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#### Abstract

Several dietary substances have been hypothesized to influence the risk of preeclampsia. Our aim in this study was to estimate the association between dietary patterns during pregnancy and the risk of preeclampsia in 23,423 nulliparous pregnant women taking part in the Norwegian Mother and Child Cohort Study (MoBa). Women participating in MoBa answered questionnaires at gestational wk 15 (a general health questionnaire) and 17–22 (a FFQ). The pregnancy outcomes were obtained from the Medical Birth Registry of Norway. Exploratory factor analysis was used to assess the associations among food variables. Principal component factor analysis identified 4 primary dietary patterns that were labeled: vegetable, processed food, potato and fish, and cakes and sweets. Relative risks of preeclampsia were estimated as odds ratios (OR) and confounder control was performed with multiple logistic regression. Women with high scores on a pattern characterized by vegetables, plant foods, and vegetable oils were at decreased risk [relative risk (OR) for tertile 3 vs. tertile 1: 0.72; 95% CI: 0.62, 0.85]. Women with high scores on a pattern characterized by processed meat, salty snacks, and sweet drinks were at increased risk [OR for tertile 3 vs. tertile 1: 1.21; 95% CI: 1.03, 1.42]. These findings suggest that a dietary pattern characterized by high intake of vegetables, plant foods, and vegetable oils decreases the risk of preeclampsia, whereas a dietary pattern characterized by high consumption of processed meat, sweet drinks, and salty snacks increases the risk. J. Nutr. 139: 1162–1168, 2009.

## Introduction

Preeclampsia is found in 3–10% of pregnancies worldwide and remains a major cause of maternal and fetal morbidity and mortality (1). The etiology of preeclampsia is unknown. Preeclamptic pregnancies are characterized by endothelial dysfunction, disturbed placentation, oxidative stress, and an exag-

gerated inflammatory response to pregnancy (2). A possible modification of these pathophysiological events by lipids, nutrients, and antioxidant supplementation has been hypothesized, but reviews of results from intervention trials do not support that supplementation with vitamin C or E during pregnancy reduce the risk of preeclampsia (3–5). Associations between various dietary components and preeclampsia have been studied in case-control and prospective cohort studies and have shown increased risk of preeclampsia with high consumption of energy, added sugar (sugar-sweetened soft drinks), PUFA, and decreased risk of preeclampsia with high consumption of milk and high intake/sufficient status of vitamin D (6–10). Causal relationships can be made probable through intervention trials, but it is virtually impossible to conduct clinical trials with normal diets as the exposure. Studies of associations between the total diet and preeclampsia using observational studies are therefore warranted.

The relationship between diet and health can be examined at the level of nutrients, foods, or dietary patterns. Analysis of dietary patterns may give a more balanced description of data

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of interest.<br><sup>3</sup> Supplemental Table 1 is available with the online posting of this paper at jn. nutrition.org.

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compared with analyses of foods or single nutrients (11). Principal component analysis  $(PCA)^7$  is a well-established method for deriving dietary patterns in a population. The patterns identified by PCA reflect dietary behavior and are not based on known health effects of diet. Thus, the identified patterns are not necessarily relevant for disease risk. However, when patterns are associated with disease risk, the results can increase insight into possibilities for dietary changes (12,13).

The aim of the present study was to investigate the relationship between dietary patterns and the risk of developing preeclampsia in a large population of nulliparous women.

### Materials and Methods

Subjects. The data set is part of the Norwegian Mother and Child Cohort Study (MoBa) database, initiated by and maintained at the Norwegian Institute of Public Health (14). This study used version 3 of the data files made available for research in 2007. In brief, MoBa is a nation-wide pregnancy cohort that aimed at including 110,000 pregnancies by the end of 2008. The majority of all pregnant women in Norway were invited to participate through a postal invitation after they signed up for the routine ultrasound examination in their local hospital. The participation rate was ~44% (14). Pregnancy and birth records from the Medical Birth Registry of Norway (MBRN) are linked to the MoBa database (15).

