A prospective cohort study of cord blood 25(OH)D₃ and food allergies in 6-month-old Chinese infants

Chunyan He,[1] Guiyuan Xiao,[1] Shijian Liu,[2] Zhang Hua,[1] Li Wang,[1] Nianrong Wang[1]

Abstract

Background: Vitamin D is closely related to childhood allergic diseases, such as food allergies, atopic dermatitis, and asthma. However, it is unclear whether vitamin D status in the cord blood from mothers is related to food allergies in infants.

Objective: We performed a prospective cohort study on the relationship between the cord blood vitamin D [i.e., 25-hydroxyvitamin $D_3(25(OH)D_3)$] level and infant food allergies.

Methods: This study selected 741 newborns to observe until 6 months of age and used open oral food challenges (OFCs) to diagnose their food allergies. Cord blood and 6-month serum $25(OH)D_3$ levels of the infants were measured by liquid chromatography-tandem mass spectrometry.

Results: The proportion of children with cord blood $25(OH)D_3$ deficiency (< 20 ng/mL) was 86.27%. Cord blood vitamin D was positively correlated with the supplementation frequency of egg yolk, multivitamins, calcium, and docosahexaenoic acid (DHA) during pregnancy and the mother's age. No significant difference was found in the cord blood $25(OH)D_3$ level between summer born and winter born infants ($p = 0.465$). After adjusting for seasonal factors, the risk of food allergies in the $25(OH)D_3$ non-deficiency group was 2.72 times that of the $25(OH)D_3$ deficiency group. Infants in the $25(OH)D_3$ non-deficiency group (≥ 20 ng/mL) had a higher risk of allergies compared with the deficiency group (< 20 ng/mL) (RR = 2.49).

Conclusions: Cord blood $25(OH)D_3$ is associated with infant food allergies. Maintaining $25(OH)D_3$ in maternal cord blood at a low level may be conducive to the prevention of infant food allergies.

Key words: cord blood, $25(OH)D_3$, food allergies, infant, gestation

Affiliations:
[1] Department of Children Healthcare, Chongqing Health Center for Women and Children, Chongqing, China
[2] Department of Biobank, Pediatric Translational Medicine Institute, Shanghai Children's Medical Center, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Corresponding author:
Nianrong Wang
120 Longshan Road, Department of Children Healthcare, Chongqing Health Center for Women and Children, Chongqing, China, 400021
E-mail: wnr2003@163.com

Introduction

Recent studies have shown that vitamin D [i.e., 25-hydroxyvitamin $D_3(25(OH)D_3)$] has many roles besides calcium homeostasis. Moreover, vitamin D receptors (VDRs) and $25(OH)D_3$ hydroxylation on different cell types have revealed the vitamin's immunomodulatory effect in the human body. It has been shown to affect the activation of T cells and the function of antigen-presenting cells, reduce T helper (Th) cell-1 cytokine secretion and inhibit of T cell proliferation.[1] These findings suggest that vitamin D is related to allergic diseases.

Given the developmental origins of health and disease, fetal life and early-life exposures are important determinants of fetal immunomodulation and subsequent development of disorders, including allergic diseases. Prior studies on the relationship between maternal vitamin D status or prenatal vitamin D supplementation and offspring allergies have shown conflicting results. Some data indicated that maternal $25(OH)D_3$ levels are associated with allergic diseases in children.[2-4] Some other data suggested that maternal $25(OH)D_3$

is only associated with some allergic diseases,[5-6] and there are also data suggesting that there is insufficient evidence to support the association between the two.[7] The World Health Organization's Guidelines for Allergic Disease Prevention also pointed out that there is insufficient evidence to support the suggestion of prenatal 25(OH)D$_3$ supplementation to prevent allergic diseases in offspring.[8]

Based on the inconsistent conclusions about the correlation between cord blood 25(OH)D$_3$ level and allergic diseases in children, there is no clear conclusion on the correlation between cord blood 25(OH)D$_3$ level and infant food allergies. Hence, we adopted a prospective cohort study that included surveying pregnant women during the third trimester regarding vitamin D supplementation. We measured the cord blood 25(OH)D$_3$ levels, and recorded the development of food allergies in infants until the age of 6 months. The correlation between the 25(OH)D$_3$ level and infant food allergies can provide a scientific basis for the early prevention of food allergies in children.

