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Prenatal, perinatal, and childhood vitamin D exposure and their association with childhood allergic rhinitis and allergic sensitization

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Abstract

Background—The role of early-life vitamin D in childhood allergy is controversial.

Objective—To assess vitamin D exposure in early life by multiple modalities and ascertain their association with childhood allergic rhinitis and allergic sensitization.

Methods—1248 mother-child pairs from a US prebirth cohort unselected for any disease were studied. Vitamin D exposure was assessed by measures of maternal intake during the first and second trimesters of pregnancy and serum vitamin D (25(OH)D) levels in mothers during

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pregnancy, cord blood, and in children at school age (median age 7.7 years, IQR 1.0 years). Tests for associations between vitamin D exposure with ever allergic rhinitis, serum total IgE, and allergen sensitization at school age were conducted.

Results—The correlations between maternal intake of vitamin D during pregnancy and serum 25(OH)D levels in pregnant mothers, cord blood, and children at school age were weak to moderate ($r = -0.03$ to 0.53). Each 100 IU/day of food-based vitamin D intake during the first and second trimesters (equivalent to the amount of vitamin D in an 8-ounce serving of milk) was associated with 21% and 20% reduced odds of ever allergic rhinitis at school age (OR 0.79 (95% CI 0.67–0.92) and OR 0.80 (95% CI 0.68–0.93), respectively). There were no associations between maternal supplemental vitamin D intake or serum 25(OH)D levels at any time point with ever allergic rhinitis. There were no associations between any vitamin D exposure and serum total IgE or allergen sensitization at school age.

Conclusions—Inclusion of foods containing vitamin D in maternal diets during pregnancy may have beneficial effects on childhood allergic rhinitis.

Keywords

Allergic rhinitis; vitamin D; atopy; prenatal; perinatal; childhood; sensitization; food; supplement; allergy

Introduction

The role of early life vitamin D exposure in the development of childhood allergy remains controversial. Vitamin D modulates both the innate and adaptive immune systems, with direct effects on B cells, T-cell activation and antigen presenting cells.^{1–3} Vitamin D deficiency may impair epithelial barrier integrity, leading to increased and inappropriate mucosal exposure to antigens and a pro-sensitization immune imbalance that compromises immunologic tolerance.^{1, 4} As such, vitamin D has been the focus of many studies examining its relationship with allergic disease. Because vitamin D may exert immunomodulatory effects *in utero* as early as the first trimester,¹ prenatal vitamin D exposure should be considered when examining the potential effects of early-life vitamin D.

Some epidemiologic studies suggest a protective effect of higher vitamin D exposure in early life, while other results point to increased odds of childhood allergy or no associations with vitamin D exposure.^{1, 2} Differences in exposure assessment, outcome definitions, study population, and study design account for many of these disparate results. The majority of studies examining the relationship between vitamin D and allergy outcomes have assessed vitamin D at single time points, either via a one-time assessment of dietary intake or serum 25-hydroxyvitamin D (25(OH)D) level.^{1, 2} These singular measures of exposure each have their limitations. While vitamin D intake assessment (via food frequency questionnaire) reflects long-term diet,¹ it does not account for sun exposure, another source of vitamin D in people. On the other hand, while 25(OH)D levels may reflect biologically available vitamin D, these levels fluctuate between measurements and season⁵ and do not capture circulating levels of other vitamin D metabolites.⁶ Distinct modalities of vitamin D assessment capture disparate dimensions of its biologic effects, and it is therefore unlikely that a single

assessment of vitamin D status is sufficient to address whether vitamin D is associated with allergic disease.^{1, 2, 7}

The hypothesis of this study was that early life vitamin D exposure is associated with allergic rhinitis at school age. This study sought to address the limitations of previous studies by examining early life vitamin D exposure in a well-characterized prebirth cohort via multiple modalities over time, including assessments of maternal vitamin D intake during the first and second trimesters of pregnancy and serum 25(OH)D levels during the prenatal, perinatal, and childhood periods. Allergic rhinitis was chosen as the primary outcome (with allergic sensitization as a secondary outcome), as few studies of vitamin D have focused on allergic rhinitis despite the high population prevalence of this disease.

