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Associations of adherence to the New Nordic Diet with risk of preeclampsia and preterm delivery in the Norwegian Mother and Child Cohort Study (MoBa)

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Abstract Preeclampsia and preterm delivery are serious complications of pregnancy and leading causes of perinatal mortality and morbidity worldwide. Dietary factors might be associated with these adverse outcomes. We investigated whether adherence to the New Nordic Diet (NND) was associated with preeclampsia and preterm delivery risks in the Norwegian Mother and Child Cohort Study (MoBa). Participants were recruited from all over Norway during the period 1999–2008. A previously constructed diet score assessing meal frequency, and the consumption of Nordic fruits, root vegetables, cabbages, potatoes, oatmeal porridge, whole grains, wild fish, game, berries, milk and water, was used to assess NND adherence. Associations between NND adherence and the outcomes were estimated in adjusted multivariate logistic regression models. Odds ratios (ORs) and 95 % confidence intervals (CIs) were calculated. A total of 72,072 women was included in the study. High versus low NND adherence was associated with lower risk of total preeclampsia (OR 0.86; 95 % CI 0.78–0.95) and early preeclampsia (OR 0.71; 95 % CI 0.52–0.96). High compared with low NND adherence was associated with a lower risk of spontaneous preterm delivery among nulliparous women (OR 0.77; 95 % CI 0.66–0.89), whereas multiparous women with high NND adherence had a marginally significant higher risk of preterm delivery (OR 1.24; 95 % CI 1.00–1.53). High NND adherence was associated with a lower relative risk of preeclampsia and of spontaneous preterm delivery among nulliparous women; however, among multiparous women there was a higher relative risk of preterm delivery.

Keywords Nordic diet · Pregnancy · Preeclampsia · Preterm delivery · Dietary pattern · Diet

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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 worldwide [1]. Frequency ranges from 2 to 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 causes of preeclampsia remain unknown, but incomplete placentation with placental ischemia is a fundamental characteristic of the disorder, and this is

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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 obstetrics care, accounting for a large share of offspring 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]. Recently 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 and Brug [10] proposed 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. 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 carried out in Nordic populations [17–20]. These beneficial metabolic influences of adherence to a healthy Nordic diet could also be of relevance to health in pregnancy because the risks of both hypertensive diseases, gestational diabetes and preterm delivery are associated with cardiovascular risk factors [4, 8, 21, 22].

Based on the documented cardioprotective effects of healthy Nordic diets, we hypothesized that NND-adherence during pregnancy might be associated with reduced risks of both preeclampsia and preterm delivery. We recently developed and described a diet score to assess adherence to a diet in line with the principles of the NND for use 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 compliance with the NND as measured by this a priori defined dietary score was associated with the risks of preeclampsia and preterm delivery in MoBa.

Subjects and methods

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 during 1999–2008. Consent for participation was obtained from 40.6 % of eligible 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 license 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 Q1 and the FFQ (Q2) (n = 86,776). We excluded plural pregnancies (n = 1,617), pregnancies with reported energy intake $<$4,500 kJ or $\geq$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, 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

The main measure was degree of adherence to the NND, assessed by a previously developed NND compliance 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 were calculated using FoodCalc and the Norwegian food composition table [25, 26]. Dietary supplements were not included in the calculations. The diet score comprised 10 subscales with each subscale addressing a specific aspect of the NND. Each subscale was constructed from one or more relevant food-frequency items. The summed score of each subscale was dichotomized by the median and participants were assigned scores of "1" if the NND intake was above the median and "0" if below the median. Adding the dichotomized subscales yielded a final NND score of 0–10, with higher scores indicating higher adherence to the NND. Similar methods have been used in many epidemiological studies to examine dietary patterns in relation to the risk of noncommunicable diseases and mortality [27].

The following subscales made up the NND score.

