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Lower risk of preeclampsia and preterm delivery with adherence to the New Nordic Diet during pregnancy – a study performed in the Norwegian Mother and Child Cohort Study (MoBa)

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Abstract

Background—Preeclampsia and preterm delivery are serious complications of pregnancy and leading causes of perinatal mortality and morbidity world-wide. Dietary factors may be implicated in the pathophysiology associated with these adverse outcomes.

Objective—The purpose of the present study was to investigate whether adherence to the New Nordic Diet (NND) is associated with preeclampsia and preterm delivery risk in the Norwegian Mother and Child Cohort Study (MoBa), a large prospective cohort study.

Design—Participants were recruited from all over Norway during the period 1999–2008. A previously constructed diet score addressing meal frequency, Nordic fruits, root vegetables, cabbages, potatoes, oatmeal porridge, whole grains, wild fish, game, berries, milk and water, was

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Conflict of interest
The authors declare that they have no conflict of interest.

used to operationalize NND adherence. Associations between NND adherence and the outcomes were estimated in multivariate logistic regression models.

Results—72,072 women were included in the study. High versus low NND-adherence was associated with lower odds of total preeclampsia (OR: 0.86; 95% CI: 0.78, 0.95) and early preeclampsia (OR: 0.71; 95% CI: 0.52, 0.96) in multivariate adjusted models. High as compared to low NND-adherence was associated with lower odds of spontaneous preterm delivery among nulliparous women (OR: 0.77; 95% CI: 0.66, 0.89), whereas multiparous women with high versus low NND adherence had borderline significant higher odds of preterm delivery (OR: 1.24; 95% CI: 1.00, 1.53).

Conclusions—High versus low NND adherence was associated with lower overall risk of preeclampsia and with spontaneous preterm delivery among nulliparous women, however, among multiparous women higher relative risk of preterm delivery was observed.

Introduction

Preeclampsia is a serious complication of pregnancy and a leading cause of maternal mortality and morbidity, perinatal deaths, preterm delivery, and intrauterine growth restriction world-wide [1]. Frequency ranges from 2–7% depending on time period, parity and diagnostic criteria [1]. In Norway the incidence of preeclampsia was 3.6% in 2008 as documented by the Medical Birth Registry of Norway (MBRN) [2].

The cause of preeclampsia remains unknown, but incomplete placentation with placental ischemia is a fundamental characteristic of the disorder and associated with an exaggerated maternal systemic inflammatory reaction to pregnancy and endothelial dysfunction with or without multi-organ involvement in later pregnancy [3, 4]. Risk factors for preeclampsia include a metabolic syndrome profile characterized by obesity, increased inflammatory markers, dyslipidemia, insulin resistance, endothelial dysfunction, and oxidative stress [5].

Preterm delivery is another serious challenge in obstetrical care, accounting for a large share of off-spring morbidity and mortality, as well as compromised long term neurologic development [6]. Preeclampsia and preterm delivery share many risk factors, among them chronic hypertension, maternal obesity, insulin resistance, and systemic inflammation [7].

Several foods, nutrients, dietary supplements, and more recently dietary patterns, have been investigated in relation to risk of both preeclampsia and preterm delivery, based on their potential influences on antioxidant defense, inflammation, immunity, insulin sensitivity, blood pressure, and blood lipids [8]. The Mediterranean diet has received much attention for its robust inverse relationship with cardiovascular risk factors and disease, mostly investigated in non-pregnant populations [9]. Lately there has been increasing interest in whether similar health benefits could be replicated with other regionally based diets, with the added advantage of being more environmentally sustainable and culturally relevant to the region in question [10, 11]. In 2009 Bere & Brug launched the concept of a 'New Nordic Diet', incorporating health-promoting properties as well as concern for environmental issues and the Nordic identity of the dietary components [10]. Later investigations have shown favorable associations and effects of variously defined healthy Nordic diets with cardiometabolic risk factors in observational [12–16] as well as randomized controlled studies (RCTs) carried out in Nordic populations [17–20]. These metabolic influences of adherence to a healthy Nordic diet could also be of relevance to pregnancy health since the risk of both hypertensive diseases, gestational diabetes and preterm delivery are associated with cardiovascular risk factors [21, 22, 4, 8].

Based on the documented cardio-protective effects of healthy Nordic diets in non-pregnant populations we hypothesized that NND-adherence would be favorably associated with risk of both preeclampsia and preterm delivery. We recently developed and described a diet score to operationalize adherence to a diet in line with the principles of the New Nordic Diet (NND) for use as an exposure in relation to health outcomes in the Norwegian Mother and Child Cohort Study (MoBa) [23]. The purpose of the present study was to investigate whether this *a priori* defined dietary score is associated with risk of preeclampsia and preterm delivery in MoBa.

Subjects and methods

The Norwegian Mother and Child Cohort Study (MoBa) is a prospective population-based pregnancy cohort study conducted by the Norwegian Institute of Public Health [24]. Participants were recruited from all over Norway from 1999–2008. The women consented to participation in 40.6% of the pregnancies. The cohort now includes 114.500 children, 95.200 mothers and 75.200 fathers.

The study was approved by The Regional Committee for Medical Research Ethics and written informed consent was obtained from all MoBa participants upon recruitment. MoBa has obtained a licence from the Norwegian Data Inspectorate. The current study is based on version 7 of the quality-assured data files released for research in May 2013.