Methods

Study design and subjects

Project Viva is a prospective, prebirth cohort study of participants recruited from Atrius Health, a large multispecialty practice in eastern Massachusetts. The goal of this longitudinal epidemiologic cohort was to study dietary factors that could influence health in early life. Participants were not selected for any disease. Study details have been previously described.⁸

Enrollment occurred between 1999 and 2002 for women with singleton pregnancy. In-person interviews and questionnaires were administered after the initial prenatal visit, at an average of 10 weeks of gestation, and at 26–28 weeks of gestation. Interviews and questionnaires on child health were administered at 6 months, 1 year, and annually thereafter. Outcome data for this study was collected between study inception and the school age in-person visit (median age 7.7 years, age range 6.6–10.9 years, IQR 1.0 years). Study protocols were approved by the institutional review boards of participating institutions. Of the 2128 children delivered in Project Viva, 1248 mother-child pairs who came to the school age in-person visit and responded to the questionnaire item regarding allergic rhinitis or had allergen sensitization measured were included in this study.

Maternal dietary and supplemental vitamin D intake assessment

Maternal dietary assessments at the first and second trimester visits were based on a validated 166-item semi-quantitative food frequency questionnaire (FFQ) modified for pregnancy⁹ that has been previously described¹⁰ and is fully available here: <https://www.hms.harvard.edu/viva/Data-collection-forms/early-preg-ffq1.pdf>. Food-based intake of vitamin D was calculated by summing the amount of vitamin D in foods in the FFQ containing vitamin D based on the Harvard nutrient composition database used for the Nurses' Health Study and other large cohort studies.¹¹ Supplement-based intake of vitamin D was calculated based on queried dose, duration, and brand/type of multivitamin, prescribed prenatal vitamin, and supplements by separate interview during the first trimester, and by self-completed questionnaire during the second trimester.¹⁰ Total vitamin D intake was the sum of vitamin D from food and supplement sources. Vitamin D intake was energy-adjusted using the nutrient residual method.¹²

Serum 25(OH)D assessment during the prenatal, perinatal, and childhood periods

Serum 25(OH)D levels were measured at three time points: in mothers during the second trimester of pregnancy, in cord blood at birth, and in children at school age. Each sample was analyzed in duplicate for 25(OH)D concentration, once using an automated chemiluminescence immunoassay,¹³ and once using a manual radioimmunoassay.¹⁴ As has been done in prior studies, two values were averaged to obtain more stable estimates of 25(OH)D level.^{15–17} For quality control, the laboratory used U.S. National Institutes of Standards and Technology level 1.

Childhood outcomes

Ever allergic rhinitis at school age was defined as positive if a mother answered yes to “Have you ever been told by a health care professional, such as a doctor, physician assistant or nurse practitioner, that your child has hay fever, seasonal allergies or allergic rhinitis (runny nose due to allergies)?” at the school age interview. This question was based on the questionnaire from the International Study of Asthma and Childhood.¹⁸ Maternal and paternal asthma, allergic rhinitis, and atopic dermatitis were each considered positive if a mother reported at week 10 of gestation that she or the child’s biological father had a history of the respective condition. Maternal allergy was considered positive if maternal asthma, allergic rhinitis, or atopic dermatitis was positive, and paternal allergy was defined analogously. Parental allergy was considered positive if maternal or paternal allergy was positive.

Of the 1248 children in the analysis sample, 702 had blood drawn at school age for additional studies, of which 616 children had sufficient sample to measure serum total IgE and allergen specific IgE (sIgE levels) by Phadia ImmunoCAP (Uppsala, Sweden). A variety of perennial and seasonal environmental allergens common to the United States Northeast were assessed, including *Dermatophagoides farinae*, *Aspergillus fumigatus*, *Alternaria alternata*, rye grass, ragweed, cat dander, dog dander, and *Blattella germanica*. Sensitization to environmental allergens was considered positive if the subject had an allergen specific IgE level ≥ 0.35 kU/L to any of the environmental allergens tested.