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

A more detailed description of the construction of the score has been published elsewhere [23]. In brief, the approximate dietary behavior associated with scoring above the median in each subscale was: (1) eating at least 24 main meals weekly; (2) eating Nordic fruits at least five times weekly; (3) eating root vegetables at least five times weekly; (4) eating cabbage at least twice weekly; (5) eating potatoes at least one-third of total occasions of eating potatoes, rice or pasta weekly; (6) choosing whole grain bread more often than refined bread; (7) eating oatmeal at least monthly; (8) eating 'foods from the wild countryside' at least twice weekly; (9) drinking more milk than juice; and (10) 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 because 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 ≥140 mm Hg 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 a dip-stick assay), 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, a combination of hemolysis, elevated liver enzymes, and low platelet count (HELLP syndrome), and preeclampsia superimposed on chronic hypertension as preeclampsia cases in the analyses. 'Early preeclampsia' was defined as preeclampsia diagnosed before 34 weeks of gestation, as registered in the MBRN.

We defined preterm delivery as delivery between 22 and 37 weeks of gestation, but chose *spontaneous* preterm delivery as the primary outcome because preeclampsia constitutes a large proportion of *indicated* preterm deliveries. The MBRN variables used to ascertain spontaneous preterm delivery were the length of gestation estimated from ultrasound examination, supplemented with the date of the 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 four 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 terms), 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 meters squared (kg/m^2). Women were categorized as being underweight (BMI < 18.5), of normal weight (BMI 18.5–24.9), overweight (BMI 25.0–29.9), obese grade I (BMI 30–35), or obese grade II (BMI ≥ 35) for description, but this information was included as a continuous variable in the regression models. Marital status was obtained from the MBRN and categorized as living with or without a 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, 13–16, 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 was 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, fewer 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 vs. ≥1–2 times a week). Information on regular dietary supplement use during pregnancy was obtained from the MBRN (yes/no). 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 for IBM 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 the mean ± standard deviation (SD) for continuous variables and proportions (%) for categorical variables. Differences in maternal characteristics across NND-adherence categories were tested with Pearson's Chi squared test for categorical data. Absolute risks of total preeclampsia, early preeclampsia, and spontaneous preterm delivery are presented according to the degree of NND adherence. We used odds ratios (ORs) to approximate relative risks of the outcomes with high compared with low NND adherence. The associations were estimated in crude and multivariate logistic regression models with NND-adherence scores modeled as a nominal variable ('low' = 1, 'medium' = 2, and 'high' = 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 (CIs), with low NND adherence as the 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, maternal height, and dietary supplement use 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, so exercise was retained in the preterm delivery model but removed from the preeclampsia models.

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

Results

Participants

A total of 72,072 women was included in this study, constituting 83 % of those having completed the relevant questionnaires. The mean age was 30.1 years (SD ± 4.6). Based on their individual NND score, participants were categorized as having '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 background information on maternal characteristics for the whole sample and according to the degree of NND adherence. Women with high NND-adherence scores were slightly older, more educated, of higher parity, more likely to exercise regularly, but less likely to smoke and be overweight/obese compared with those with low NND adherence.

Diet

Obviously, from the way the score was constructed women with high NND-adherence scores reported substantially higher intake of whole grain bread, oatmeal, fruits, vegetables, potatoes, fish and seafood, meat, unsweetened milk,

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)[a,b] (n = 72,072)