Methods

Research participants

This study selected 343 and 398 healthy pregnant women (no comorbidities or complications during pregnancy that required treatment; no history of abnormal pregnancy; no infectious diseases, such as hepatitis B, syphilis, or human immunodeficiency virus infection; and no smoking, alcoholism, drug abuse, or other bad habits) in the Department of Obstetrics at Chongqing Maternal and Child Health Care Hospital in Chongqing, China from June 1 to August 31, 2018 (born in summer) and from November 1, 2018 to January 31, 2019 (born in winter), respectively. The normal full-term singleton newborns of these pregnant women were the research subjects of this study and were followed up with until the age of 6 months to collect the basic information of their families (e.g., the parents' age, occupation, family financial status, and family residence) ,information on the vitamin D consumption and outdoor activities of their mothers during pregnancy, childbirth outcomes, and family history of allergies using a self-developed questionnaire. This study was approved by the Ethics Committee of Chongqing Maternal and Child Health Hospital. The guardians of all selected subjects provided their written informed consent before the study began.

Collection and testing of cord blood samples

A 5-ml venous cord blood sample was collected aseptically within 2 min after the newborn was delivered, which was followed by detecting the cord blood 25(OH)D$_3$ level using a commercially available kit from King Create Biotechnology on a liquid chromatography tandem mass spectrometer (4500MD, AB Sciex, Framingham, MA).

Categorization of vitamin D

Referring to the reference value of vitamin D recommended for the Chinese adult population, cord blood 25(OH)D$_3$ levels < 20 ng/mL were classified as vitamin D deficiency, cord blood 25(OH)D$_3$ levels between 20 and 29 ng/mL were classified as vitamin D insufficiency, and cord blood 25(OH)D$_3$ levels ≥ 30 ng/mL were classified as vitamin D sufficiency.[9]

Food allergy determination

Definition of food allergies

Food allergies are abnormal and excessive immune responses of the body caused by food proteins. They affect the skin and the digestive system, respiratory system, and cardiovascular systems. As the subjects of this study were all infants, open oral food challenges (OFCs) were used for the diagnosis of food allergies.[10]

The following signs and symptoms were classified as food allergies: (1) Infants' response: mouth or skin itching, throat discomfort, cough, wheezing, abdominal pain, vomiting, diarrhea, depression or other discomfort symptoms; (2) Vital signs monitoring: blood pressure, pulse, respiration, transcutaneous oxygen saturation, and continuous monitoring until the end of the OFCs; (3) Physical examination of the skin and mucous membrane: Infants with eczema and atopic dermatitis needed the Scoring Atopic Dermatitis Index (SCORAD) score before and after the OFCs to observe the change in skin rash; (4) Physical examination of the respiratory system: observe whether there was dyspnea, laryngeal sound, and wheezing sound, for example; (5) Abdominal physical examination: observe whether there was tenderness, or active bowel sounds, for example; (6) Physical examination of the cardiovascular system: observe changes in the blood pressure and heart rate, and whether the heart sounds were low and blunt.[11]

A physical examination or questionnaires were performed every month following birth until 6 months of age. The caretaker was asked "Which foods is the child allergic to?" Possible responses included egg, milk, wheat, peanuts, soy products, fish, other nuts, and shellfish. The OFCs was performed for infants aged 6 months, because children were fed complementary foods starting at 6 months of age in our cohort. In the OFCs experiment, infants were monitored every 15 minutes. If the parents in the interim reflected that the child was allergic, we recorded that immediately. Food allergies in OFCs mainly depended on the clinicians' observation and diagnosis. During the observation period of 2-4 weeks at home, we provided a form for parents to monitor their infants' allergies and fill out, including signs and symptoms of each system (skin, gastrointestinal, and cardiovascular), and contacted parents in Wechat (a social app for mobile phones) every day.

