


Season, dietary factors, and physical activity modify 25-hydroxyvitamin D concentration during pregnancy

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Abstract

Purpose The objectives of this cross-sectional study were to define maternal and umbilical cord blood (UCB) 25-hydroxyvitamin D (25(OH)D) to characterize maternal factors modifying 25(OH)D during pregnancy and predict UCB 25(OH)D in two subgroups with Declined [$\Delta 25(\text{OH})\text{D} < 0 \text{ nmol/l}$] and Increased [$\Delta 25(\text{OH})\text{D} > 0 \text{ nmol/l}$] 25(OH)D concentration.

Methods A complete dataset was available from 584 women. 25(OH)D was determined at gestational weeks 6–13 and in UCB. Baseline characteristics were collected retrospectively using questionnaires. $\Delta 25(\text{OH})\text{D}$ was calculated as UCB 25(OH)D–early pregnancy 25(OH)D. Dietary patterns were generated with principal component analysis. Multivariate regression models were applied.

Results Vitamin D deficiency was scarce, since only 1% had 25(OH)D concentration $< 50 \text{ nmol/l}$ both in early

pregnancy and in UCB. Shared positive predictors of UCB 25(OH)D in the subgroups of Declined and Increased, were early pregnancy 25(OH)D ($P < 0.001$) and supplemental vitamin D intake ($P < 0.04$). For the Increased subgroup summer season at delivery ($P = 0.001$) and “sandwich and dairy” dietary pattern characterized with frequent consumption of vitamin D fortified margarine and milk products ($P = 0.009$) were positive predictors of UCB 25(OH)D. Physical activity ($P = 0.041$) and maternal education ($P = 0.004$) were additional positive predictors in the Declined group

Conclusions Maternal and newborn vitamin D status was sufficient, thus public health policies in Finland have been successful. The key modifiable maternal determinants for 25(OH)D during pregnancy, and of the newborn, were supplemental vitamin D intake, frequent consumption of vitamin D fortified foods, and physical activity.

Keywords Maternal vitamin D status · Newborn vitamin D status · 25-hydroxyvitamin D concentration · Pregnancy · Dietary pattern

The project protocol is registered at ClinicalTrials.gov (NCT01723852).

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Abbreviations

DP	Dietary pattern
FFQ	Food frequency questionnaire
PA	Physical activity
UCB	Umbilical cord blood
VIDI	Vitamin D intervention in infants
25(OH)D	25-hydroxyvitamin D concentration

Introduction

Vitamin D deficiency is a major health concern among pregnant women across the globe [1]. In the northern

latitudes, solar ultraviolet B radiation during the winter months is insufficient for cutaneous vitamin D synthesis, and the main sources of vitamin D are food and supplements.

A high prevalence of vitamin D deficiency has existed in several age groups in Finland [2] including pregnant women [3, 4]. In 2007, we observed vitamin D deficiency, defined as serum 25-hydroxyvitamin D concentration [25(OH)D] <50 nmol/l, in 77% of women during early pregnancy and in 60% of mother–infant pairs measured from umbilical cord blood (UCB) at delivery [5].

Poor maternal vitamin D status has been associated with gestational morbidities such as increased risk of gestational diabetes and pre-eclampsia [6, 7]. In addition, poor maternal vitamin D status and low maternal intake of vitamin D have both short-term and long-term consequences on child health; they are associated with poor intrauterine growth [7, 8] and childhood obesity [9, 10]. Furthermore, poor vitamin D status increases the risk of asthma and allergic rhinitis [11], infantile eczema [12], and poor bone mass accrual in the offspring [13, 14].

In 2010, vitamin D fortification in Finland was doubled in fluid dairy products and dietary fats, which now contain vitamin D₃ 1 µg/100 ml and 20 µg/100 g, respectively. The national recommendation for vitamin D supplementation for pregnant and breastfeeding women was revised in 2011 to year-round daily 10 µg supplementation, instead of solely winter-time supplementation. Probably due to these actions, vitamin D status in Finland has improved [15, 16].

The objectives of this study were to define maternal and UCB 25(OH)D, to characterize maternal factors which modify the tracking of 25(OH)D during pregnancy and predict UCB 25(OH)D in two subgroups where 25(OH)D concentration declines, or increases during pregnancy. To disentangle the impact of diet on 25(OH)D, we investigated maternal diet in the form of dietary patterns (DP) that take into account the interactions of foods and their nutrients and identify foods that are usually eaten together [17, 18].

The study is part of the longitudinal Vitamin D Intervention in Infants (VIDI) study.

Subjects and methods

Recruitment

At Kättilöopisto Maternity Hospital, Helsinki, Finland, 987 families were recruited to the study between January 2013 and May 2014; recruitment took place during the mother's hospital stay for delivery. Mothers were of Caucasian origin without regular medication and with an uneventful and singleton pregnancy. The infants, 492 girls and 495 boys, were born at term (37.0–42.0 weeks) and birth weight

was appropriate for gestational age (birth weight SD score between −2.0 and +2.0). Exclusion criteria for the newborns included nasal continuous positive airway pressure treatment >1 day, intravenous glucose infusion, seizures, duration of phototherapy >3 days, and a need for nasogastric tube >1 day. Of the informed eligible families, 29% agreed to participate in the VIDI study (Fig. 1). For the present cross-sectional study, we included subjects who had complete baseline background data, and both early pregnancy (gestational weeks 6–13) and UCB 25(OH)D available ($n=584$) (Fig. 1). Thus, subjects had no missing values.