Informed consent was obtained from each participant before the study. The Regional Committee for Medical Research and the Norwegian Data Inspectorate approved the study.

When preparing the dataset, 29,888 nulliparous women had answered the first MoBa questionnaire. Of these, 28,472 (95%) were also recorded in MBRN and had singleton births and 23,856 (80%) had, in addition, answered version 2 of the FFQ (16). A final number of 23,423 (78%) had a registered food intake  $> 4500$  kJ and  $< 20,000$  kJ/d and were included in the analyses.

Dietary information. The MoBa FFQ is completed around wk 22 of gestation. Data have been collected from February 2002 and onwards (16). The MoBa FFQ is a semiquantitative questionnaire designed to capture dietary habits and intake of dietary supplements during the first 4–5 mo of pregnancy. Nutrient calculations were performed with the use of FoodCalc (17) and the Norwegian food composition table (18). The FFQ has been thoroughly validated with regard to nutrients, foods, and dietary supplement use (19,20). The daily intakes (g/d) of the 255 food and beverage items in the FFQ were aggregated into 58 nonoverlapping food items or food groups based on structure, nutrient profile, or culinary usage (Supplemental Table 1).

Preeclampsia. The main outcome was preeclampsia in the present pregnancy as registered in MBRN (15). Information provided to the registry is based on forms completed by the midwives after birth. The form has 5 check-off boxes relevant to preeclampsia: hemolysis, elevated liver enzymes, and low platelet count; eclampsia; early preeclampsia (diagnosed before 34 wk); mild preeclampsia; and severe preeclampsia. For our study, the diagnosis of preeclampsia was given if any of the above-mentioned diagnoses were present. Women with chronic hypertension were included in the case group only if they also developed proteinuria. The diagnostic criteria for preeclampsia in Norway, according to guidelines issued by the Society for Gynecology, are blood pressure  $>140/90$  after 20 wk of gestation, combined with proteinuria  $>+1$  dipstick on at least 2 occasions (21).

Gestational age at the time of diagnosis was not known, but mean  $\pm$ SD gestational age when the FFQ was completed was  $20.7 \pm 3.7$  wk.

Extraction of dietary patterns. Dietary patterns were obtained by principal component factor analysis. Four dietary patterns with eigenvalues  $> 1.6$ , which together accounted for 18% of the total variation, were extracted on the basis of the scree plot and evaluation of the factor loading matrix after orthogonal (varimax) rotation (22). With PCA, one reduces the dimension of the data by forming a few linear combinations of the original observed variables containing as much as possible of the variation in the original data. By this method correlated variables are grouped together. The coefficients defining these linear combinations, called factor loadings, are the correlations of each food item with that factor. Foods with loadings  $> 0.3$  on a factor were used to describe the dietary patterns. Factor scores were created by multiplying factor loadings with the corresponding standardized value for each food and summing across the food items. For each participant, the factor scores indicate the extent to which her diet conformed to the respective dietary patterns. A high factor score for a given pattern indicated high intake of the foods constituting that food pattern and a low score indicated low intake of those foods (11,22).

Other variables. We adjusted for the following confounding variables: maternal prepregnant BMI, maternal height, educational attainment, smoking status, hypertension prior to pregnancy, dietary supplement use, and total energy intake. These factors have previously been shown to influence the risk of preeclampsia and they were also associated with the dietary pattern scores. In MoBa,  $>99\%$  of the participants are of Caucasian ethnicity and ethnicity is not a relevant confounder. Selfreported prepregnancy height and weight were used to calculate BMI (kg/m<sup>2</sup>). BMI was divided into 4 categories (<20, 20-24.9, 25-29.9, and  $\geq$ 30 kg/m<sup>2</sup>), maternal height into 4 categories (quartiles) (<165, 166– 168, 169–172,  $\geq$ 1.73 cm), educational attainment into 4 categories (less than high school, high school, 3 y of college/university, or  $\geq$  4 y of college/university education), and smoking in 3 categories (daily smokers, occasional smokers, and nonsmokers). A dichotomous variable denoting chronic hypertension was included in the adjusted model. Dietary supplement use reported in the FFQ was computed as a categorical variable with 3 categories: no supplement use, use of any supplement without vitamin D, and use of a vitamin D-containing supplement. Maternal age at delivery was retrieved from MBRN. Maternal age was used as a continuous variable except in Table 2, where it was divided into 4 categories (<20 y, 20–29 y, 30–39 y,  $\geq 40$  y).