We used data from two questionnaires completed by the participants upon recruitment in the second trimester, and from the Medical Birth Registry of Norway (MBRN) which is linked to the MoBa database. In questionnaire 1 (Q1) women provided information about education, lifestyle, health, medications, and socioeconomic factors. Questionnaire 2 (Q2) was a semi-quantitative food frequency questionnaire (FFQ) covering diet from conception to mid-pregnancy, completed by participants around week 22 of pregnancy.

Exclusion criteria

Pregnant women were considered for the present study if they had completed the baseline questionnaire (Q1) and the FFQ (Q2) (n=86,776). We excluded plural pregnancies (n=1,617), pregnancies with reported energy intake < 4,500 kJ or ≥ 20,000 kJ (n=1,376), abortions/ deliveries < 22 gestational weeks (n=89) and > 42 weeks (n=170), and pregnancies with missing information on length of gestation (n=295). We only included the first pregnancy contributed, and excluded additional pregnancies by the same mother (n=11,157). This resulted in a final sample of 72,072 women.

The New Nordic Diet

Main exposure was degree of adherence to the New Nordic Diet (NND), operationalized by a previously developed NND score [23]. Information on diet was collected from a validated semi-quantitative 255-item FFQ completed around week 22 of pregnancy, covering the period from conception until mid-pregnancy [25]. Food intake and daily energy and nutrient intakes was calculated by use of FoodCalc and the Norwegian food composition table [25, 26]. Dietary supplements were not included. The diet score comprised ten subscales with each subscale addressing a specific aspect of the NND. Each subscale was constructed from one or more relevant food frequency-items. The sum score of each subscale was dichotomized by the median and participants were assigned scores of "1" if intake was above the median and "0" if below the median. Adding the dichotomized subscales yielded the final NND-score that could take values from 0 to 10, with higher score indicating higher adherence to the NND. Similar methods have been used in many epidemiological studies to examine dietary patterns in relation to risk of non-communicable diseases and mortality [27].

The following subscales made up the NND-score:

1. 'Meal frequency' as number of main meals/week (breakfast, lunch, dinner and evening meal)
2. 'Nordic fruits' as frequency of eating apples, pears, plums and strawberries
3. 'Root vegetables' as frequency of eating carrots, rutabaga, and various types of onions
4. 'Cabbages' as frequency of eating kale, cauliflower, broccoli and Brussels sprouts
5. 'Potatoes' as frequency of eating potatoes relative to rice and pasta combined
6. 'Whole grain breads' as frequency of eating whole grain bread relative to more refined breads (refined bread containing < approximately 1/3 wholegrain flour)
7. 'Oatmeal porridge' as frequency of eating oatmeal porridge
8. 'Foods from the wild countryside' as frequency of eating wild fish, seafood, game, and wild berries.
9. 'Milk' as consumption of milk relative to fruit juice
10. 'Water' as consumption of water relative to artificially-sweetened and sugar-sweetened beverages.

A detailed description of the construction of the score has been published elsewhere [23]. In brief, the approximate dietary behavior associated with scoring (as defined by the median sumscore) in each subscale was: (i) eating at least 24 main meals per wk, (ii) eating Nordic fruits at least 5 times/wk, (iii) eating root vegetables at least 5 times/wk, (iv) eating cabbage at least twice weekly, (v) eating potatoes at least one-third of total occasions of eating potatoes, rice or pasta, (vi) choosing whole grain bread more often than refined bread, (vii) eating oatmeal at least monthly, (viii) eating wild fish/game/wild berries at least twice weekly, (viiii) drinking more milk than juice, and (x) drinking at least six times as much water as sugar-sweetened beverages. With the ambition of achieving three equally sized adherence groups, participants were categorized according to their total NND score into 'low', 'medium' or 'high' NND-adherence, representing NND scores of 0–3 (n=19,349, 27%), 4–5 (n=25,544, 35%) or 6–10 (n=27,179, 38%) NND points respectively.

Outcome variables

The primary outcomes in the present study were the complication of pregnancy by preeclampsia and preterm delivery. We included 'Early preeclampsia' as a secondary outcome since this subgroup of preeclampsia is likely to represent a more severe type of disease with larger fetal consequences [2]. The diagnostic criteria for preeclampsia as applied by the Norwegian Federation of Obstetricians and Gynecologists is an increase in blood pressure to at least ≥ 140 systolic or 90 mm Hg diastolic, after the 20th gestational week, combined with proteinuria (protein excretion of at least 0.3 g/24 h or ≥ 1+ on dip-stick), both measured at least twice [2]. Preeclampsia and hypertensive disorders are recorded in the birth notification form completed by midwives after birth by checking one or more of the following alternatives: 'Preeclampsia, mild', 'Preeclampsia, severe', 'Preeclampsia, before 34 weeks', 'Eclampsia', 'Gestational hypertension (without proteinuria)', and 'Pre-existing hypertension' [2]. We included reported preeclampsia, eclampsia, HELLP-syndrome, and preeclampsia superimposed on chronic hypertension as preeclampsia cases in the analyses. 'Early preeclampsia' was defined as preeclampsia before 34 weeks of gestation, as registered in the MBRN.