25(OH)D analysis

Maternal early pregnancy serum samples were collected at communal prenatal clinics at gestational weeks 6–13

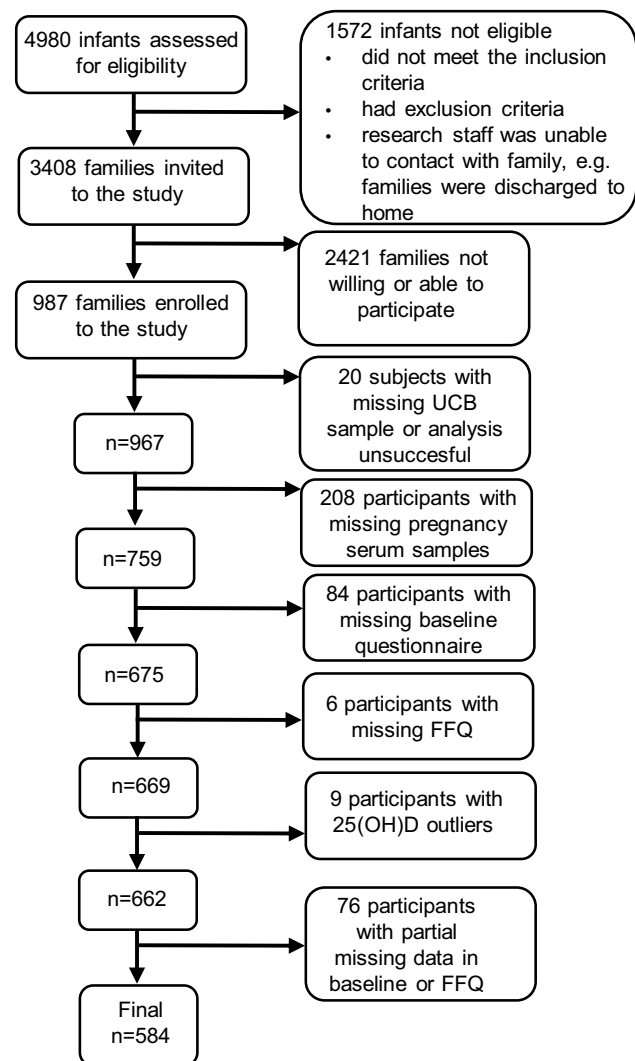


Fig. 1 Flow chart of subjects included in the study. FFQ, food frequency questionnaire; UCB, umbilical cord blood; 25(OH)D, 25-hydroxyvitamin D

between June 2012 and November 2013 as part of the mothers' normal follow-ups. Samples were stored in the Finnish Maternity Cohort serum bank, which is organized by the National Institute for Health and Welfare. At birth, 20 ml of UCB was obtained, stored at +8 °C, and processed within 12 h. Blood plasma and cells were separated and samples were frozen at –20 °C and later transferred to –80 °C for storage until analysis.

From the UCB plasma and pregnancy serum samples, 25(OH)D was analyzed simultaneously using the IDS-iSYS fully automated immunoassay system (Immunodiagnostic Systems Ltd., Bolton, UK) with chemiluminescence detection. Inter-assay variation was avoided by analyzing all samples in the same patch. The intra-assay variation was <5% for early pregnancy samples and <13% for UCB samples. The quality and accuracy of the serum 25(OH)D analysis is validated on an on-going basis by participation in the vitamin D External Quality Assessment Scheme (DEQAS, Charing Cross Hospital, London UK). The method utilized in the present study shows a 3% positive bias against all laboratory trimmed mean values and a 10% positive bias compared with NIST standards in international comparisons [19]. There is a minor tendency to overestimate the actual concentration. Plasma UCB 25(OH)D concentrations were corrected with formula $19.13 + 0.897 * \text{UCB } 25(\text{OH})\text{D}$ to be comparable with serum 25(OH)D concentrations. The equation is based on the comparison of paired 25(OH)D measurements in EDTA-plasma and serum UCB samples in 84 individuals at birth.

We employed UCB 25(OH)D to reflect both the mother's vitamin D status at the end of pregnancy and the infant's vitamin D status at birth. Our previous study indicated that 25(OH)D in UCB and in the mother's circulation at the time of delivery were linked, the UCB 25(OH)D being on average (SD) 103% (16) of the maternal postpartum concentration [5].

Maternal baseline data

Maternal baseline data were obtained using a self-administered questionnaire which was filled in after delivery. This included maternal height (cm) and weight (kg) before pregnancy. Body mass index (BMI) (kg/m^2) was categorized into underweight (<18.5), normal weight (18.5–24.9), overweight (25.0–29.9), obese (30.0–34.9), and severely obese (>35). Education level was graded from 1 (=comprehensive school/lower secondary education) to 6 (university degree/first or second stage of tertiary education) or marked as "other" if none of the grades were applicable. Education level was recategorized from six to two categories (1=lower or upper secondary or post-secondary non-tertiary education, 2=first or second stage of tertiary education). Parity was determined by the number of biological

children and used as a dichotomous variable (1=primipara, 2=multipara). History of physical activity before pregnancy was obtained. Guided exercise, unsupervised exercise, and exercise related to everyday travel between home and workplace were recorded. Only guided exercise (PA) was used in analyses due to collinearity issues. Current and prepregnancy smoking status was assessed by number of cigarettes per day. Alcohol consumption before pregnancy was assessed by number of dosages per week. Duration of gestation at pregnancy sampling and at delivery was applied as days or weeks as appropriate. Maternal age was determined at the sampling date in early pregnancy.