Determination of OFCs results

The results of the OFCs were divided into four categories: rapid positive results, delayed positive results, negative results, uncertain results.

Statistical analysis

Data were analyzed using SPSS 25.0 statistical software (IBM Corp., Armonk, NY). The measurement data were presented as the mean ± standard deviation ($\bar{x} \pm s$). The count data were presented as n (%). The relative risk (RR) of different groups of cord blood 25(OH)D$_3$ was analyzed by unconditional logistic regression. The difference in food allergies in different seasons was analyzed by chi-square stratified analysis.

The risk factors of food allergies were analyzed using univariate analysis and multivariate logistic regression analysis. The Mantel-Haenszel test was used to control seasonal factors for stratified analysis ($p < 0.05$ was considered statistically significant).

Results

General information of research subjects

This study included a total of 741 subjects, including 343 summer born infants (46.29%) and 398 winter born infants (53.71%), 385 males (52.03%) and 355 females (47.97%), with an average gestational age of 38.69 ± 1.27 weeks and an average birth weight of 3,309.96 ± 430.02g. The average delivery age of the pregnant women was 30.15 ± 4.22 years old, and the percentage with a family allergy history was 55.88%.

Among the 6-month-old infants, 51 cases were diagnosed with food allergies (total incidence of 6.88%), and 690 cases did not develop food allergies. There were 18 cases of milk allergy, 1 case of egg yolk allergy, 16 cases of egg white and egg yolk allergy, 1 case of peanut allergy, and 15 cases who were allergic to two or more kinds of food. Among the allergic infants, 32 (62.75%) showed symptoms of skin mucous membrane allergy (e.g., erythema of the skin, aggravation of eczema, edema of the eyelids, edema of the lips), and 19 (37.25%) showed symptoms of digestive system allergy (e.g., blood in the stool, vomiting, diarrhea). None of the babies showed signs of other systemic allergies. In addition, 34 showed immediate reactions, and 17 showed delayed reactions.

No significant differences in birth weight, body length, mode of delivery, gestational age (weeks), number of pregnancies, parity, infant's gender, parents' age, parents' education level, family's sources of income, place of residence, smoking/secondhand smoking during pregnancy, pet ownership during pregnancy, or genetic risks that could cause the allergies were found between the food allergy group and non-food allergy group ($p > 0.05$, **Table 1**).

Table 1. Comparison of demographic information between the food allergy group and the control group.

Variable		Food allergy group	Control group	*t*/Chi-square value	*p*-value
Birth weight (g) (mean ± SD)		3289.3 ± 464.8	3311.5 ± 427.7	−0.36	0.72
Birth length (cm) (mean ± SD)		49.73 ± 2.14	49.83 ± 1.81	−0.40	0.69
Mode of delivery [n (%)]	Vaginal delivery	24 (47.06)	360 (52.25)	0.5125	0.47
	Caesarean section	27 (52.94)	329 (47.75)		
Gestational week [weeks, n (%)]	< 38	6 (11.76)	94 (13.62)	0.1405	0.71
	≥ 38	45 (88.24)	596 (86.38)		
Number of pregnancies [n (%)]	1	26 (50.98)	308 (44.70)	0.7578	0.68
	2	12 (23.53)	181 (26.27)		
	≥ 3	13 (25.49)	200 (29.03)		
Parity [n (%)]	1	37 (72.55)	475 (69.04)	0.2746	0.6
	≥ 2	14 (27.45)	213 (30.96)		
Infant's gender [n (%)]	Male	28 (54.90)	357 (51.81)	0.1814	0.67
	Female	23 (45.10)	332 (48.19)		
Paternal age [years, n (%)]*	< 30	20 (39.22)	238 (34.49)	0.4668	0.49
	≥ 30	31 (60.78)	452 (65.51)		
Maternal age [years, n (%)]*	< 30	6 (11.76)	94 (13.62)	0.1405	0.71
	≥ 30	45 (88.24)	596 (86.38)		
Place of residence [n (%)]*	Urban area	39 (92.86)	400 (87.72)	- (Fisher's test)	0.14
	Non-urban area	3 (7.14)	56 (12.28)		
Paternal educational level [n (%)]*	High school or below	4 (8.33)	64 (14.55)	1.3926	0.24
	College degree or above	44 (91.67)	376 (85.45)		
Maternal educational [n (%)]*	High school or below	8 (16.67)	64 (14.48)	0.1652	0.68
	College degree or above	40 (83.33)	378 (85.52)		