We defined preterm delivery as *spontaneous* delivery between 22 and 37 weeks of gestation since preeclampsia constitutes a large proportion of *indicated* preterm deliveries. The MBRN variables used to ascertain spontaneous preterm delivery was length of gestation estimated from ultrasound examination, supplemented by date of last menstrual cycle if information from ultrasound examination was lacking and combined with information on type of delivery. Misclassification of gestational age is an acknowledged problem, especially in the preterm weeks. Reported gestational age was therefore validated by calculating sex-specific birth weight-by-gestational week Z-scores [28]. Infants reported to be born before 37 completed weeks of pregnancy with birth weight Z-scores above 4 for a given gestational week were viewed as having misclassified gestational age and were excluded from the analyses.

Other variables

Potential confounders considered were maternal age (linear and quadratic term), height, pre-pregnancy body mass index (BMI), parity, educational attainment, present smoking status, exercise during pregnancy, chronic hypertension, diabetes, marital status, and energy intake. Maternal age at delivery was obtained from the MBRN. Maternal height was obtained from the baseline questionnaire and categorized according to quartiles as defined in earlier MoBa studies (1.40–1.64, 1.65–1.68, 1.69–1.72, and ≥1.73 m). Pre-pregnancy BMI was calculated from self-reported weight divided by height in squared meters (kg/m^2) and categorized as underweight (BMI < 18.5), normal weight (BMI 18.5–24.9), overweight (BMI 25.0–29.9), obese grade I (BMI 30), or obese grade II (BMI ≥35) for description, but included as a continuous variable in the regression models. Marital status was obtained from the MBRN and categorized as living with or without cohabitant. Information on parity was obtained from the MBRN and presented with all categories for description but as nulliparous versus multiparous in the regression models. Educational attainment was categorized as ≤12 years, 13–16 years, and ≥17 years of education as reported in Q1. Smoking in mid-pregnancy was obtained from Q1 and categorized as "never", "occasional", or "regular smoking" for description, but were collapsed into two categories (smoking in mid-pregnancy yes/no) for regression modeling. Exercise in mid-pregnancy was obtained from Q1 with four categories for description (never, less than once a week, 1–2 times a week, or 3 times a week or more), but was collapsed into two categories in the logistic regression models (less than once a week versus ≥ 1–2 times a week). Information on chronic hypertension was obtained from the MBRN (yes/no). The original MBRN Diabetes Mellitus variable with five categories was redefined into a variable with three categories denoting 'no diabetes', 'pre-gestational diabetes', and 'gestational diabetes'.

Statistics

All statistical analyses were performed with SPSS statistical software package version 19.0 (IBM Corporation, Armonk, NY, USA). A two-sided p-value of 0.05 was considered significant.

Maternal characteristics are presented as mean (SD) for continuous variables and proportions (%) for categorical variables. Differences in maternal characteristics across NND-adherence categories were tested with Pearson Chi-Squared test for categorical data. Food and nutrient intake variables were generally skewed and are therefore presented as median with interquartile range. The non-parametric Kruskal-Wallis test was used for testing trends of food intake as well as energy and nutrient intake across the three NND-adherence categories. Absolute risk of total preeclampsia, early preeclampsia, and total and spontaneous preterm delivery are presented according to degree of NND-adherence. We used odds ratios (OR) to approximate relative risks of the outcomes with high as compared to low NND-adherence. The associations were estimated in crude and multivariate logistic regression models with NND-adherence modeled as a nominal variable ('low' =1, 'medium'=2 and 'high' NND-adherence =3) and the outcomes modeled as 'preeclampsia' yes/no, 'early preeclampsia' yes/no, and 'spontaneous preterm delivery' yes/no. Odds ratios are presented with 95% confidence intervals (CI), with low NND-adherence as reference category.

Covariates suspected to be confounders or effect-modifiers of the association between NND-adherence and the outcomes were assessed in univariate logistic regression models and included in preliminary models. The models were evaluated by inspecting changes in the estimates and overall model fit upon removal of covariates. Marital status, family income, and maternal height changed the parameter estimates by less than 10%, and were removed from the models. Removing the exercise variable changed the estimate by more than 10% in the preterm delivery model and exercise was therefore retained in the preterm delivery model but removed from the preeclampsia models.

We evaluated potential interactions between NND-adherence and covariates by including the product terms of NND-adherence and each covariate in the models. A p-value for the product term of less than 0.10 was defined as effect modification. When effect modification by a covariate was identified, results were presented both for the whole sample as well as stratified according to the relevant covariate levels.

Results

Participants

A total of 72,072 women were included in the present study, constituting 83% of those having completed the relevant questionnaires. Mean age was 30.1 years (SD 4.6). Based on their individual NND score, participants were categorized as having either ‘low’ (27%), ‘medium’ (35%), or ‘high’ (38%), NND-adherence. The score cut-offs were decided upon with the aim of obtaining three approximately equally sized groups. Table 1 contains information on maternal characteristics for the whole sample and according to degree of NND-adherence. Women with high NND-adherence were slightly older, more educated, of higher parity, more likely to exercise regularly, but less likely to smoke and be overweight/ obese compared to those with low NND-adherence.