	Whole sample N = 72,072 n (%)	Degree of NND adherence		
		Low N = 19,349 (%)	Medium N = 25,544 (%)	High N = 27,179 (%)
Age in years, mean (SD)	30.1 (4.6)	29.1 (4.7)	30.0 (4.5)	30.8 (4.5)
<25	8,271 (11.5)	16.8	11.3	7.9
25–29	24,410 (33.9)	36.3	34.6	31.4
30–34	27,018 (42.4)	38.3	42.4	45.4
≥35	12,373 (12.2)	8.6	11.7	15.3
Parity				
Nulliparous	37,945 (52.6)	58.1	53.9	47.6
Para 1	21,445 (29.8)	28.6	29.3	31.0
Para 2	9,914 (13.8)	10.5	13.2	16.6
Para 3	2,121 (2.9)	2.1	2.7	3.7
Para 4 or more	647 (0.9)	0.7	0.8	1.1
Education				
≤12 years	22,430 (31.1)	37.5	31.4	26.3
13–16 years	29,864 (41.4)	39.0	41.4	43.2
≥17 years	18,235 (25.3)	20.9	25.0	28.7
Missing	1,543 (2.1)	2.5	2.2	1.8
Height (m) Mean (SD)	1.66 (0.19)	1.66 (0.19)	1.66 (0.19)	1.67 (0.18)
1.40–1.64	19,428 (27.0)	29.3	27.0	25.2
1.65–1.68	18,180 (25.2)	24.8	25.5	25.2
1.69–1.72	17,153 (23.8)	23.1	23.6	24.5
≥1.73	16,509 (22.9)	21.6	22.7	24.1
Missing	802 (1.1)	1.2	1.2	1.0
BMI mean (SD)	24.0 (4.3)	24.4 (4.5)	24.1 (4.3)	23.7 (4.0)
<18.5	2,141 (3.0)	3.2	3.0	2.8
18.5–24.9	46, 188 (64.1)	59.7	63.7	67.5
25–29.9	15,187 (21.1)	23.0	21.0	19.8
30–34.9	4,852 (6.7)	7.9	7.1	5.5
≥35	1,830 (2.5)	3.2	2.6	2.0
Missing	1,874 (2.6)	2.8	2.6	2.4
Smoking in mid-pregnancy				
No smoking	65,807 (91.3)	88.6	91.1	93.4
Occasional	1,970 (2.7)	3.3	2.8	2.3
Daily	3,778 (5.2)	7.4	5.4	3.6
Missing	517 (0.7)	0.7	0.7	0.7
Exercise in pregnancy				
Never	10,172 (14.1)	20.6	14.3	9.3
Less than weekly	13,854 (19.2)	22.4	19.9	16.3
1–2 times per week	21,315 (29.6)	27.1	29.9	31.1
3 times per week or more	20,748 (28.8)	20.3	27.5	36.0
Missing	5,983 (8.3)	9.6	8.4	7.2
Dietary supplements				
Regular use	52,665 (73.1)	71.3	73.1	74.3
No regular use	19,407 (26.9)	28.7	26.9	25.7
Marital status				
Without cohabitant	2,945 (4.1)	4.9	4.1	3.5

Table 1 continued

	Whole sample N = 72,072 n (%)	Degree of NND adherence		
		Low N = 19,349 (%)	Medium N = 25,544 (%)	High N = 27,179 (%)
Comorbidity				
Diabetes, all categories	1,064 (1.5)	1.2	1.5	1.6
Pregestational diabetes[c]	435 (0.6)	0.5	0.6	0.7
Gestational diabetes[d]	629 (0.9)	0.7	0.9	1.0
Chronic hypertension	364 (0.5)	0.5	0.4	0.4
Pregnancy outcomes				
Preeclampsia[e]	2,908 (4.0)	4.6	4.1	3.6
Early preeclampsia[f]	300 (0.4)	0.5	0.4	0.3
Preterm delivery (total)[g]	3,729 (5.2)	5.5	5.4	4.7
Spontaneous preterm delivery	2,127 (3.0)	3.2	3.1	2.6

[a] One-way ANOVA; $p < 0.01$for all comparisons of continuous variables

[b] Chi squared test $p < 0.01$ for all comparisons of covariates across NND-adherence groups except for those subjects with chronic hypertension where the result was not significant

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

[d] Including those subjects reporting the use of antidiabetic drugs during pregnancy n = 56

[e] Preeclampsia was defined as an increase in blood pressure to ≥140 mm Hg 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 a dipstick assay), both measured at least twice

[f] Early preeclampsia was defined as that resulting in delivery between 22 and 34 completed weeks of gestation

[g] Preterm delivery was defined as delivery between 22 and 37 weeks of gestation

and drinking water, and a lower intake of sugar-sweetened and artificially sweetened beverages compared with women with low NND adherence. They also reported higher intakes of fermented milk and yoghurt and slightly lower intakes of sweets and salty snacks. However, they did report higher intakes of cakes and desserts. A detailed presentation of differences in food and nutrient intakes according to the degree of NND adherence is included as supplementary material (supplementary tables 1 and 2). Differences in macronutrient distribution between groups were small, but generally favored a healthier distribution with increasing NND adherence. Micronutrient intake per 10 MJ increased across NND-adherence scores for all micronutrients (supplementary table 2). 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 cases of preeclampsia was identified, giving a 4.0 % prevalence of preeclampsia in our study population. High compared with 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 a 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). Because diabetes and chronic hypertension are strong risk factors for preeclampsia, we reran the models after removing any participants with those disorders. This did not substantially change the overall estimate (OR 0.87; 95 % CI 0.79–0.96).