Maternal use of supplements, specific brand names, dosing, and date of commencement were recorded. We calculated the average daily intake of vitamin D from supplementation during the last two months of pregnancy. Diet including alcohol consumption during the last month of pregnancy was collected retrospectively using a 22-item semi-quantitative food frequency questionnaire (FFQ) [20]. Participants were asked about frequency of food groups with given standard portion size. If participant's portion size differed from the standard they reported the applicable portion size, and we took this into account when calculating the final frequencies. The frequency of food groups consumed was recorded as follows: 0=not used, 1=once a month or less, 2=two to three times a month, 3=once a week or four times a month, 4=two to three times a week, 5=four to five times a week, 6=once a day, 7=two to three times a day, and 8=four to six times a day or more. Subjects filled out the questionnaire before the study visit and study personnel reviewed it at the study visit.

Statistical analysis

The normality of the variables was visually inspected. Outliers of UCB 25(OH)D ($n=7$) and early pregnancy 25(OH)D ($n=2$) concentrations were removed to obtain reliable results with linear regression. Season, with four categories, was coded using dummy variables (with fall as a reference) in linear regression models. Winter was defined as December, January, and February; spring as March, April, and May; summer as June, July, and August; and fall as September, October, and November. In this study, we defined vitamin D sufficiency as $25(\text{OH})\text{D} \geq 50 \text{ nmol/l}$ [21]. $\Delta 25(\text{OH})\text{D}$ was calculated as $\text{UCB } 25(\text{OH})\text{D} - \text{early pregnancy } 25(\text{OH})\text{D}$. Independent sample t-tests or Mann–Whitney *U*-tests as appropriate were applied to compare maternal characteristics between the Declined [$\Delta 25(\text{OH})\text{D} < 0 \text{ nmol/l}$] and Increased [$\Delta 25(\text{OH})\text{D} > 0 \text{ nmol/l}$] subgroups. Seasonal differences were tested using One-way ANOVA and Bonferroni post hoc tests.

DPs were created based on food group frequencies using principal component analysis. This was performed with

varimax (orthogonal) rotation. If a food group appeared in multiple DPs, the highest loading determined the DP to which it was assigned. Regression-based principal component analysis scores were calculated for 584 individuals. These scores rank individuals according to their adherence to the specific DP. The means (SD) for scores are 0 (1).

We applied an elaboration model [22] to study the tracking of 25(OH)D from early pregnancy to UCB. To do this, we applied series of regression models to investigate how the different factors affected the relationship between early pregnancy and UCB 25(OH)D. In the crude model, only pregnancy 25(OH)D was employed to explain UCB 25(OH)D. Next, potential explanatory variables were added into the model in the following packages: (1) lifestyle (including PA, smoking and alcohol consumption before pregnancy, and smoking after delivery), (2) maternal background (including education, prepregnancy BMI, age in early pregnancy, and parity), (3) season and duration of gestation (including spring, winter and summer season at early pregnancy and at delivery, duration of gestation at pregnancy sampling and at delivery), and (4) nutrition (including five DPs, number of daily supplements, and supplemental vitamin D intake during pregnancy). The combination of the specific factors in packages was based on the similar characteristics of the factors.

We examined changes in the B coefficient of early pregnancy 25(OH)D after adding each factor one by one and after adding the whole package into the crude model. A decline in B coefficient means that the added factor promotes, and an increase in B coefficient means that the added factor prevents the tracking of 25(OH)D from early pregnancy to UCB.

The elaboration model enabled us to select the modifiers associating with UCB 25(OH)D for further analysis. All of the selected modifiers were included in the same linear regression model to determine the most important explanatory factors of UCB 25(OH)D in the two subgroups of Declined and Increased. In addition, determinants for clinically relevant decline in 25(OH)D during pregnancy [$\Delta 25(\text{OH})\text{D} \leq -10.0$; $n = 209$] were investigated.

Associations were considered significant at $P < 0.05$. All statistical analyses were conducted using the IBM SPSS program for Windows version 22 (IBM, Chicago, IL, USA).

Results

Maternal characteristics

The mean age of mothers was 31.6 years (range 18.8–43.7); most of the mothers were primiparous (63%), had normal weight (72%), and were non-smokers (before pregnancy

86% and after delivery 97%), and 76% had at least Bachelor's level education (Table 1). Of the mothers, 18% were overweight and 6% obese. Altogether 95% of women used vitamin D supplementation during pregnancy, and for 54% the daily vitamin D supplementation was 10 μg , as recommended. During pregnancy, the average daily supplemental vitamin D intake was 15.7 μg (range 0.0–197.5, interquartile range 10.0–20.0).

25(OH)D concentrations

In general, the maternal and newborn concentrations of 25(OH)D were considered sufficient, as only 1% of early pregnancy 25(OH)D and UCB 25(OH)D concentrations were below 50 nmol/l. Both early pregnancy and UCB 25(OH)D showed seasonal variation (Table 2) (early pregnancy, One-way ANOVA: $P < 0.036$; UCB, One-way ANOVA: $P < 0.010$), highest concentrations being in the summer. The lowest UCB 25(OH)D in the spring and fall, and for early pregnancy 25(OH)D in the winter.