Diet

As follows from the way the score was constructed, women with high NND-adherence reported substantially higher intake of whole grain bread, oatmeal, fruits, vegetables, potatoes, fish and seafood, meat, unsweetened milk, and drinking water, and lower intake of sugar-sweetened as well as artificially sweetened beverages compared to women with low NND-adherence. They reported higher intake of fermented milk and yoghurt and slightly lower intake of sweets and salty snacks. They did, however, report higher intake of cakes and desserts. A detailed presentation of differences in food and nutrient intake according to degree of NND-adherence in the MoBa cohort has been presented elsewhere [23]. Macronutrient distribution differences between groups were small, but generally in favor of a healthier distribution with increasing NND-adherence. Micronutrient intake per 10 MJ increased across NND-adherence for all micronutrients [23]. Differences in energy-adjusted intakes between extreme categories of NND-adherence were most pronounced for added sugar, dietary fiber and the micronutrients calcium, phosphorus, beta-carotene, vitamin C, vitamin D, folate, magnesium, potassium and selenium.

Preeclampsia

A total of 2,908 preeclampsia cases were identified, yielding a prevalence of preeclampsia 4.0% in our study population. High as compared to low NND-adherence was associated with lower adjusted odds of preeclampsia (OR: 0.86; 95% CI: 0.78, 0.95) (Table 2). Smoking in mid-pregnancy was identified as an effect modifier of the association between NND-adherence and preeclampsia (interaction term p=0.083). High versus low NND-adherence yielded substantially lower adjusted odds of preeclampsia among smokers than non-smokers (smokers OR: 0.57; 95% CI: 0.37, 0.87, non-smokers: OR: 0.88; 95% CI: 0.80, 0.98) (Table 2).

Since diabetes and chronic hypertension are strong risk factors for preeclampsia we reran the models upon removing participants with chronic hypertension and diabetes. This did not substantially change the overall estimate (OR: 0.87; 95% CI: 0.79, 0.96).

Early preeclampsia

A total of 300 women developed preeclampsia before 34 weeks of gestation. High as compared to low NND-adherence was associated with lower odds of early preeclampsia (OR: 0.71; 95% CI: 0.52, 0.96) (Table 3). Running the model without participants with chronic hypertension and diabetes did not substantially change the estimate (OR: 0.70; 95% CI: 0.51, 0.97).

Preterm delivery

A total of 3,729 (5.2%) delivered preterm, of which 2129 (3.0%) were spontaneous deliveries. A total of 16 cases born before week 37 had birth-weight z-score > 4 and were excluded from further analyses because of suspected misclassification. Two of these were spontaneous deliveries, yielding 2127 spontaneous preterm deliveries in the logistic regression analyses. The observed associations between NND-adherence and spontaneous preterm delivery are shown in Table 4. High as compared to low NND-adherence was not significantly associated with preterm delivery in the whole sample (OR: 0.91; 95% CI: 0.80, 1.03). Parity was, however, identified as an effect modifier of the relationship between NND-adherence and preterm delivery (interaction term p=0.001), so analyses were completed stratified by parity. Absolute risk of spontaneous preterm delivery was lower in the multiparous compared to the nulliparous group (2.4% versus 3.5%)(Table 6). Among nulliparous women high as compared to low NND-adherence implied lower odds of preterm delivery (OR: 0.77; 95% CI: 0.66, 0.89), whereas borderline significant higher odds of preterm delivery was observed (OR: 1.24; 95% CI: 1.00, 1.53) among multiparous women.

Subgroup analyses

We ran all models stratified by parity and established risk factors for preeclampsia and preterm delivery including smoking, BMI, diabetes and chronic hypertension. Stronger associations were generally observed among nulliparous and normal weight women whereas weaker or non-significant associations were observed among multiparous and obese women (data not shown). For some of the strata there was insufficient power to detect true differences in risk as judged by the number of cases and the width of the confidence intervals.

Among participants with pre-gestational diabetes, high versus low NND-adherence was associated with reduced odds of preeclampsia (OR: 0.38; 95% CI: 0.15, 0.95). No association with NND-adherence was observed among participants with gestational diabetes (OR: 0.86; 95% CI: 0.36, 2.02). High versus low NND-adherence was non-significantly associated with lower odds of spontaneous preterm delivery among women with pre-gestational diabetes (OR: 0.89; 95% CI: 0.79, 1.01), but not among women with gestational diabetes (OR: 1.44; 95% CI: 0.41, 5.13).

Sensitivity analysis

To assess whether a stricter definition of 'high' NND-adherence would strengthen the observed associations, we moved the NND score cut-off from 6 to 7, resulting in a smaller percentage of participants in the highest NND-adherence category (n=15,635, 22%). This led to a marginally strengthened inverse association of NND-adherence with preeclampsia and a slight attenuation of the association of NND-adherence with early preeclampsia and preterm delivery (data not shown).

Missing data

The number of women with missing information for the covariates BMI, smoking, and education were low (< 3.0%), but 8.3% had missing information on the exercise variable. This led to a total of 12.9% missing participants in the preterm delivery analysis in which exercise was retained as confounder.

Discussion

In this study we found lower overall risk of preeclampsia with high as compared to low adherence to the New Nordic Diet (NND). NND-adherence was differently associated with the risk of spontaneous preterm delivery according to parity, with lower relative risk of spontaneous preterm delivery with high versus low NND-adherence among nulliparous women and an unexpected higher relative risk among multiparous women.

