Eater n (%)	Mean intake (SD), g/d	Factor loading on dietary pattern				
			Vegetable pattern	Meat pattern	Fruit pattern	Snack pattern	Wheat staple pattern
Food items							
Flammulina	834 (84.5)	3.2 (5.0)	0.51				
Oyster mushroom	727 (73.7)	3.0 (4.6)	0.47				
Shiitake	791 (80.1)	7.2 (9.8)	0.47				
Cauliflower	813 (82.4)	11.5 (13.6)	0.45				
Black fungus	755 (76.5)	6.1 (8.0)	0.42				
Cucumber	935 (94.7)	53.1 (44.6)	0.42				
Tomato	954 (96.7)	65.2 (46.2)	0.42				
Kelp	721 (73.0)	3.9 (5.2)	0.41				
Broccoli	552 (55.9)	9.4 (12.0)	0.40				
Leek	840 (85.1)	9.2 (11.9)	0.40				
Cabbage	835 (84.6)	9.7 (11.9)	0.40				
Eggplant	865 (87.6)	18.5 (21.7)	0.40				
Carrot	827 (83.8)	10.5 (11.8)	0.38				
Legume	840 (85.1)	13.9 (15.7)	0.37				
Potato	966 (97.9)	46.0 (30.4)	0.37				
Leaf-used lettuce	800 (81.1)	17.5 (21.8)	0.37				
Radish	758 (76.8)	15.4 (20.9)	0.36				
Spinach	903 (91.5)	28.7 (29.2)	0.36				
Fresh chili	816 (82.7)	18.6 (16.0)	0.35				
Bean sprout	787 (79.7)	12.8 (16.2)	0.32				
Laver	610 (61.8)	3.7 (5.1)	0.32				
Zucchini	802 (81.3)	13.8 (16.6)	0.31				
Lotus root	576 (58.4)	8.4 (10.4)	0.30				
Beef	476 (48.2)	4.9 (6.2)		0.65			
Mutton	350 (35.5)	5.0 (7.3)		0.59			
Poultry	701 (71.0)	6.2 (8.0)		0.41			
Pumpkin	446 (45.2)	7.9 (9.9)		0.36			
Freshwater fish	705 (71.4)	6.1 (8.4)		0.33			
Pork	776 (78.6)	13.2 (16.1)		0.32			
Asparagus lettuce	363 (36.8)	8.5 (11.6)		0.32			
Pluck	17 (1.7)	3.1 (2.4)		0.31			
White gourd	462 (46.8)	13.3 (14.3)		0.31			
Cantaloupe	518 (52.5)	3.7 (4.8)			0.37		
Pineapple	694 (70.3)	9.7 (16.6)			0.36		
Muskmelon	682 (69.1)	45.6 (68.3)			0.35		
Watermelon	855 (86.6)	167.5 (234.7)			0.34		
Grape	821 (83.2)	27.7 (43.8)			0.33		
Chinese snack	337 (34.1)	1.4 (2.0)			0.31	0.37	
Cakes	524 (53.1)	4.6 (7.4)				0.37	
Biscuit	482 (48.8)	3.0 (6.2)				0.32	
Bread	660 (66.9)	8.4 (13.4)				0.31	
Noodles	974 (98.7)	231.3 (105.0)					0.35
Liangpi	692 (70.1)	22.6 (25.5)					0.34
Eigenvalue			5.58	2.86	2.31	1.80	1.60
Explained variance			20.7%	10.6%	8.5%	6.7%	6.0%

* Food items with factor loadings > 0.3 or greater were listed.

based cohort study (2.5%) in Eastern China (N = 193, 554) from 1993 to 1995[42] and reported in a hospital-based national cross-sectional survey (2.8%) in China (N = 112, 386) in 2011[43]. Variation in reported risk of preeclampsia across those studies might be attributed to the differences in study design and sampled population.

Among Chinese pregnant women, we first observed the inverse association between high adherence to the vegetable dietary pattern and preeclampsia. This novel finding was consistent with that from the Norwegian Mother and Child Cohort study in which high adherence to the vegetable dietary pattern characterized by high intakes of vegetables, fruits, and vegetable oils was associated with decreased risk of preeclampsia: 6.3% in the 1st tertile, 5.3% (adjusted OR, 0.84 [95% CI, 0.73–0.97]) in the 2nd tertile, and 4.6% in the 3rd tertile (0.72 [0.62–0.85]) [33].