Statistical methods. We used linear regression to calculate P-trend in dietary pattern scores across ordered categories, including maternal age, length of education, prepregnancy BMI, height, and energy intake, and we used the Mann-Whitney and the Kruskall Wallis tests for nominal categories, including smoking, hypertension, and dietary supplement use. Due to skewed distribution of nutrient intakes, we used nonparametric correlation coefficients (Spearman) to examine the associations between the dietary pattern scores and nutrient intakes.

Relative risks were estimated as odds ratios (OR) and calculated for tertiles of factor scores using logistic regression and were adjusted for confounding using multiple logistic regression. All dietary patterns were entered in the same model. The model was adjusted for potential confounding by maternal age, length of education, prepregnancy BMI, height, smoking, total energy intake, hypertension prior to pregnancy, and dietary supplement use. For all tests,  $P < 0.05$  was considered significant. All analyses were performed using SPSS version 14.

### Results

Among 23,423 nulliparous women, 1267 (5.4%) developed preeclampsia. We extracted 4 dietary patterns by factor analysis (Table 1). The first pattern had high positive loadings on vegetables, cooking oil, olive oil, fruits and berries, rice, and chicken and this pattern was denoted the vegetable pattern. The second pattern, which was denoted the processed food pattern, had high positive loadings on processed meat products, white bread, French fries, salty snacks, and sugar-sweetened drinks and high negative loadings on oily fish, high-fiber breakfast cereals, and lean fish. The high-loading foods on the 3rd pattern were cooked potatoes, processed fish, lean fish, fish spread and

<sup>&</sup>lt;sup>7</sup>Abbreviations used: MBRN, Medical Birth Registry of Norway; MoBa, the Norwegian Mother and Child Cohort Study; OR, odds ratio; PCA, principal component analysis.





 $1$  Factor loadings are the correlation coefficients ( $n$ ) between the original variables (food consumption) and the extracted factors. Food groups are sorted by the size of loading coefficients. Negative loadings are listed at the foot. Food groups with factor loadings below  $\pm$  0.3 are not listed.

shellfish, and margarine, and this pattern was denoted the potato and fish pattern. The 4th pattern, denoted the cakes and sweets pattern, was characterized by high loadings on cakes, waffles

and pancakes, buns, ice cream, sweet biscuits, sweets, and chocolate.

Within each dietary pattern, we looked at the distribution in terms of participant characteristics (Table 2). For the vegetable pattern, the mean factor score increased with maternal age, education, and height, decreased with BMI, and was higher in nonsmokers than smokers. The processed food pattern score was inversely associated with maternal age, education, and height and positively associated with BMI and smoking. The mean scores for the potato and fish and the cakes and sweets patterns also differed for these characteristics, but the associations were not as clear as for the first 2 patterns. Similarly, dietary supplement users had significantly higher vegetable pattern scores and lower processed food pattern scores, whereas the potato and fish and the cakes and sweets pattern scores were not related to dietary supplement use. Pattern scores increased with increasing energy intake for all patterns, but the relative increase was less within the vegetable pattern than within the other patterns (Table 2).