Table 1. (Continued)

Variable		Food allergy group	Control group	*t*/Chi-square value	*p*-value
Main source of family income [n (%)]*	Salary or bonus	36 (75.00)	332 (76.32)	0.0416	0.8383
	Agriculture, self-employment, part-time job, and other incomes	12 (25.00)	103 (23.68)		
Monthly income of the family [n (%)]*	Low(≤ $772)	3 (6.52)	27 (6.31)	0.0033	1
	Middle($772~$1544)	10 (21.74)	93 (21.73)		
	High(> $1544)	33 (71.74)	308 (71.96)		
Smoking habit of mother [n (%)]*	Daily or often	0 (0.00)	1 (0.15)	- (Fisher's test)	1
	Occasionally or never	51 (100.00)	676 (99.85)		
Second-hand smoking exposure in mother [n (%)]*	Daily or often	11 (21.57)	162 (24.04)	0.1588	0.69
	Occasionally or never	40 (78.43)	512 (75.96)		
Pet keeping [n (%)]*	Yes	4 (8.33)	20 (4.16)	1.7568	0.19
	No	44 (91.67)	461 (95.84)		
Genetic risk of infant allergies [n (%)]*	Yes	9 (17.65)	180 (26.09)	1.7804	0.1821
	No	42 (82.35)	510 (73.91)		

*Missing value

The link between cord blood 25(OH)D₃ and infant food allergies

Cord blood 25(OH)D₃

The average value of cord blood 25(OH)D₃ was 13.10 ± 6.15 ng/mL. Among the infants, 86.27% had cord blood 25(OH)D₃ deficiency, 12.25% had cord blood 25(OH)D₃ insufficiency, and 0.81% had sufficiency (6 infants, all in the non-food allergy group). The average value of cord blood 25(OH)D₃ of the summer birth group was 13.28 ± 6.28 ng/mL, and the average of cord blood 25(OH)D₃ of the winter birth group was 12.94 ± 6.04 ng/mL, showing no significant difference in the cord blood 25(OH)D₃ between the infants born in the two seasons ($t = 0.731$, $p = 0.465$).

The number of cases with sufficient cord blood 25(OH)D₃ was relatively small, so we combined the data of cord blood 25(OH)D₃ insufficient levels and cord blood 25(OH)D₃ sufficient levels to perform a comparative analysis between the cord blood 25(OH)D₃ deficiency (< 20 ng/mL) and non-deficiency (≥ 20 ng/mL) groups. Among the summer born infants, the proportions of infants with food allergies in the cord blood 25(OH)D₃ deficiency group was higher than that in the cord blood 25(OH)D₃ non-deficiency group ($p < 0.01$). Among the winter born infants, the proportions of infants with food allergies in the cord blood 25(OH)D₃ deficiency group and non-deficiency group were similar (Fisher's test, $p = 0.1800$).

For the correlation between 25(OH)D₃ deficiency and food allergies, the Mantel-Haenszel test was used to control the factor of season for stratified analysis. The results of summer born infants and winter born infants were not heterogeneous ($p = 0.124$); that is, correlation between 25(OH)D₃ deficiency and food allergies was not affected by the season. After adjusting for season, the risk of food allergies in the 25(OH)D₃ non-deficiency group was 2.72 times that of the deficiency group (95% CI: 1.37–5.41; $p = 0.004$, **Table 2**).

Table 2. Seasonal stratified analysis of cord blood 25(OH)D₃ and food allergies.