Differences between extreme categories of NND-adherence were most pronounced for added sugar, dietary fiber and micronutrients like calcium, phosphorus, beta-carotene, vitamin C, vitamin D, folate, magnesium, potassium and selenium, many of which may influence metabolic pathways involved in the pathophysiology of preeclampsia and preterm delivery [8]. A nutritious and well-balanced diet may enhance functionality and efficiency of maternal and fetal metabolism through substrate availability, reductive capacity, immunologic mechanisms, and insulin sensitivity, and the metabolic stress induced by disturbed placentation could possibly be attenuated or counterbalanced by a high quality diet [8, 29]. In a meta-analysis by Thangaratinam et al. (2012) investigating potential effects of dietary interventions on risk of adverse pregnancy outcomes, interventions which generally improve diet quality pregnancy were associated with a 33% reduced risk of preeclampsia and a 32% reduced risk of preterm delivery [30].

In an earlier study confined to nulliparous women in MoBa, principal component analysis was used to identify underlying dietary patterns that were subsequently investigated in relation to preeclampsia risk. Women with high as compared to low scores on a dietary pattern characterized by vegetables, plant foods, and vegetable oils, had 28% lower risk of preeclampsia, whereas those with high versus low scores on a processed food pattern characterized by processed meat, salty snacks, and sweet drinks had 21% higher risk of preeclampsia [31]. Our *a priori* defined New Nordic Diet score to some extent integrates these patterns and produced comparable associations despite the fact that fat quality differed minimally between NND-adherence groups. Qiu et al. used dietary fiber as a proxy for a healthy diet and found high versus low fiber intake to be associated with a 72% lower risk of preeclampsia in a prospective study in pregnant women [32]. One of the largest nutritional differences between high and low NND-adherence in our study was in fact the intake of dietary fiber and micronutrients associated with whole grains, fruits and vegetables.

The stronger association of NND-adherence with preeclampsia observed among smokers was unexpected, but could possibly reflect a larger metabolic benefit by a healthier diet in this group. Relatively more smokers than non-smokers were categorized with low NND-adherence as can be observed in Table 2. The slightly stronger association of high versus low NND-adherence with risk of early preeclampsia compared to total preeclampsia indicates that a protective influence of diet might apply from early gestation and contribute to avoid or postpone the development of fulminant disease. Another possible explanation might be that early preeclampsia could be associated with a different phenotype compared to term preeclampsia, potentially more responsive to lifestyle [2]. The combination of compromised intrauterine fetal conditions due to inadequate placentation, and being born prematurely, leaves the infant at especially high risk for perinatal morbidity and later adverse health [29, 33]. Even a small protective effect of diet could therefore be of public health relevance.

The pathophysiology leading to preterm delivery is multifactorial and complex, and even though individual causal factors have been difficult to establish, it has been demonstrated that clusters of beneficial or adverse behavioral and dietary aspects may substantially influence risk [34]. Khoury et al. reported a 90% reduction in incidence of preterm delivery in the intervention group randomized to following a cholesterol-lowering diet during pregnancy [35]. Aiming to replicate this finding, two coordinated observational studies were carried out in the Norwegian and Danish birth cohorts, with predefined dietary criteria adapted to resemble the intervention diet in the study by Khoury [36, 37]. Significant associations were only observed in the Danish study, but few women fulfilled the relatively strict criteria. A recent study applied principal component analysis to extract underlying dietary patterns in the MoBa dataset, and documented 12% lower hazard rate of preterm delivery with high versus low adherence to a ‘prudent’ dietary pattern as well as 9% lower hazard rate with a so-called ‘traditional’ dietary pattern [38]. Our *a priori* New Nordic Diet score applied in the same dataset captures a combination of these two dietary patterns that could be described in detail, high in whole grains, drinking water, fruits, vegetables, and fish, but including potatoes and milk to a larger extent than the ‘prudent’ pattern, and not taking into account oils and fat spreads.

The borderline significant higher risk of preterm delivery with high versus low NND-adherence observed among multiparous women is difficult to explain. As can be viewed from table 4, multiparous women had an absolute lower risk of preterm delivery compared to nulliparous women in all NND-adherence categories, documenting clinical heterogeneity according to parity. Moreover, more multiparous than nulliparous women were categorized with high NND-adherence and fewer with low NND-adherence. It is possible that the maximal benefit of a healthy diet in relation to risk of preterm delivery had already been achieved in the multiparous women, making other risk factors and bias introduced by potential reverse causation more influential. The single most important predictor of preterm delivery in multiparous women is prior preterm delivery which increases the risk for subsequent preterm delivery by an estimated six-fold [39]. Women with a history of earlier preterm delivery may thus be at considerable risk of repeat preterm delivery regardless of diet. We were not able to adjust for earlier preterm delivery in our analyses. Other unmeasured potential confounding factors, like inter-pregnancy interval, breastfeeding, and previous adverse reproductive outcomes, likely contributes to the observed heterogeneity by parity.

Strengths and limitations

Strengths of our study are the prospective, population-based design of MoBa and the large sample of pregnant women recruited from all parts of Norway and from all socioeconomic groups. The FFQ used in MoBa has been thoroughly validated and was completed by the participants in advance of the outcomes in question [40]. The investigation of a comprehensive dietary pattern as exposure allows cumulative, synergistic and interactive effects of diet to be taken into account, unlike investigations with single nutrients or foods as exposures [27, 41, 42]. This approach also made possible the categorization of participants into three distinct diet categories for description, comparison and analysis. The MBRN preeclampsia variable has recently been validated against medical records according to broader diagnostic criteria requiring one measurement of hypertension and proteinuria, as well as to the present more restricted diagnostic criteria requiring two measurements [43]. High positive predictive value (PPV) was demonstrated using both broader and restricted criteria (90.3 and 82.0% respectively, for the period of 2003–2005), confirming that MBRN-registered preeclampsia corresponds well with medical records in the period relevant to the present study [43].