25(OH)D concentration was maintained during pregnancy which was confirmed in pairwise comparison of 25(OH)D concentrations, the mean (95% CI) change being -0.6 ($-1.5, 2.6$) nmol/l ($P = 0.585$). We observed an association between early pregnancy and UCB 25(OH)D ($B = 0.32$; 95% CI 0.23, 0.41; $P < 0.001$). Maternal characteristics were compared between subgroups with Declined [$\Delta 25(\text{OH})\text{D}$ range: -63.3 (-0.1)] and Increased [$\Delta 25(\text{OH})\text{D}$ range: 0.2 – 115.6] vitamin D status (Table 1). Compared with mothers in the Declined group, those in the Increased group showed lower early pregnancy 25(OH)D, earlier sampling and lower parity, but higher UCB 25(OH)D (Table 1). In the Declined group 5.9% and in the Increased group 4.6% did not use vitamin D supplements during pregnancy (χ^2 Test $P = 0.467$).

Dietary patterns

Five DPs were identified using principal component analysis, explaining 45.7% of the variation in maternal diet (Table 3). Correlations between food groups and DPs are shown as loadings in Table 3. The first DP consisted of sweets/candy/lollipops, pudding/chocolate/ice cream, sweet and salty pastries, snacks, and squash/soft drink, and was interpreted as “goodies and snacks.” The second DP consisted of fresh and cooked vegetables (including potato), fruits/berries (including fruit or berry juice), fish, and seeds/beans, and was interpreted as “health conscious.” The third DP consisted of meat, chicken or egg-based foods, cold cuts from sausages, sausages, and ready-made marinated meat or fish products, and was interpreted as “meat.” The fourth DP consisted of rye bread/other whole grain bread/muesli, cheese, margarine, and fluid dairy or

Table 1 Maternal characteristics of the entire study population and comparison between subgroups with Declined and Increased 25(OH)D concentration during pregnancy^a

	All (n=584)	Declined (n=321)	Increased (n=263)
Maternal characteristics	Mean ± SD	Mean ± SD	Mean ± SD
Alcohol use (portion/wk) ^b	1.9 ± 2.0	1.8 ± 2.0	1.9 ± 2.1
Smoking (number of daily cigarettes) ^b	1.3 ± 3.8	1.3 ± 3.8	1.2 ± 3.8
Guided exercise (min/d) ^b	10.6 ± 19.1	9.9 ± 18.1	11.4 ± 20.2
BMI (kg/m ²) ^b	23.3 ± 3.8	23.1 ± 3.7	23.6 ± 3.9
Duration of gestation at pregnancy sampling (wk)	11.0 ± 1.0	11.1 ± 1.0	10.8 ± 1.0**
Age (year)	31.1 ± 4.2	31.1 ± 4.4	31.0 ± 4.0
Early pregnancy 25(OH)D (nmol/l)	88.8 ± 19.0	95.8 ± 18.3	80.4 ± 16.1***
UCB 25(OH)D (nmol/l)	88.3 ± 22.0	78.3 ± 14.6	100.5 ± 23.4***
Δ25(OH)D (nmol/l)	-0.6 ± 24.8	-17.5 ± 13.7	20.1 ± 18.8***
Number of daily supplements ^c	2.3 ± 1.4	2.2 ± 1.3	2.3 ± 1.4
Supplemental vitamin D intake (μg/d) ^c	15.7 ± 16.9	15.2 ± 18.6	16.3 ± 14.6
Duration of gestation at delivery (wk)	40.2 ± 1.1	40.1 ± 1.1	40.3 ± 1.1
Parity	1.5 ± 0.7	1.6 ± 0.8	1.4 ± 0.6**
Level of education ^d	4.9 ± 1.3	4.9 ± 1.4	5.0 ± 1.3
Smoking (number of daily cigarettes) ^e	0.2 ± 1.4	0.3 ± 1.4	0.2 ± 1.3

BMI body mass index; 25(OH)D 25-hydroxyvitamin D; UCB umbilical cord blood; Δ25(OH)D change between UCB 25(OH)D and early pregnancy 25(OH)D; Declined group Δ25(OH)D < 0.00 nmol/l; Increased group Δ25(OH)D > 0.00 nmol/l

Significant difference between declined and increased groups: *P < 0.05, ** P < 0.01, *** P < 0.001

^aMean differences tested using independent sample T-test or Mann–Whitney U-test where suitable

^bBefore pregnancy

^cDuring pregnancy

^dScale from 1 = lower secondary education to 6 = first or second stage of tertiary education

^eAfter delivery

Table 2 Seasonal differences in 25(OH)D concentrations in early pregnancy and UCB

Season of sampling	Early pregnancy 25(OH)D (nmol/l) ^a		UCB 25(OH)D (nmol/l) ^b	
	n	Mean ± SD	n	Mean ± SD
Spring	81	88.7 ± 25.4	256	85.1 ± 19.6
Summer	158	91.7 ± 16.7	123	94.1 ± 23.8
Fall	220	89.2 ± 16.9	97	85.8 ± 21.9
Winter	125	84.6 ± 19.7	108	91.4 ± 23.9

UCB umbilical cord blood; 25(OH)D 25-hydroxyvitamin D

^aOne-way ANOVA: P = 0.036 (Brown–Forsythe), significant difference between summer and winter (P = 0.010) (Bonferroni)

^bOne-way ANOVA: P = 0.001, significant difference between summer and spring (P = 0.001) and between summer and fall (P = 0.033) (Bonferroni)

vegetable milk products, and was interpreted as “sandwich and dairy.” The fifth DP consisted of mild and strong alcoholic drinks, and was interpreted as “alcohol.” The five DPs explained 13.5, 10.6, 8.5, 7.1, and 6.0% of the variation in diet, respectively. No interaction existed between dietary patterns and seasons. To summarize, we identified five maternal dietary patterns apparent in advanced pregnancy:

“goodies and snacks,” “health conscious,” “meat,” “sandwich and dairy,” and “alcohol.”