Spearman correlations between pattern scores and key nutrients showed that the vegetable pattern was significantly correlated with dietary intake of nutrients such as folate  $(r =$ 0.52), vitamin B-6 ( $r = 0.50$ ), fiber ( $r = 0.47$ ), vitamin C ( $r =$ 0.43),  $\beta$ -carotene ( $r = 0.49$ ), tocopherol ( $r = 0.37$ ), potassium ( $r =$ 0.42), and magnesium  $(r = 0.39)$ , whereas the processed food pattern significantly correlated with nutrients such as SFA  $(r =$ 0.35), added sugar ( $r = 0.33$ ), and sodium ( $r = 0.28$ ). The potato and fish pattern significantly correlated with the intake of sodium ( $r = 0.60$ ), fiber ( $r = 0.48$ ), folate ( $r = 0.48$ ), and tocopherol ( $r = 0.46$ ). The cakes and sweets pattern significantly correlated with the intake of SFA ( $r = 0.45$ ) and added sugar ( $r =$  $(0.56)$ .

Women who developed preeclampsia had lower mean factor scores of the vegetable pattern and higher mean factor scores of the processed food pattern ( $P < 0.001$ ) than those who did not develop preeclampsia (Table 3). These results were not adjusted for confounders.

The highest incidence of preeclampsia was in the upper tertile of the processed food pattern (6.4%) and the lowest incidence (4.5%) was in the lower tertile of the same pattern and in the upper tertile of the vegetable pattern  $(4.6\%)$  (Table 4).

In the crude analysis, women ranked in the 2 upper tertiles of the vegetable pattern had significantly lower risk of developing preeclampsia than those in the lowest tertile and the effect remained significant after adjusting for maternal characteristics and dietary supplement use. Independent of this, women in the upper tertile of the processed food pattern had significantly higher risk of developing preeclampsia than those in the lowest tertile and the effect was evident in both the crude and adjusted analyses (Table 4). No significant independent effect on the risk of preeclampsia was found for the potato and fish and the cakes and sweets patterns.

Because the associations of preeclampsia with the dietary patterns may be modified by other covariates, we further examined the risk estimates after stratifying participants according to some established risk factors. The observed associations with preeclampsia according to tertiles of dietary pattern scores did not differ according to maternal age, height, education, smoking status, prior hypertension, or prepregnancy BMI (data not shown).

We also examined the effects of the vegetable and processed food patterns according to different combinations of factor scores (tertiles). The effect of having high scores on the vegetable pattern were strongest within the lowest tertile of the processed



#### **TABLE 2** Factor scores according to maternal characteristics in 23,423 nulliparous women from the MoBa, 2002–2006

<sup>1</sup> Values are mean factor scores obtained by extraction of 4 dietary factors by PCA. The scores are not adjusted for confounders

<sup>2</sup> Test for linear trend.

<sup>3</sup> Test for trend excludes missing.

<sup>4</sup> Kruskall Wallis test.

<sup>5</sup> Mann-Whitney U-test.





<sup>1</sup> Values are means  $\pm$  SEM. The scores are not adjusted for confounders (Mann-Whitney U-test).

food pattern (35–40% risk reduction), whereas having high scores on the processed food pattern did not significantly increase the risk in any of the vegetable pattern tertiles.

## **Discussion**

In this study, we investigated the relationship between dietary behavior during the first half of pregnancy and the risk of developing preeclampsia. Two dietary patterns influenced the risk of developing preeclampsia after adjustment for measured confounders and dietary supplement use. Adherence to a dietary pattern characterized by high intake of vegetables, fruits, rice, vegetable oils, and poultry was associated with a reduced risk of preeclampsia, whereas adherence to a dietary pattern characterized by high intake of processed foods including sausages, hamburgers, white bread, salty snacks, sugar-sweetened drinks, and sweets increased the risk of preeclampsia.