Early preeclampsia

Three hundred women developed preeclampsia before 34 weeks of gestation. High compared with 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 or diabetes did not change the estimate substantially (OR 0.70; 95 % CI 0.51–0.97).

Preterm delivery

A total of 3,729 women (5.2 %) delivered babies preterm. High versus low NND adherence was associated with

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

NND adherence	No.	No. cases	Crude risk (%)	Crude OR	95 % CI	Adjusted OR[c,d]	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

* $p < 0.05$

[a] Preeclampsia was defined as an increase in blood pressure to ≥140 mm Hg 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 a dipstick assay), both measured at least twice. Participants with eclampsia and HELLP syndrome (see definition in the text), as well as preeclampsia superimposed on chronic hypertension are included in the model

[b] Interaction term $p = 0.083$

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

[d] Numbers of missing data points in the multivariate models: 3,831 (5.3 %) for the whole sample; 351 (6.1 %) for smokers' and 2,963 (4.5 %) for nonsmokers

OR odds ratio, *CI* confidence interval

Table 3 Associations of adherence to a New Nordic Diet (NND) during pregnancy with risk of early preeclampsia[a,b] 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[c,d]	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

* $p < 0.05$

[a] Early preeclampsia was defined as preeclampsia before gestational week 34

[b] Preeclampsia was defined as an increase in blood pressure to ≥140 mm Hg 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 a dipstick assay), both measured at least twice. Participants with eclampsia and HELLP syndrome (see definition in the text), as well as preeclampsia superimposed on chronic hypertension are included in the model

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

[d] Number of missing data points in the multivariate model: 3,830 (5.3 %)

lower odds of preterm delivery (OR 0.90; 95 % CI 0.81–0.98). A total of 2,129 (3.0 % of the total cohort) were spontaneous deliveries. Sixteen neonates born before week 37 had birthweight z-scores >4 and were excluded from further analyses because of suspected misclassification. Two of these were spontaneous deliveries, yielding 2,127 spontaneous preterm deliveries in the logistic regression analyses. The observed associations between NND adherence and spontaneous preterm delivery are shown in Table 4. High compared with low NND adherence was not significantly associated with spontaneous preterm delivery in the whole sample (OR 0.91; 95 % CI 0.80–1.03). Parity was identified as an effect modifier of the relationship between NND adherence and spontaneous

Table 4 Associations of adherence to a New Nordic Diet (NND) during pregnancy with the risk of spontaneous preterm delivery[a] in the Norwegian Mother and Child Cohort Study (MoBa), presented for the whole sample and by parity[b] (n = 72,037)

NND adherence	No.	No. Cases	Crude risk (%)	Crude OR	95 % CI	Adjusted OR[c,d]	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

* $p < 0.05$

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

[b] Interaction term $p < 0.001$

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

[d] Number of missing data points 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

preterm delivery (interaction term $p = 0.001$), so analyses were completed stratified by parity. Among nulliparous women, high compared with low NND adherence implied lower odds of preterm delivery (OR 0.77; 95 % CI 0.66–0.89), whereas a marginally significant higher odds of preterm delivery was observed among multiparous women (OR 1.24; 95 % CI 1.00–1.53). The absolute risk of spontaneous preterm delivery was lower in the multiparous compared with the nulliparous group (2.4 vs. 3.5 %; Table 4).