The biological mechanisms for the observed association between the vegetable dietary pattern and the risk of preeclampsia are unclear [6]. Our in-depth analysis on associations between the vegetable dietary pattern and the two diagnostic criteria of preeclampsia (i.e. gestational hypertension and proteinuria) could help to understand the underlying mechanisms. Pathogenesis of gestational hypertension is complex and can be triggered by abnormal vasoconstriction due to derangement of endothelial-derived vasoactive factors, an early gestational exaggeration of cardiac output, enhanced vascular sensitivity to the renin-angiotensin system, and high autoimmune activity [20]. In our study, the vegetable dietary pattern was not associated with risk of gestational hypertension. In the other studies, however, high adherence to the Mediterranean-style dietary pattern was inversely associated with higher blood pressure [44] and the risk of gestational hypertension [6]. The difference between these studies might be partly due to the difference in these two dietary patterns. Although high in vegetable consumption, Mediterranean-style dietary pattern also contains high consumption of nuts, red wine, and rye bread, which may have larger contributions to its potential association with a lower risk of gestational hypertension.

Instead, for the first time we found an inverse association between the vegetable dietary pattern and the risk of proteinuria. Proteinuria reflects glomerular and widespread endothelial dysfunction, a key component in the pathophysiology of preeclampsia [45–48]. Although

Table 3
Association between dietary pattern scores and risk of preeclampsia (N = 987).

Dietary pattern	N	Risk of preeclampsia, n (%)	Adjusted RR (95% CI) of preeclampsia*		
			Model 1	Model 2	Model 3
Vegetable					
Quartile 1	246	9 (3.7)	Reference	Reference	Reference
Quartile 2	247	4 (1.6)	0.43 (0.13–1.42)	0.44 (0.13–1.46)	0.40 (0.12–1.35)
Quartile 3	247	4 (1.6)	0.42 (0.13—1.40)	0.42 (0.12–1.43)	0.38 (0.11–1.33)
Quartile 4	247	2 (0.8)	**0.20 (0.04–0.97)**	**0.20 (0.04–0.96)**	**0.20 (0.04–0.98)**
P for trend**			**0.035**	**0.036**	**0.041**
Meat					
Quartile 1	246	2 (0.8)	Reference	Reference	Reference
Quartile 2	247	6 (2.4)	3.09 (0.62–15.51)	2.78 (0.55–14.10)	2.87 (0.56–14.76)
Quartile 3	247	7 (2.8)	3.59 (0.74–17.46)	3.36 (0.68–16.70)	3.59 (0.71–18.14)
Quartile 4	247	4 (1.6)	2.00 (0.36–11.01)	2.00 (0.35–11.40)	2.01 (0.35–11.67)
P for trend**			0.74	0.71	0.72
Fruit					
Quartile 1	246	3 (1.2)	Reference	Reference	Reference
Quartile 2	247	7 (2.8)	2.55 (0.63–10.29)	2.11 (0.52–8.62)	1.94 (0.47–8.01)
Quartile 3	247	6 (2.4)	2.16 (0.52–8.96)	1.95 (0.44–8.63)	1.76 (0.40–7.84)
Quartile 4	247	3 (1.2)	1.08 (0.21–5.52)	1.14 (0.20–6.40)	1.03 (0.18–5.76)
P for trend**			0.99	0.91	0.96
Snack					
Quartile 1	246	4 (1.6)	Reference	Reference	Reference
Quartile 2	247	5 (2.0)	1.25 (0.33–4.73)	1.20 (0.31–4.62)	1.25 (0.32–4.87)
Quartile 3	247	9 (3.6)	2.32 (0.70–7.66)	2.34 (0.67–8.20)	2.68 (0.76–9.46)
Quartile 4	247	1 (0.4)	0.25 (0.03–2.27)	0.31 (0.03–3.13)	0.33 (0.03–3.35)
P for trend**			0.39	0.65	0.72
Wheat staple					
Quartile 1	246	4 (1.6)	Reference	Reference	Reference
Quartile 2	247	6 (2.4)	1.52 (0.42–5.45)	1.24 (0.34–4.55)	1.43 (0.38–5.35)
Quartile 3	247	3 (1.2)	0.74 (0.16–3.36)	0.62 (0.13–2.84)	0.65 (0.14–3.03)
Quartile 4	247	6 (2.4)	1.49 (0.41–5.36)	1.44 (0.38–5.39)	1.58 (0.41–6.08)
P for trend**			0.71	0.74	0.69