Preeclampsia is a pregnancy-specific condition that resolves with delivery. The risk factors for preeclampsia include obesity, dyslipidemia, insulin resistance, and other factors that are also risk factors for atherosclerosis (5). Diet has been suggested for many years to play a role in preeclampsia, but with focus on

specific nutrients, few questions about nutrient involvement in preeclampsia have been definitely answered. Our finding of an increased risk of preeclampsia with the processed food pattern corroborates the results of a previous prospective study from Norway that found an increased risk of preeclampsia with an increasing intake of sugar-containing soft drinks (6). In that study, however, no associations were found for intakes of meat, fish, vegetables, and fruits. A study from a very different cultural and socioeconomic setting in central Africa reported that women who had frequent intake of vegetables had lower risk of preeclampsia than women with infrequent intake of vegetables (23). A study from the US reported a strong protective effect of dietary fiber on the risk of preeclampsia and also a negative association between dietary fiber intake and maternal plasma lipid and lipoprotein concentration (24). The vegetable pattern in our study was positively correlated with dietary fiber intake, whereas the processed food pattern was inversely associated with dietary fiber. On the other hand, we found no independent effect on the risk of preeclampsia for the cakes and sweets pattern, although this pattern was characterized by high intake of refined carbohydrates.

Several mechanisms for a biological effect of dietary factors on the risk of preeclampsia may exist. In nonpregnant populations, dietary patterns characterized by high consumption of vegetables and fruit and low consumption of processed meats and foods rich in sugar and fats have been shown to reduce markers of the metabolic syndrome, inflammation, and cardiovascular disease (25–27). The vegetable pattern in our study resembles the traditional Mediterranean diet, which has also been shown to be beneficial in the prevention of many chronic diseases (28–30). Furthermore, adherence to a Mediterranean diet during pregnancy has been associated with a lower risk of preterm birth (31,32). Dietary factors are also known predictors of plasma homocysteine, with levels of plasma homocysteine being inversely related to diets rich in fruit, vegetables, whole grain, and fish, and positively associated with high intake of refined cereals, fat, and sugar (33–35). Moreover, elevated

**TABLE 4** Associations between tertiles of dietary pattern scores and risk of preeclampsia from the MoBa, 2002–2006

Dietary pattern	Total, $n = 23,423$	Preeclampsia	Model $1$ OR <sup>1</sup> (95% CI)	Model $2$ $OR2$ (95% CI)	Model $3 \text{ OR}^3$ (95% CI)
Tertile 1	7807	495 6.3			
Tertile 2	7808	415 5.3	$0.82$ (0.72, 0.94)	0.84(0.74, 0.97)	$0.84$ (0.73, 0.97)
Tertile 3	7808	357 4.6	$0.71$ $(0.62, 0.82)$	0.76(0.66, 0.87)	$0.72$ (0.62, 0.85)
Processed food					
Tertile 1	7807	354 4.5			
Tertile 2	7808	410 5.3	1.15(0.99, 1.33)	1.08 (0.94, 1.26)	$1.06$ (0.91, 1.23)
Tertile 3	7808	503 6.4	1.45 (1.26, 1.67)	1.30(1.13, 1.50)	1.21(1.03, 1.41)
Potato and fish					
Tertile 1	7807	404 5.2			
Tertile 2	7808	420 5.4	1.05(0.91, 1.21)	1.04(0.90, 1.19)	0.99(0.86, 1.15)
Tertile 3	7808	443 5.7	$1.11$ (0.97, 1.29)	1.10(0.96, 1.26)	$1.00$ $(0.84, 1.18)$
Cakes and sweets					
Tertile 1	7807	435 5.6			
Tertile 2	7808	435 5.6	$0.98$ $(0.86, 1.13)$	1.02 (0.88, 1.17)	$1.00$ $(0.86, 1.15)$
Tertile 3	7808	397 5.1	$0.89$ $(0.78, 1.03)$	0.98(0.85, 1.13)	$0.90$ $(0.76, 1.06)$

<sup>1</sup> Adjusted for other dietary patterns.

<sup>2</sup> Adjustment for other dietary patterns and prepregnant BMI.