Modifiers affecting the tracking of 25(OH)D from early pregnancy to UCB

The results of elaboration analysis using several multiple linear regression models in each package are shown in Fig. 2. From the lifestyle package, PA (P = 0.005) and smoking before pregnancy (P = 0.014) were selected for further analysis. PA promoted the tracking of 25(OH)D from early pregnancy into UCB, while smoking had no effect (Fig. 2a). Although smoking after delivery associated with UCB 25(OH)D, due to collinearity issues, it was not chosen for further analysis.

Summer season at delivery (P < 0.001) was selected for further analysis from season and duration of gestation package. Summer season prevented the tracking of 25(OH)D from early pregnancy into UCB (Fig. 2b). Although winter, spring, and duration of gestation at pregnancy sampling also associated with UCB 25(OH)D, these were not chosen for further analysis due to minor changes in B coefficient compared with summer season at delivery.

Table 3 Principal component analysis^a loadings of food groups for maternal dietary patterns^a

Food groups	Dietary patterns				
	Goodies and snacks	Health conscious	Meat	Sandwich and dairy	Alcohol
Sweets, candy, lollipops (containing sugar)	0.661	-0.239	-0.029	0.058	0.004
Pudding, chocolate, ice cream	0.657	0.081	0.071	-0.062	-0.085
Sweet pastries (bun, doughnut, sweet pie)	0.647	0.244	0.000	0.007	-0.099
Salty pastries (pizza, meat pastry, savory pie)	0.577	0.112	0.094	-0.035	0.076
Snacks (potato chips, popcorn, salted peanuts)	0.541	-0.131	0.122	-0.002	0.167
Squash, soft drink (containing sugar)	0.540	-0.250	0.079	0.047	-0.081
Fresh vegetables (tomato, cucumber, salad, pepper)	-0.028	0.675	-0.133	0.281	-0.040
Cooked vegetables (potato, carrot, broccoli, green peas)	-0.115	0.618	0.049	0.005	0.010
Fruits and berries (apple, banana, mandarin, tangerine, blackcurrant, blueberry, juice)	0.137	0.590	-0.166	0.290	-0.035
Fish (fish soup, raw spiced or smoked fish product)	-0.102	0.587	0.094	-0.118	0.110
Seeds, beans (chick pea, soya bean, sunflower seed, linseed)	0.028	0.542	-0.478	-0.039	0.040
Meat, chicken or egg foods (meat sauce, chicken fillet, omelet)	0.022	0.245	0.714	-0.043	0.071
Cold cut from sausages	0.103	-0.225	0.623	0.184	-0.048
Sausages	0.192	0.014	0.613	-0.025	-0.005
Ready-made marinated meat products (chicken, fish, meat)	-0.005	-0.178	0.545	-0.006	-0.041
Rye bread, other whole grain bread, muesli	-0.026	0.117	-0.071	0.734	-0.009
Cheese (on bread or salad but not cheese spread)	0.082	0.069	0.036	0.697	0.002
Margarine, vegetable oil-based fat spreads	-0.077	-0.190	0.069	0.613	-0.003
Fluid dairy products and vegetable milk products (milk, yogurt, sour whole milk)	-0.018	0.174	0.114	0.487	-0.138
Mild alcohol drinks (beer, cider, wine)	0.084	0.053	-0.005	-0.018	0.829
Strong alcohol drinks (spirit, cognac, liquor)	-0.112	0.014	-0.021	-0.080	0.801
Ready meals (meat-macaroni casserole, ham-potato casserole, spinach pancake)	0.175	-0.043	0.075	0.075	-0.018
Eigenvalue	2.97	2.33	1.87	1.56	1.32
Cumulative variance explained %	13.5	24.1	32.6	39.7	45.7
Dietary pattern score, min–max	-3.2 to 3.7	-4.2 to 2.8	-3.4 to 3.3	-5.1 to 1.8	-1.0 to 9.0

^aAnalysis conducted with Varimax rotation method

From the maternal background package, education ($P=0.042$) and parity ($P<0.001$) were chosen for further analysis. Education promoted and parity prevented the tracking of 25(OH)D from early pregnancy into UCB (Fig. 2c). Prepregnancy BMI and maternal age had no effect on 25(OH)D.

From the nutrition package, “sandwich and dairy” DP ($P=0.025$), supplemental vitamin D intake ($P<0.001$), and number of daily supplements ($P<0.001$) were selected. Supplemental vitamin D intake and number of daily supplements promoted the tracking of 25(OH)D from early pregnancy to UCB, while “sandwich and dairy” DP had no impact (Fig. 2d).

Predictors for declining and increasing 25(OH)D concentration during pregnancy

Shared positive predictors of UCB 25(OH)D in the subgroups Declined and Increased were early pregnancy 25(OH)D concentration and supplemental vitamin D intake during pregnancy (Table 4). For the Declined group, other positive predictors were physical activity ($P=0.041$) and higher education ($P=0.004$). Correspondingly, for the Increased group, positive predictors were “sandwich and dairy” dietary pattern ($P=0.009$) and summer season at delivery ($P=0.001$), while multiparity was an inverse predictor ($P=0.013$) (Table 4).