RR, relative risk; CI, confidence interval.
Bold values means the signicifance of P value less than 0.05.
* Model 1 was adjusted for calories. Model 2 was further adjusted for the other four dietary patterns. Model 3 was further adjusted for baseline systolic and diastolic blood pressure.
** P for trend was evaluated using the median score for each quartile as a continuous variable in the regression model.

there is no published study on roles of dietary patterns in endothelial dysfunction among pregnant women, previous studies among non-pregnant populations supported the beneficial effects of vegetable consumption on vascular endothelial function and renal function [49–52]. For example, in the Multi-Ethnic Study of Atherosclerosis, the dietary pattern characterized by green leafy vegetables, whole grains, fruit, and nuts was inversely (the 5th quintile vs the 1st quintile: 253 vs 262 pg/ml, P for trend = 0.044) related to plasma concentrations of sICAM-1, a strong marker of endothelial dysfunction [52]. A 8-week dietary intervention study in the U.K. reported that an additional portion (80 g) of daily consumption of vegetables and fruits led to 6.2% improvement in endothelium-dependent forearm blood flow response (P = 0.032) [51], an indicator of good endothelial function. In addition, in a study from Taiwan, high adherence to the vegetable and fish dietary pattern was significantly correlated with a lower plasma creatinine level (the 3rd tertile vs the 1st tertile: 0.84 vs 0.88, P for trend = 0.032) [50], an indicator of renal dysfunction. The effect of high consumption of vegetables on improving endothelial function may be partly attributed to ample amounts of antioxidant phytochemicals and dietary fiber as well as relatively low protein amount in vegetables [50,53,54].

Our study had several strengths. First, to our knowledge, it was the

Table 4
Associations of the vegetable dietary pattern scores with risk of gestational hypertension and proteinuria (N = 987).*

Vegetable dietary pattern	N	Gestational hypertension		Proteinuria	
		Risk, n (%)	Adjusted RR (95% CI)†	Risk, n (%)	Adjusted RR (95% CI)†
Quartile 1	246	32 (13.0)	Reference	35 (14.2)	Reference
Quartile 2	247	39 (15.8)	1.17 (0.70–1.95)	23 (9.3)	**0.54 (0.30–0.94)**
Quartile 3	247	24 (9.7)	0.66 (0.37–1.17)	28 (11.3)	0.62 (0.35–1.07)
Quartile 4	247	29 (11.7)	0.88 (0.50–1.53)	19 (7.7)	**0.44 (0.24–0.80)**
P for trend‡			0.35		**0.015**

RR, relative risk; CI, confidence interval.
Bold values means the signicifance of P value less than 0.05.
* Assuming 431 participants without urine protein test result being proteinuria negative.
† Adjusted for calories, the other four dietary patterns and baseline systolic and diastolic blood pressure.
‡ P for trend was evaluated using the median score for each quartile as a continuous variable in the regression model.

first study to investigate the associations between dietary patterns and risk of preeclampsia among Chinese pregnant women. Our novel findings from the dietary pattern analysis are informative for clinical practice and public health. Secondly, we first examined the associations of dietary patterns with two diagnostic criteria of preeclampsia (i.e. gestational hypertension and proteinuria). This in-depth analysis could help to explore the biological mechanisms through which dietary patterns might impact the risk of preeclampsia.

Serval limitations should be considered in interpreting our findings. First, the substantial proportion (about 32%) of missing data on FFQ data might cause selection bias. The influence of missing data on our results seemed to be limited, as adjustment for variables that differed between the analytic and excluded samples only led to small changes (e.g., 5% for vegetable dietary pattern) in associations between dietary patterns and preeclampsia. Secondly, diet during pregnancy was subject to recall bias, as it was retrospectively self-reported right for delivery. Thirdly, the generalization of our results might be limited, as this study was conducted in only 3 rural counties in northwestern China. Finally, our *post hoc* power analysis suggested our available sample size could provide sufficient (> 80%) statistical power for detecting the association between vegetable dietary pattern and the risk of preeclampsia, but not for other four dietary patterns.

5. Conclusion

In conclusion, we found that high adherence to the vegetable dietary pattern was significantly associated with a decreased risk of preeclampsia in relatively healthy pregnant women. This might be explained by the lower risk of proteinuria associated with high vegetable consumption. If confirmed by future studies, our findings support an intervention promotion vegetable consumption to preeclampsia prevention. Further research is needed to identify the biological mechanisms through which the vegetable dietary pattern may associate with preeclampsia pathogenesis.

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Declaration of interest

The authors report no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.preghy.2019.03.013.

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