<sup>3</sup> Additional adjustment for maternal age, maternal education, maternal height, maternal smoking, total energy intake, hypertension prior to pregnancy, and dietary supplement use.

maternal concentrations of homocysteine have been reported in women who later develop preeclampsia (36,37). Plant foods are rich in micronutrients (phytochemicals, antioxidants, vitamins, and minerals) and dietary fiber, whereas processed foods are rich in added sugar, salt, and SFA. No individual dietary component is responsible for the positive associations reported above and the general view is that the interaction between many components of the diet, or the overall diet quality, offers protection against disease.

Among the 4 patterns identified, the vegetable pattern was most clearly associated with characteristics commonly understood to indicate or be predictive of good health, i.e. higher level of education, lower BMI, and less smoking, whereas the processed food pattern was most clearly associated with characteristics indicative of poor health (Table 2). Use of vitamin D supplementation was positively associated with the vegetable pattern and negatively associated with the processed food pattern. As we have previously reported that vitamin D supplement use reduced the risk of preeclampsia (10), vitamin D supplement use might confound the association between the dietary patterns and preeclampsia. However, adjusting for vitamin D supplement use did not change the association (Table 4).

We reduced the possibility of confounding by controlling for relevant factors. The associations between preeclampsia and risk factors like parity, maternal BMI, smoking, and maternal age in our study were similar to those described on other study populations. BMI is strongly associated with both diet quality and preeclampsia (38,39). Adjusting for BMI, education, maternal age, smoking, and height is likely to capture a large part of the variability in socioeconomic background and health behavior. Additional confounders like household income and marital status were also considered, but did not influence the reported estimates. However, it is possible that our results could be due to confounding by factors not included in the present analysis and the results must be interpreted with caution with regard to causal inference between dietary habits and the risk of preeclampsia.

The strength of this study is the large sample of nulliparous women. MoBa is a large pregnancy cohort with participants from both urban and rural regions, representing all age groups and all socioeconomic groups (14). The FFQ assessed diet over the first 4–5 mo of pregnancy. The food frequency method challenges the participants with complex cognitive tasks and is particularly difficult to answer during the first part of pregnancy when many women experience nausea/vomiting and changes in appetite and eating patterns. The MoBa FFQ was developed and validated for use in pregnancy (16). The validation study demonstrated that relative to a dietary reference method and several biological markers, the FFQ produces a realistic estimate of the habitual intake and is a valid tool for ranking pregnant women according to high and low intakes of energy, nutrients, and food. However, the correlation coefficients between the test and reference methods were generally weaker than correlations found in nonpregnant populations (19).

The proportion of women in MoBa with preeclampsia is similar to the proportion in the overall Norwegian population (MBRN). The validity of the preeclampsia diagnosis in MBRN has never been assessed. However, a recent study from Denmark examined the validity of preeclampsia and related diagnoses recorded in a mandatory Danish national discharge registry, which is comparable to the MBRN. They reported a high positive predictive value of the preeclampsia diagnosis and all registrations of serious subtypes reflected true cases (40). We think similar results will apply to the MBRN. In this prospective cohort study, dietary information and information on potential confounding factors were collected prior to onset of preeclampsia. Thus, systematic (differential) misclassification of preeclampsia according to dietary pattern seems unlikely. However, nondifferential misclassification may exist. Thus, any misclassification of preeclampsia is likely to be randomly distributed across all dietary pattern groups. Such nondifferential misclassification is likely to underestimate the true association between dietary patterns and development of preeclampsia. Low precision in the dietary assessment may also attenuate the diet-disease association.

In conclusion, we cannot establish a causal relationship between dietary behavior in pregnancy and the risk of preeclampsia, but our results suggest that a lifestyle including a dietary pattern characterized by high intake of vegetables, plant foods, and vegetable oils and low intake of processed meats and sweet beverages may be beneficial. Pregnancy is a period when most women are highly motivated for advice on a healthy diet and changes toward a healthy diet may also benefit their children. Dietary changes have low cost and low risk compared with medical interventions and even a moderate increase in the intake of vegetables and plant foods may be of public health importance.

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