Cord blood 25(OH)D₃ (ng/mL)	Summer born infants			Winter born infants		
	Food allergy group (n = 10)	Control group (n = 333)	Total (n = 343)	Food allergy group (n = 41)	Control group (n = 357)	Total (n = 398)
Deficiency (< 20 ng/mL)	5 (1.71%)	288 (98.29%)	293 (85.42%)	33 (9.40%)	318 (90.60%)	351 (88.19%)
Non-deficiency (≥ 20 ng/mL)	5 (10.00%)	45 (90.00%)	50 (14.57%)	8 (17.02%)	39 (82.98%)	47 (11.81%)
RR (95%CI)	2.72 (1.374-5.411)					
p	0.004*					

*$p < 0.05$; RR, relative risk; CI, confidence interval.

Table 3. Unconditional logistic regression analysis of cord blood 25(OH)D$_3$ and food allergies

Cord blood 25(OH)D$_3$ (ng/mL)	Food allergy group [n (%)]	Control roup [n (%)]	OR (95% CI)	aOR_1 (95% CI)	aOR_2 (95% CI)
Deficiency (< 20 ng/mL)	38 (5.90%)	606 (94.10%)	1	1	1
Non-deficiency (≥ 20 ng/mL)	13 (13.40%)	84 (86.60%)	2.485 (1.269–4.865)	3.256 (1.494–7.096)	3.968 (1.769–8.902)

Note: OR refers to the unadjusted odds ratio value; aOR_1 refers to the OR value adjusted for basic conditions; aOR_2 refers to the OR value adjusted for basic conditions and infant allergic risk. OR, odds ratio; CI, confidence interval.

Table 4. Univariate analysis of the influencing factors of cord blood 25(OH)D$_3$

Variable		Number of cases	Mean value	Standard deviation	Standard error	F	p-value
Supplementation of egg yolk	Daily	357	13.7717	5.89271	0.31188	4.864	0.002*
	Often	219	12.6881	6.35636	0.42952		
	Occasionally	96	11.3083	6.17679	0.63042		
	Rarely or never	49	13.9714	6.27681	0.89669		
Supplementation of multivitamins	Daily	565	14.0991	6.02951	0.25366	25.279	0.000*
	Often	38	10.5368	5.26074	0.8534		
	Occasionally	38	8.1474	4.5053	0.73086		
	Rarely or never	83	9.8952	5.39444	0.59212		
Supplementation of calcium	Daily	625	13.6398	6.0245	0.24098	11.176	0.000*
	Often	50	9.412	5.98661	0.84663		
	Occasionally	24	9.7917	4.85359	0.99073		
	Rarely or never	25	10.672	6.60041	1.32008		
Supplementation of DHA	Daily	241	14.8822	6.36441	0.40997	14.496	0.000*
	Often	55	14.6418	6.34842	0.85602		
	Occasionally	44	13.1182	5.67943	0.85621		
	Rarely or never	384	11.7922	5.69594	0.29067		
Maternal age	< 30 years old	368	12.4179	6.0605	0.3159	t = −3.01	0.0027*
	≥ 30 years old	369	13.7732	6.1669	0.321		

*$p < 0.05$

Table 5. Multiple linear regression analysis of the influencing factors of cord blood 25(OH)D$_3$

Variable	Regression coefficient	Standardized regression coefficient	Standard error	t	p-value
Egg yolk supplementation during pregnancy	0.50003	0.07497	0.23286	2.15	0.0321*
Multivitamins supplementation during pregnancy	1.39566	0.23229	0.21883	6.38	< 0.0001*
Calcium supplementation during pregnancy	0.71258	0.07833	0.33162	2.15	0.032*
DHA supplementation during pregnancy	0.82492	0.18496	0.15798	5.22	< 0.0001*
Maternal age at childbirth	0.11265	0.07768	0.05073	2.22	0.0267*

*$p < 0.05$

Unconditional logistic regression analysis of cord blood 25(OH)D₃ and food allergies

The results showed that the percentage of infants with food allergies was 13.40% in the cord blood $25(OH)D_3$ non-deficiency group (≥ 20 ng/mL) and 5.90% in the cord blood $25(OH)D_3$ deficiency group (< 20 ng/mL) (RR = 2.49, 95% CI: 1.269–4.865, **Table 3**).