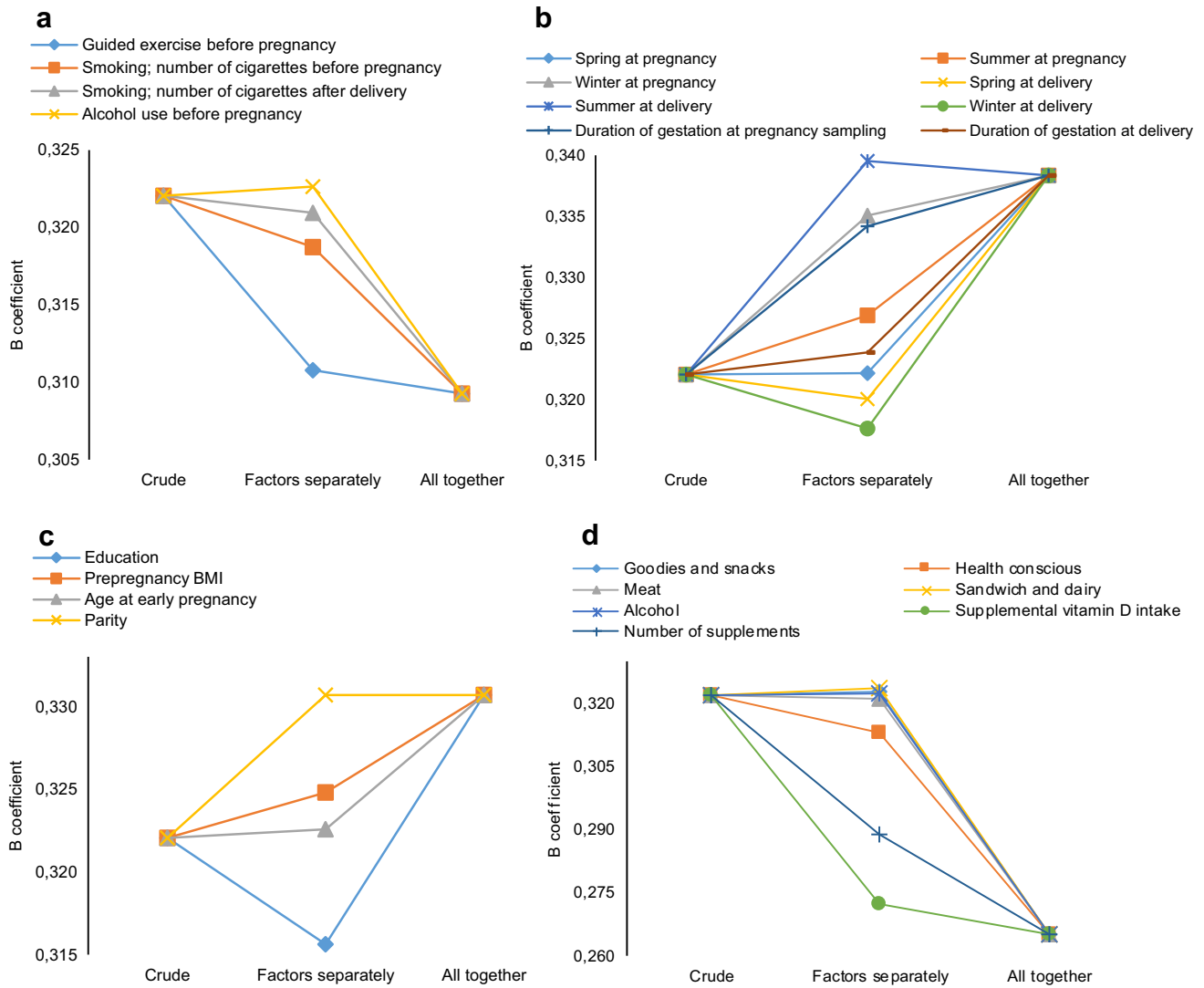


Fig. 2 Modifiers affecting the tracking of 25(OH)D from early pregnancy to UCB. B Coefficient for early pregnancy 25(OH)D when explaining the UCB 25(OH)D in crude model, after adding factors separately and after adding whole factor package together. Factor packages were: lifestyle (a), season, and duration of gestation (b),

maternal background (c), and nutrition (d). A decline in B coefficient means that the added factor promotes and an increase in B coefficient means that the added factor prevents the tracking of 25(OH)D from early pregnancy to UCB. UCB, umbilical cord blood; 25(OH)D, 25-hydroxyvitamin D

Together the predictors explained 49 and 42% of the variation in UCB 25(OH)D in the Declined and Increased group, respectively.

Ultimately, determinants for a clinically relevant decline in 25(OH)D concentration during pregnancy [$\Delta 25(OH)D \leq -10.0$; $n=209$] were examined. The determinants for more severe decline in 25(OH)D were as follows: higher early pregnancy 25(OH)D ($B = -0.45$; 95% CI $-0.52, -0.37$; $P < 0.001$), smoking before pregnancy ($B = -0.45$; 95% CI $-0.83, -0.07$; $P = 0.021$), and multiparity ($B = -2.79$; 95% CI $-5.39, -0.18$; $P = 0.036$).