Subgroup analyses

We ran all models stratified by the women's parity and established risk factors for preeclampsia and preterm delivery including smoking, BMI, diabetes and chronic hypertension. Stronger associations were generally observed among nulliparous women and women with BMI < 30, whereas weaker or nonsignificant associations were observed among multiparous and obese women (data not shown). In some strata, there was insufficient power to detect differences in risk as judged by the number of cases and the range of the CIs. Among participants with pregestational 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 nonsignificantly associated with lower odds of spontaneous preterm delivery among women with pregestational 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 analyses

To assess whether a stricter definition of 'high' NND adherence would strengthen the observed associations, we moved the NND score cutoff 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 spontaneous preterm delivery (data not shown). A large proportion of the participants reported regular use of dietary supplements during pregnancy (Table 1). To assess the associations between NND adherence and the outcomes without a potential influence of dietary supplements we reran the models in the subset of women reporting no regular use of dietary supplements during pregnancy as documented in the birth notification form (26.9 %). The association between NND adherence and risk of preeclampsia was essentially the same as in the whole sample (OR 0.85; 95 % CI 0.70–1.04). The association between NND adherence and risk of spontaneous preterm delivery was likewise in the same direction and of similar magnitude in the 'no supplements' group as in the whole sample (nulliparous: OR 0.75; 95 % CI 0.57–0.99, multiparous: OR 1.32; 95 % CI 0.95–1.82).

Missing data

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

Discussion

In this study, we found lower overall risk of preeclampsia with high compared with low adherence to the NND. Adherence to the diet 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.

Dietary differences between extreme categories of NND adherence were most pronounced for added sugar, dietary fiber, and micronutrients such as calcium, phosphorus, beta-carotene, vitamin C, vitamin D, folate, magnesium, potassium, and selenium, many of which might influence metabolic pathways involved in the pathophysiology of preeclampsia and preterm delivery [8]. A nutritious and well-balanced diet might enhance the function and efficiency of maternal and fetal metabolism through substrate availability, reductive capacity, immunological mechanisms and insulin sensitivity. Thus, the metabolic stress induced by disturbed placentation could possibly be attenuated or counterbalanced by a high quality diet [8, 29]. A meta-analysis by Thangaratinam et al. [30] in 2012 investigated the effects of dietary interventions on maternal weight and obstetric outcomes; in this, general interventions during pregnancy to improve diet quality were associated with a 33 % reduced risk of preeclampsia and a 32 % reduced risk of preterm delivery.

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 compared to low scores on a dietary pattern characterized by the consumption of vegetables, plant foods, and vegetable oils, had a 28 % lower risk of preeclampsia, whereas those with high versus low scores on a processed food pattern characterized by eating processed meat, salty snacks, and sweet drinks had a 21 % higher risk of preeclampsia [31]. Our previously defined NND score to some extent integrates these patterns and produced similar associations even though fat quality differed minimally between the NND-adherence groups. Qiu et al. [32] used dietary fiber as a proxy for a healthy diet and found a high versus a low fiber intake to be associated with a 72 % lower risk of preeclampsia in a prospective study on pregnant women. Notably, one of the largest nutritional differences between high and low NND adherence in our study was the intake of dietary fiber and micronutrients associated with whole grains, fruits and vegetables.

The strong 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 nonsmokers were categorized with low NND adherence, as can be observed in Table 2. The slightly stronger association of high versus low NND adherence with the risk of early preeclampsia compared with total preeclampsia indicates that a protective influence of diet might apply from early gestation, and help to avoid or postpone the development of fulminant disease. Another possible explanation is that early preeclampsia could be associated with a different phenotype compared with term preeclampsia, and—potentially—might be more responsive to lifestyle [2]. The combination of compromised intrauterine fetal conditions caused by inadequate placentation—and being born prematurely—leaves the infant at an especially high risk for perinatal morbidity and later impaired health [29, 33]. Therefore, even a small protective effect of diet could be of relevance to public health.

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 might influence risk substantially [34]. Khoury et al. [35] reported a 90 % reduction in the incidence of preterm delivery in an intervention group randomized to following a cholesterol-lowering diet during pregnancy. Aiming to replicate this finding, two coordinated observational studies were carried out on Norwegian and Danish birth cohorts, with predefined dietary criteria adapted to resemble the intervention diet in the study by Khoury et al. [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 a 12 % lower hazard rate of preterm delivery with high versus low adherence to a 'prudent' dietary pattern as well as a 9 % lower hazard rate with a so-called 'traditional' dietary pattern [38]. Our NND score applied to the same dataset captured a combination of these two dietary patterns that could be described in detail, namely 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 significantly higher risk of spontaneous preterm delivery with high versus low NND adherence observed among multiparous women is difficult to explain. As seen in Table 4, multiparous women had an absolute lower risk of spontaneous preterm delivery compared with 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 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 sixfold [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, such as intervals between pregnancies, breastfeeding, and previous adverse reproductive outcomes, likely contributed to the observed heterogeneity by parity.