Influencing factors of cord blood 25(OH)D₃

The results of univariate analysis suggested that supplementation of egg yolk (F = 4.864, p = 0.002), multivitamins (F = 25.279, p = 0.000), calcium (F = 11.176, p = 0.000), and docosahexaenoic acid (DHA) (F = 14.494, p = 0.000), and maternal age (t = −3.01, p = 0.0027) were factors associated with cord blood $25(OH)D_3$ (**Table 4**).

Logistic stepwise regression analysis was performed with the supplementation of egg yolk, multivitamins, calcium, and DHA; and maternal age during pregnancy as independent variables. The results showed that cord blood $25(OH)D_3$ was positively correlated with the frequency of supplementation of egg yolk, multivitamins, calcium, and DHA during pregnancy, as well as maternal age (**Table 5**).

Discussion

Deficiency in $25(OH)D_3$ is common in pregnant women around the world.[12] The rate of vitamin D deficiency in pregnant women in Spain is 96.8%, and that of severe deficiency rate is 34.6%.[13] The rate of serum vitamin D deficiency (< 10 ng/mL) in pregnant women is 45% in South Asia, 40% in the Middle East, and 26% in sub-Saharan Africa.[14] Among pregnant women in Shanghai China, 9.9% have severe vitamin D deficiency [$25(OH)D_3$ < 10 ng/mL], 60.1% have vitamin D deficiency [10 ng/mL ≤ $25(OH)D_3$ < 20 ng/mL], 28.4% have insufficient vitamin D [20 ng/mL ≤ $25(OH)D_3$ < 30 ng/mL], and only 1.6% have sufficient vitamin D [$25(OH)D_3$ ≥ 30 ng/mL].[15] All pregnant women in this study were from Chongqing, China. Among them, 86.27% had cord blood $25(OH)D_3$ deficiency, 12.25% had insufficient cord blood $25(OH)D_3$, and 0.81% had sufficient cord blood $25(OH)D_3$. Shanghai is located on the east coast of China. Shanghai has a higher latitude, longer sunshine time, and lower vitamin D deficiency rate in pregnant women than Chongqing. The cord blood $25(OH)D_3$ was previously found to be associated with serum $25(OH)D_3$ in infants, with infants of vitamin D-deficient mothers also showing low circulating $25(OH)D_3$ levels.[16]

In this study, cord blood $25(OH)D_3$ was positively correlated with the frequencies of egg yolk, multivitamin, calcium, and DHA supplementation as well as the mother's age. It is possible that older pregnant women may pay more attention to a balanced diet and nutrient supplementation, whereas younger pregnant women are more concerned about not tanning and thereby adopt more sun protection measures. In this study, these mothers took multivitamins from the first trimester until delivery, resulting in increased $25(OH)D_3$ levels in cord blood, among those who had taken vitamin D ranging from 200 to 500 IU. It has been reported that combined use of vitamin D and calcium may increase the risk of premature delivery, however, the clinical significance of elevated serum $25(OH)D_3$ is unclear,[17] and given this, we need to explain

these results cautiously. A study by Gurol et al. indicated that omega-3 fatty acid supplementation may lead to an increase in vitamin D levels.[18] In a study by An et al., a significant increase in 1,25 (OH) 2D levels was observed in dialysis patients taking omega-3 fatty acids (without vitamin D) for 3 months compared to baseline levels.[19] Therefore, this study collected data on maternal supplementation of extra nutrients during the third trimester, however, at no point in time were cord blood $25(OH)D_3$ and multivitamins, calcium and DHA supplementation in the mother related.