Discussion

Maternal and newborn 25(OH)D concentrations were sufficient in our study. We observed that seasonal and lifestyle-related factors modify 25(OH)D during pregnancy. Being born in summer resulted in higher UCB 25(OH)D compared with other seasons. The most important maternal lifestyle determinants of vitamin D status in newborn were supplemental vitamin D intake, “sandwich and dairy” dietary pattern (DP) characterized by frequent consumption of vitamin D fortified foods, and physical activity, while the risk factors for impaired vitamin

Table 4 Key modifiers of UCB 25(OH)D concentration in subgroups with Declined and Increased 25-OHD concentration^a

	Declined (<i>n</i> = 321)				Increased (<i>n</i> = 263)			
	β	B (95% CI)	pr^2	<i>P</i> value	β	B(95% CI)	pr^2	<i>P</i> value
Smoking before pregnancy (number of daily cigarettes)	-0.06	-0.24 (-0.57, 0.09)	0.007	0.152	0.09	-0.54 (-1.13, 0.06)	0.012	0.075
Guided exercise before pregnancy (min/d)	0.08	0.07 (0.00, 0.13)	0.013	0.041	0.04	0.05 (-0.06, 0.16)	0.003	0.397
Early pregnancy 25(OH)D (nmol/l)	0.61	0.49 (0.42, 0.55)	0.391	<0.001	0.59	0.86 (0.73, 1.00)	0.373	<0.001
Supplemental vitamin D intake (μ g/d)	0.09	0.07 (0.00, 0.14)	0.014	0.037	0.11	0.17 (0.02, 0.32)	0.018	0.031
“Sandwich and dairy” dietary pattern	0.02	0.27 (-0.85, 1.39)	0.001	0.633	0.13	3.07 (0.77, 5.38)	0.027	0.009
Summer season at delivery (yes vs. no)	0.07	2.58 (-0.53, 5.69)	0.009	0.104	0.17	8.81 (3.81, 13.81)	0.045	0.001
Parity (multi- vs. primiparous)	0.05	-1.51 (-3.85, 0.83)	0.005	0.204	-0.12	-6.11 (-10.93, -1.29)	0.024	0.013
Education (higher educated vs. lower educated)	0.13	4.32 (1.42, 7.22)	0.027	0.004	-0.09	-4.96 (-10.35, 0.43)	0.013	0.071

25(OH)D 25-hydroxyvitamin D; UCB umbilical cord blood; Δ 25(OH)D change between UCB 25(OH)D and early pregnancy 25(OH)D; Declined group Δ 25(OH)D < 0.00 nmol/l; Increased group Δ 25(OH)D > 0.00 nmol/l; pr^2 partial correlation squared

^aAnalysis conducted using standard multiple linear regression

D status during pregnancy were maternal smoking and multiparity.

To the best of our knowledge, we are the first to report that vitamin D status of pregnant women and newborns in Finland has substantially improved during the past decade as a result of increased fortification of foods and revised recommendation on vitamin D supplementation. Vitamin D deficiency was scarce in our cohort both in the mothers in early pregnancy and in the infants at birth. Compared with our previous study [5], the prevalence of maternal and newborn vitamin D deficiency has diminished from 60 to 70% to only 1%. In addition, Holmlund-Suila et al. reported that average 25(OH)D concentration in UCB was 53 nmol/l [23] (as measured in 113 infants), while in our current cohort it was 88 nmol/l. In line with our findings, recent Finnish studies on elderly subjects [16, 24] and children [15] showed improvement in the overall vitamin D status following the enhanced food fortification. On the other hand, according to the Institute of Medicine 25(OH)D concentrations above 125 nmol/l are potentially harmful [25]. In our study, 3.8% (*n* = 22) in early pregnancy, and 6.8% (*n* = 40) in UCB had 25(OH)D above 125 nmol/l. In comparison with national prevalence, mothers in our cohort more often had higher education (76 vs. 36%) [26], were less likely obese (6 vs. 19%) [27], mostly primiparous, used vitamin D supplements, and were willing to participate in a vitamin D intervention study of infants. As indicated previously [28], these factors could explain the sufficient 25(OH)D status in our cohort. Thus, a selection bias may exist and at population level the vitamin D status may be inferior to our cohort. On the other hand, the proportion of women smoking daily prior to pregnancy was almost the same as at population level (13 vs. 14%) [29] which speaks against selection bias.

The crude association between early pregnancy and UCB 25(OH)D was unexpectedly weak. Others have reported 25(OH)D in UCB to reflect 68–108% [30] and 50–100% [31] of the concurrent maternal concentrations. Here maternal vitamin D status on average was stable during pregnancy, which is in accordance with some studies but not all [5, 32, 33].

The proportion of pregnant women using vitamin D supplements in Finland has increased during the last decade from 40 to 80%, evidently due to revised national recommendations and increased awareness [5, 34–36]. In our cohort, the proportion of pregnant women using vitamin D supplements was high (95%). Before the extended vitamin D fortification, the daily maternal intake of vitamin D from food and supplements was on average 6 μ g [37]. Our results are in line with the latest national FINDIET study, where the average daily intake of vitamin D from food was 9 μ g and from supplements 17 μ g in women of reproductive age [38].

Supplemental vitamin D intake is an acknowledged predictor of vitamin D status during pregnancy [33]. Our study confirmed that supplemental vitamin D intake during pregnancy promoted the tracking of 25(OH)D from early pregnancy to UCB. Finnish adults using vitamin D supplements had over 9 nmol/l higher mean 25(OH)D compared with non-users after adjusting for possible confounders [39]. Similarly, Moon et al. concluded that vitamin D supplementation was the strongest determinant of tracking 25(OH)D during pregnancy when compared with those who did not use or discontinued vitamin D supplementation [40].