Some limitations should be addressed. Causality cannot be inferred from observational studies, and we cannot exclude the possibility of residual and unmeasured confounding. Low NND-adherence was associated with maternal characteristics such as younger age at delivery, overweight, less education, more smoking, and less exercise, all of which are associated with both socioeconomic status and with preeclampsia and preterm delivery risk. Even though we adjusted for these factors in the multivariate models, residual confounding from other traits or behaviors associated with social class is possible.

The NND score is a crude instrument designed to rank and categorize participants according to dietary behavior and some behaviors will necessarily be overlapping across NND-adherence categories. We did not have data on biomarkers. We believe that the substantial differences in diet across NND-adherence described in our previous paper indicate that the score discriminates degree of adherence to the dietary pattern we intend to describe [23]. Potential under-reporting of unhealthy, as well as over-reporting of healthy dietary behaviors, may have led to some degree of misclassification of NND-adherence, and a potential larger degree of misreporting by high-risk groups may have attenuated associations [44]. Women with chronic conditions like diabetes, chronic hypertension, or obesity may adhere to a healthy diet during pregnancy, but still have considerably increased risk for the outcomes compared to other pregnant women. Such reverse causation bias would, however, tend to attenuate true associations. The observed lower odds of preeclampsia with high versus low NND-adherence in the subgroup of women with pre-gestational diabetes is interesting, but should be interpreted with caution since the number of cases was small and confounding of this association by overall disease management and compliance with medical advice is likely. Since diabetes is a strong risk factor for preeclampsia this association warrants further investigation.

Dietary patterns have been shown to be fairly stable over time [45]. It is therefore likely that NND-adherence in the present study to some extent reflects longer term NND-adherence. Parts of the observed associations between diet during pregnancy and the outcomes may thus be explained by longer term NND-adherence and corresponding maternal pre-pregnancy nutritional status. This does not challenge the validity of the association between NND adherence and the risk of preeclampsia and preterm delivery, but rather whether the short time frame of pregnancy is the critical window for nutritional factors to alter pregnancy risk. Long-term diet is a determinant of a range of interrelated risk factors associated with preeclampsia and preterm delivery, such as BMI, serum lipids, insulin resistance, type 2-diabetes and chronic hypertension, and may therefore exert its influence both indirectly mediated through modification of pre-pregnancy risk factors, and directly by its influence on other aspects of nutritional status. Since we removed the effect of baseline risk factors by adjusting for them in the statistical analyses, the observed estimates between diet during pregnancy and the outcomes may overestimate the associations between pregnancy NND-adherence and the outcomes, but underestimate true associations of long-term NND-adherence with risk of preterm delivery and preeclampsia. Only a carefully conducted randomized controlled study could confirm whether a diet in line with the New Nordic Diet during the time frame of pregnancy influences risk of preeclampsia and preterm delivery. Meanwhile, the intervention study by Khoury et al. [35], and the meta-analysis by Thangaratinam et al. [30] support that diet during the time frame of pregnancy matters.

The diet captured by a high NND score is largely in line with Food Based Dietary Guidelines supported by health authorities in many countries, advocating a larger representation of fruits and vegetables, whole grains, potatoes, fish, lean meat, and drinking water in the diet with the aim of preventing ill-health and non-communicable diseases. Our primary aim with the development of the score was to be able to measure adherence to a *potentially* regionally based and environmentally friendly diet, and secondly to investigate its association with various pregnancy-related health outcomes in the MoBa cohort. The score items were established a priori to reflect adherence the concept of a New Nordic Diet as described by Bere & Brug [10] and Mithril et al. [11]. The food items to be included in each subscale were limited by the availability of food data, but could have comprised most food items that can potentially be cultivated, grown or harvested in a Nordic climate without extensive use of fertilizers or excessive emissions of greenhouse gases. We were not able to take into account potential seasonal variation in availability of Nordic fruits that may have influenced consumption. Apples and pears are, however, available throughout the year in all parts of Norway, so large seasonal variation is unlikely to have influenced intake.

Young women, women with more than two children, women with previous stillbirths, smokers, and mothers living alone have been shown to be strongly under-represented in MoBa, whereas folic acid and multivitamin users are over-represented [46]. Since the healthier lifestyle documented in MoBa participants compared to the background population could reduce the likelihood of detecting true associations, the observed favorable associations between NND-adherence and the outcomes in our study are likely to be valid for pregnant women in general, and may possibly be stronger in subsets of women with a less health-conscious lifestyle. The individual contribution of each dietary component to the overall associations with preeclampsia and preterm delivery in our study cannot be reliably disentangled from the totality of the diet. We believe that this is of lesser relevance since dietary recommendations forwarded to the public needs to address complex diets. Most of the foods addressed by the NND score are not confined to the Nordic traditional diet, but widely consumed in other European regions as well [47].