Comparing the levels of the cord blood $25(OH)D_3$ of infants born in summer and winter, we found that the relationship between cord blood $25(OH)D_3$ and food allergies was not affected by the season. This was consistent with the results of a study by Shannon et al. in the United States.[20] Some studies have indicated that winter born and winter born infants may have lower levels of vitamin D owing to the low level of environmental ultraviolet radiation of the mother in the third trimester of pregnancy.[21,22] There is a significant correlation between food allergies in children and the intensity of ultraviolet radiation. Children born in the summer are 55% less likely to have food allergies than children born in other seasons.[23] Under normal circumstances, adequate and effective sunlight is beneficial to increasing the vitamin D level of pregnant women. However, the application of sunscreen under outdoor exposure to the sun complicates the $25(OH)D_3$ state.[24] Sun exposure and a diet rich in vitamin D are not enough to maintain the vitamin D level of pregnant women. Additional vitamin D supplementation helps pregnant women to reach the optimal serum vitamin D level.[25] Vitamin D supplementation during pregnancy improves the vitamin status of pregnant women and newborns.[26] Evidence of the importance of macronutrients and micronutrients during pregnancy is evolving rapidly and continuously. However, important knowledge gaps remain in nutrition interactions, the optimal time and dose of nutrients required during pregnancy, and the impact of specific nutrients on immediate, short-term and long-term outcomes.

The results of this study showed that the $25(OH)D_3$ non-deficiency group (≥ 20 ng/mL) had a higher risk of food allergies than the $25(OH)D_3$ deficiency group (< 20 ng/mL). Some birth cohort studies reported conflicting results on the risk of allergy and prevention after vitamin D exposure.[27] Early correction of vitamin D deficiency might promote mucosal defense, maintain healthy microbial ecology and allergen tolerance, and decrease the risk of food allergies in children.[28,29] These findings support the hypothesis of an increased incidence of allergic diseases and the immunological side effects of vitamin D supplementation initiated during infancy.[30] Gale et al. reported that maternal levels of 25OHD > 75 nM in the third trimester of pregnancy have been linked to increased odds of developing visible eczema in children at 9 months and having asthma at 9 years.[29] Potential explanations to reconcile these conflicting results are that the relationship between the $25(OH)D_3$ concentration and allergies may not be linear, which supports a U-shaped association, i.e., both high and low levels of vitamin D in serum may increase the risk of allergic diseases.[31,32] It is speculated that the balance between the systemic T-helper (Th)2 skews the effect of vitamin D,

and its local tissue anti-inflammatory effect may differ depending on different circulating concentrations of 25(OH)D$_3$.[27] Excessive vitamin D supplementation in pregnant women during pregnancy causes higher vitamin D levels in pregnant women and cord blood, resulting in high levels of vitamin D during pregnancy and birth, which may lead to a higher risk of food allergies.[33] Cord blood 25(OH)D$_3$ levels are negatively correlated with the regulation of T cell numbers, and vitamin D supplementation is opposed for preventing allergies.[34] There have also been conflicting or inconsistent results in studies on vitamin D and allergic diseases. A meta-analysis showed that owing to the lack of a recognized standard definition of vitamin D deficiency and the appropriate level of vitamin D needed to affect immune function, a longitudinal study between vitamin D levels and food allergies is needed to evaluate whether vitamin D may be involved in the development of food allergies.[35]

In summary, this study was one of the few to have analyzed the relationship between cord blood 25(OH)D$_3$ levels and food allergies in 6-month-old infants under low cord blood 25(OH)D$_3$ conditions, and our findings, indicated that cord blood 25(OH)D$_3$ at an insufficient level is more associated with predisposition to food allergy in infancy than a deficient state, and cord blood 25(OH)D$_3$ deficiency seems to have a protective effect on the occurrence of food allergy in infancy. The first limitation of the present study was that the number of cases with sufficient cord blood 25(OH)D$_3$ was relatively small, which could have led to an indeterminable the relationship between cord blood 25(OH)D$_3$ sufficiency and food allergy in 6-month-old infants. The second limitation was that the follow-up time of infants was only 6 months. The longer the follow-up period, the more kinds of complementary foods infants will consume, and the more children who may be diagnosed with food allergy. The use of vitamin D in the primary prevention of food allergies needs to be supported by large randomized controlled trials to demonstrate the potential of vitamin D to improve the management of food allergies.

Funding

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