In previous studies, the quality of Finnish maternal diet has been reported to be good, with the exception of inadequate intakes of vitamin D and folate [34, 35, 41]. We found five different DPs during pregnancy that

revealed interesting behaviors. “Goodies and snacks” together with “meat” and “alcohol” DPs can be considered as less favorable for pregnant women. Of all women, only 16% consumed 1 to 5 dosages of alcohol in total during the last month of pregnancy. However, the “health conscious” DP also existed strongly. These findings are in line with observations by Arkkola et al. [42]. It remains to be seen how these translate into health and well-being of the children.

“Sandwich and dairy” DP was the only dietary pattern associating with newborn 25(OH)D, and it consisted of vitamin D fortified margarine and milk products, which are the major dietary sources of vitamin D, together with fish [38]. Concordantly, intakes of vitamin D, fish, and margarine intake are associated positively with 25(OH)D in Finnish adults [39]. The effect of “sandwich and dairy” DP was confirmed in those with Increased 25(OH)D during pregnancy implying that constant maternal intake of vitamin D from diet contributes to higher 25(OH)D concentration in the newborn.

Summer season at delivery determined newborn 25(OH)D. Season is an established factor influencing vitamin D status, especially in the northern latitudes [43]. In the present study, mean 25(OH)D concentration in UCB was on average 9 nmol/l higher in summer compared with spring and winter. Despite the high frequency of supplement users, the effect of season was evident suggesting an active lifestyle and outdoor activities.

Physical activity, measured as guided exercise before pregnancy, was a promoting factor for 25(OH)D during pregnancy. This may reflect an overall healthy lifestyle. In addition, as increased fat mass reduces serum 25(OH)D [44], physical activity may improve vitamin D status by preventing excessive weight gain. However, in our cohort, prepregnancy BMI itself was not associated with 25(OH)D. Our finding is parallel with results from the Southampton Women’s Survey that greater physical activity is associated with positive changes in 25(OH)D during pregnancy [40].

Higher education level promoted the tracking of 25(OH)D from early pregnancy to UCB, and higher education was a positive predictor for UCB 25(OH)D concentration in the Declined group, while surprisingly an opposite trend was observed for the Increased group. We suggest that such a difference illuminates a distinctive behavior in the use of supplements. Higher education may reduce the likelihood of extreme behaviors, and women with a higher education level may use supplements more discreetly than less educated women. In a previous study, the use of dietary supplement in pregnant Finnish women correlated positively with education [34]. Among adults, Aronsson et al. found that higher education was not associated with vitamin D supplement use in Finland, as it was positively associated in USA and Sweden [36].

In the present study, smoking and multiparity were identified as risk factors for inferior vitamin D status and for clinically relevant decline of 25(OH)D during pregnancy, whereas in a recent systematic review the associations of smoking with maternal 25(OH)D concentration were considered controversial [45]. In line with our results, inverse associations between parity and 25(OH)D concentration have been reported previously [46, 47]. Overall, lifestyle-related predictors explained only a small part of the variation in 25(OH)D, and a larger cohort is needed to verify these findings.

We recognize several strengths and limitations in our study. This is a unique cohort with healthy Caucasian mothers from the capital region of Finland, northern Europe. A strength of the study lies in the subject recruitment, which took place in a single hospital, enabled standardized data collection, and covered all seasons. However, a multi-center study would have resulted in a wider variety of socio-economic backgrounds. Only one-third of all eligible mothers participated in the study. Thus, our results may not be generalized to population level. Another limitation was several missing values, which constrained the final number of participants in the present study. Our data rely heavily on a self-administered questionnaire postpartum; however, at the first study visit, the study nurse reviewed the questionnaire with the participant. The FFQ was designed to measure bone affecting food components and not for dietary pattern analysis. A limitation was that the FFQ was not validated. Still, our finding implies that current FFQ is a valid method since “sandwich and dairy” dietary pattern, which was loaded with vitamin D fortified foods, correlates with 25(OH)D. Furthermore, we did not have data on maternal absolute dietary intake of vitamin D, nor supplemental vitamin D intake specifically in early pregnancy. However, we had the information of vitamin D intake from supplements during the last two months of pregnancy, which most likely reflects the supplemental vitamin D intake during the whole pregnancy.

Conclusions

We acknowledge that public health policies to improve vitamin D status in Finland have been successful, since the prevalence of vitamin D deficiency was low in pregnant women and their newborn. Yet, season and maternal lifestyle-related factors modified 25(OH)D during pregnancy and in the newborn. Being born in summer resulted in higher UCB 25(OH)D compared with other seasons. Supplemental vitamin D intake, dietary pattern characterized by frequent consumption of vitamin D fortified margarine and milk products, and physical activity before pregnancy were the key determinants of vitamin D status

during pregnancy and of the newborn. These modifiable lifestyle factors are of importance when counseling families in prenatal clinics on health promotion, and on the prevention of vitamin D deficiency during pregnancy. Our results underscore the importance of maternal diet with regular consumption of vitamin D fortified foods and daily supplemental vitamin D intake for sustaining sufficient vitamin D status throughout the pregnancy and for providing a healthy start for the newborn.

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Compliance with ethical standards

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

Ethical standards This study was conducted according to the guidelines laid down in the 1964 Declaration of Helsinki and its later amendments. Ethical approval was obtained from the Research Ethics Committee of the Hospital District of Helsinki and Uusimaa (107/13/03/03/2012). Written informed consent was obtained from the participants at recruitment prior to their inclusion in the study. The project protocol is registered on ClinicalTrials.gov (NCT01723852).

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