Conclusion

The focus of this study was to investigate whether a more holistic, regionally based and environmentally friendly diet during pregnancy would have the additional benefit of being associated with favorable pregnancy health. We have shown that a dietary pattern in line with the concept of the New Nordic Diet during pregnancy is associated with lower risk of preeclampsia, and a lower risk of spontaneous preterm delivery confined to nulliparous women. An unexplained higher relative risk with high versus low NND-adherence was, however, observed among multiparous women. Many of the foods captured by the New Nordic Diet are likely to be available throughout the year and should be culturally acceptable to pregnant women in many European countries. Similar regionally based wholesome diets could probably be adapted to cover pregnancy needs in most regions of the world.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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ERH, EB and NCØ conceived the project and designed the present study; MH was involved in the development and calculations of the MoBa food frequency questionnaire; SE, KK and QH were involved in the validation of the MBRN preeclampsia variable and contributed to the interpretation of the results, ERH prepared the dataset, analyzed data and wrote the paper; ERH, EB and NCØ had primary responsibility for final content. All authors read and approved the final manuscript.

Abbreviations

FFQ food frequency questionnaire

MBRN Medical Birth Registry of Norway

MoBa the Norwegian Mother and Child Cohort Study

NND New Nordic Diet

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TABLE 1

Maternal characteristics according to degree of adherence to a New Nordic Diet (NND) during pregnancy in the Norwegian Mother and Child Cohort Study (MoBa)[1,2]. N=72,072.

		Degree of NND-adherence		
	Whole sample N=72,072 n	**Low N=19,349 %**	**Medium N=25,544 %**	**High N=27,179 %**
Age in years, mean (SD)		29.1 (4.7)	30.0 (4.5)	30.8 (54.5)
< 25	8,271	16.8	11.3	7.9
25–29	24,410	36.6	34.6	31.4
30–34	27,018	38.3	42.4	45.4
≥ 35	12,373	8.6	11.7	15.3
Parity				
Nulliparous	37,945	58.1	53.9	47.6
Para 1	21,445	28.6	29.3	31.0
Para 2	9,914	10.5	13.2	16.6
Para 3	2,121	2.1	2.7	3.7
Para 4 or more	647	0.7	0.8	1.1
Education				
≤ 12 years	22,430	37.5	31.4	26.3
13–16 years	29,864	39.0	41.4	43.2
≥ 17 years	18,235	20.9	25.0	28.7
Missing	1,543	2.5	2.2	1.8
Height (m) Mean (SD)		1.66 (0.19)	1.66 (0.19)	1.67 (0.18)
1.40–1.64	19,428	29.3	27.0	25.2
1.65–1.68	18,180	24.8	25.5	25.2
1.69–1.72	17,153	23.1	23.6	24.5
≥1.73	16,509	21.6	22.7	24.1
Missing	802	1.2	1.2	1.0
BMI mean (SD)		24.4 (4.5)	24.1 (4.3)	23.7 (4.0)
<18.5	2,141	3.2	3.0	2.8
18.5–24.9	46, 188	59.7	63.7	67.5
25–29.9	15,187	23.0	21.0	19.8
30–34.9	4,852	7.9	7.1	5.5
≥35	1,830	3.2	2.6	2.0
Missing	1,874	2.8	2.6	2.4
Smoking in mid-pregnancy				
-No smoking	65,807	88.6	91.1	93.4
-Occasional	1,970	3.3	2.8	2.3
-Daily	3,778	7.4	5.4	3.6
-missing	517	0.7	0.7	0.7
Exercise in pregnancy				
-never	10,172	20.6	14.3	9.3

		Degree of NND-adherence		
	Whole sample N=72,072 n	Low N=19,349 %	Medium N=25,544 %	High N=27,179 %
-less than weekly	13,854	22.4	19.9	16.3
-1–2 times per week	21,315	27.1	29.9	31.1
-3 times per week or more	20,748	20.3	27.5	36.0
-missing	5,983	9.6	8.4	7.2
Marital status				
Without cohabitant	2,945	4.9	4.1	3.5
Comorbidity				
Diabetes, all categories	1,064	1.2	1.5	1.6
-pregestational diabetes[3]	435	0.5	0.6	0.7
-gestational diabetes [4]	629	0.7	0.9	1.0
Chronic hypertension	364	0.5	0.4	0.4
Pregnancy outcomes				
Preeclampsia[5]	2,908	4.6	4.1	3.6
Early preeclampsia[6]	300	0.5	0.4	0.3
Preterm delivery (total)[7]	3,729	5.5	5.4	4.7
Spontaneous preterm delivery	2,127	3.2	3.1	2.6

[1]One-way Anova p<0.01 for all comparisons of continuous variables

[2]Chi Square test p<0.01 for all comparisons of covariates across NND-adherence except chronic hypertension that was not significant (p=0.604)

[3]Type 1 diabetes n=295, type 2 diabetes n= 127, unspecified diabetes n= 13

[4]Including those reporting use of anti-diabetic drugs during pregnancy n=56

[5]Preeclampsia defined as an increase in blood pressure to at least ≥ 140 systolic or 90 mm Hg diastolic, after the 20th gestational week, combined with proteinuria (protein excretion of at least 0.3 g/24 h or ≥ 1+ on dip-stick), both measured at least twice. Participants with eclampsia and HELLP-syndrome, as well as preeclampsia superimposed on chronic hypertension are included in the model.

[6]Early preeclampsia defined as preeclampsia resulting in delivery between 22 and 34 completed weeks of gestation.

[7]Preterm delivery defined as spontaneous delivery between 22 and 37 weeks of gestation.