Strengths and limitations

The 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 [25]. The investigation of a comprehensive dietary pattern as exposure allows for the cumulative, synergistic and interactive effects of diet to be taken into account, unlike investigations with single nutrients or foods as exposures [27, 40, 41]. This approach also made possible the categorization of participants into three distinct diet categories for description, comparison and analysis. The MBRN preeclampsia variable has been validated recently 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 [42]. High positive predictive values were 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 [42].

Some limitations in our study 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, being overweight, having less education, smoking more, and taking less exercise, all of which are associated with both lower 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 groups described in our previous paper indicate that the score discriminates the degree of adherence to the dietary pattern we intended to describe [23]. Potential under-reporting of unhealthy dietary behaviors, as well as over-reporting of healthy ones, might 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 [43]. Women with chronic conditions such as diabetes, chronic hypertension, or obesity might adhere to a healthy diet during pregnancy, but still have considerably increased risk for the outcomes compared with other pregnant women. However, such reverse causation bias would tend to attenuate true associations. The observed lower odds of preeclampsia with high versus low NND adherence in the subgroup of women with pregestational diabetes is interesting, but should be interpreted with caution because the number of cases was small, and confounding of this association by overall disease management and compliance with medical advice is likely. Given that having diabetes is a strong risk factor for preeclampsia, this association warrants further investigation.

Dietary patterns have been shown to be fairly stable over time as documented by the assessment of the diets of 12,572 nonpregnant women aged 20–34 years from Southampton, UK, of whom 2,270 and 2,649 became pregnant and provided complete dietary data in early and late pregnancy, respectively [44]. 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 might thus be explained by longer term NND adherence and corresponding maternal nutritional status before pregnancy. 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 a critical window for nutritional factors to alter pregnancy-related risks. Long-term diet is a determinant of a range of interrelated risk factors associated with preeclampsia and preterm delivery, such as BMI, serum lipid levels, insulin resistance, type 2 diabetes and chronic hypertension. Therefore, it might exert its influence both indirectly, mediated through modification of pre-pregnancy risk factors, and directly by its influence on other aspects of nutritional status. Because 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 might overestimate the associations between NND adherence during pregnancy and the outcomes. However, they might underestimate the 'true' associations of *long-term* NND adherence with the risk of preterm delivery and preeclampsia. Only a carefully conducted randomized controlled study could confirm whether a diet in line with the NND during pregnancy really influences the risk of preeclampsia and preterm delivery. Meanwhile, the intervention study referred to by Khoury et al. [35] and the meta-analysis by Thangaratinam et al. [30] both support the idea that diet during the timeframe of pregnancy matters.

The diet indicated by a high NND score is largely in line with Food Based Dietary Guidelines adopted 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 noncommunicable diseases. Our primary aim for the development of the score was to be able to measure adherence to a *potentially* regionally based and environmentally friendly diet, and beyond that to investigate its association with various pregnancy-related health outcomes in the MoBa cohort. The score items were established in advance to reflect adherence to the concept of an NND as described by Bere and 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 the availability of Nordic fruits that might have influenced consumption. However, apples and pears are 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 single mothers have been shown to be strongly under-represented in MoBa, whereas consumers of folic acid and multivitamin users are over-represented [45]. Because the healthier lifestyle documented in MoBa participants compared with 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 might potentially 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 disentangled reliably from the totality of the diet. We believe that this is of lesser relevance because dietary recommendations communicated to the public need to address complex diets. Most of the foods addressed by the NND score are not confined to the Nordic traditional diet, but are widely consumed in other European regions as well [46].

Conclusions

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 outcomes. We have shown that a dietary pattern in line with the concept of the NND during pregnancy is associated with lower risk of preeclampsia, and a lower risk of spontaneous preterm delivery among nulliparous women. However, an unexplained higher relative risk of spontaneous preterm delivery with high versus low NND adherence was observed among multiparous women. Many of the foods captured by the NND 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.

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Conflict of interest None.

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