TABLE 2

Associations of adherence to a New Nordic Diet during pregnancy with risk of preeclampsia[1] in the Norwegian Mother and Child Cohort study (MoBa), presented for the whole sample and by smoking status[2] (n=72,072).

NND-adherence	No.	No. cases	Crude risk %	Crude OR	95% CI	Adjusted OR[3,4]	95% CI
Whole sample	72,072	2,908	4.0				
Low	19,349	892	4.6	1.00		1.00	
Medium	25,544	1,045	4.1	0.88*	0.81, 0.97	0.91	0.83, 1.00
High	27,179	971	3.6	0.77*	0.70, 0.84	0.86*	0.78, 0.95
Smokers	5,748	187	3.3				
Low	2,060	90	4.4	1.00		1.00	
Medium	2,091	59	2.8	0.64*	0.46, 0.89	0.63*	0.44, 0.90
High	1,597	38	2.4	0.53*	0.36, 0.78	0.57*	0.37, 0.87
Non-smokers	65,807	2,710	4.1				
Low	17,145	800	4.7	1.00		1.00	
Medium	23,271	981	4.2	0.90*	0.82, 0.99	0.94	0.85, 1.04
High	25,391	929	3.7	0.78*	0.70, 0.86	0.88*	0.80, 0.98

* $P < 0.05$

1 Preeclampsia is defined as an increase in blood pressure (BP) to at least ≥ 140 systolic or 90 mm Hg diastolic after 20th week of gestation, combined with proteinuria (protein excretion of ≥ 0.3 g/24 h or ≥ 1+ on dip-stick), both measured at least twice. Participants with eclampsia and HELLP-syndrome, as well as preeclampsia superimposed on chronic hypertension are included in the model.

2 Interaction term p=0.083

3 Adjusted for maternal age, maternal age squared, parity, pre pregnancy BMI, educational attainment, smoking in mid-pregnancy, diabetes, chronic hypertension, and energy intake.

4 Number of missing in the multivariate models were 3,831 (5.3%) for the whole sample, 351 (6.1%) for smokers, and 2,963 (4.5%) for non-smokers.

Abbreviations: NND, New Nordic Diet.

TABLE 3

Associations of adherence to a New Nordic Diet during pregnancy with risk of early preeclampsia[1,2] in the Norwegian Mother and Child Cohort study (MoBa) (n=72,037).

NND-adherence	No.	No. cases	Crude risk %	Crude OR	95% CI	Adjusted OR[3,4]	95% CI
Whole sample	72,037	300	0.4				
Low	19,344	96	0.5	1.00		1.00	
Medium	25,532	112	0.4	0.88	0.67, 1.16	0.84	0.63, 1.12
High	27,161	92	0.3	0.68*	0.51, 0.91	0.71*	0.52, 0.96

* $P < 0.05$

1 Early preeclampsia was defined as preeclampsia before gestational week 34.

2 Preeclampsia is defined as at least one visit after 20 weeks of gestation with a systolic blood pressure (SBP) ≥ 140 or diastolic blood pressure (DBP) ≥ 90 after the 20th week of gestation, combined with proteinuria (urinary protein of 1+ or greater), both measured at least twice. Participants with hospital-confirmed eclampsia and HELLP-syndrome were included as valid cases, as well as those with PE superimposed on chronic hypertension (cHTN).

3 Adjusted model comprised maternal age (linear and quadratic), parity, pre pregnancy BMI, educational attainment, smoking, any diabetes, chronic hypertension, and energy intake.

4 Number of missing in the multivariate model was 3,830 (5.3%).

Abbreviations: NND, New Nordic Diet

TABLE 4

Associations of adherence to a New Nordic Diet during pregnancy with risk of spontaneous preterm delivery[1] in the Norwegian Mother and Child Cohort study (MoBa), presented for the whole sample and by parity[2] (n=72,037).

NND-adherence	No.	No. Cases	Crude risk %	Crude OR	95% CI	Adjusted OR[3,4]	95% CI
Whole sample	72,037	2,127	3.0				
Low	19,344	615	3.2	1.00		1.00	
Medium	25,532	794	3.1	0.98	0.88, 1.09	1.06	0.94, 1.19
High	27,161	718	2.6	0.83*	0.74, 0.92	0.91	0.80, 1.03
Nulliparity	37,924	1,320	3.5				
Low	11,237	445	4.0	1.00		1.00	
Medium	13,763	499	3.6	0.91	0.80, 1.04	0.95	0.85, 1.12
High	12,924	376	2.9	0.73*	0.63, 0.84	0.77*	0.66, 0.89
Multiparity	34,113	807	2.4				
Low	8,107	170	2.1	1.00		1.00	
Medium	11,769	295	2.5	1.20	0.99, 1.45	1.28*	1.03, 1.58
High	14,237	342	2.4	1.15	0.95, 1.38	1.24*	1.00, 1.53

*P < 0.05

[1]Preterm delivery defined as delivery before 37 weeks of pregnancy

[2]Interaction term p<0.001

[3]Adjusted for maternal age, parity, pre pregnancy BMI, educational attainment, smoking, exercise during pregnancy, any diabetes, chronic hypertension, and energy intake.

[4]Number of missing in the multivariate models: 9,285 (12.9%) for the whole sample, 4,177 (11.0%) in the nulliparity model, and 4,270 (15.0%) in the multiparity model.

Abbreviations: NND, New Nordic Diet