Statistical analyses

Spearman rank correlation was used to assess the pairwise correlation between measures of vitamin D. Unadjusted and multivariable adjusted logistic regression models were used to examine associations between vitamin D measures and ever allergic rhinitis at school age. For ease of interpretation, 100 IU of vitamin D (the amount of vitamin D in an 8 ounce glass of milk) was used as the unit of exposure for vitamin D intake, and 25 nmol/ml of serum 25(OH)D was used as the unit of exposure for serum measures of vitamin D. Models included as covariates factors that could confound the association of vitamin D with allergic rhinitis, including maternal education, maternal pre-pregnancy body mass index (BMI), smoking during pregnancy, parity at enrollment, parental allergy, and child sex, ethnicity, season of birth, breastfeeding history, and child BMI at school age. To explore potential bias related to follow up at school age, sensitivity analyses limited to subjects with school age 25(OH)D levels (n=652) were performed. In the 616 subjects for whom serum total IgE levels and environmental allergen sensitization status were available, association testing was

performed for vitamin D and these intermediate phenotypes of allergy. All analyses were performed using R 2.15.2 (R Foundation for Statistical Computing, Vienna, Austria) and SAS 9.3 (SAS Institute, Cary, NC).

Results

Study population

The baseline characteristics of the participants are shown in Table 1. Compared to the 880 participants excluded, the 1248 participants with school age data included showed higher proportions of maternal Caucasian ethnicity (69% vs. 63%), maternal college or graduate education (69% vs. 58%), annual household income exceeding \$70,000 (63% vs. 58%), and parental allergy (59% vs. 57%). Compared to the general US population,¹⁹ the study population contained a higher proportion of African Americans and lower proportion of Hispanics. The majority of mothers were college-educated and most households were not low income. Rates of parental asthma, allergic rhinitis, and atopic dermatitis were consistent with those for the general US population.^{20–22}

Maternal intake of vitamin D by food, supplement, and all sources was higher during the second trimester than the first trimester (Table 1). Serum 25(OH)D levels were < 50 nmol/L (“deficient” per Endocrine Society guidelines²³) in 33% of mothers during the second trimester, 61% of infants, and 18% of children at school age. Of note, norms for cord blood 25(OH)D are not well-established, and guidelines for adult serum 25(OH)D are typically applied.²³

Among the 616 children in with IgE levels, serum total IgE levels ranged from 2 to 3284 kU/L with a geometric mean level of 48.5 kU/L (Table 1). 42% of children were sensitized to at least one of the 8 environmental allergens tested at school age. The prevalence of ever allergic rhinitis at school age (23.8%) was consistent with the 10–30% prevalence of allergic rhinitis reported for Americans.²¹

Weak to moderate correlations between pairs of vitamin D measures

There was moderate correlation between total maternal vitamin D intake during the first and second trimesters ($r=0.38$), and relatively low correlation between these intake measures and maternal, cord blood, and childhood serum 25(OH)D levels (Figure 1A). Maternal serum 25(OH)D levels modestly correlated with cord blood levels ($r=0.53$), and cord blood levels modestly correlated with childhood serum levels ($r=0.46$), but maternal and child levels were not well correlated ($r=0.29$).

Comparisons of the mode of maternal vitamin D intake during the first and second trimesters showed no significant correlation between vitamin D intake by food and by supplement during the first trimester, and low correlation during the second trimester ($r=0.10$) (Figure 1B). Intake of vitamin D by food sources was moderately correlated between the first and second trimesters ($r=0.54$), while intake of supplemental vitamin D weakly correlated between the first and second trimesters ($r=0.28$).

Food-based vitamin D intake during pregnancy is associated with reduced odds of ever allergic rhinitis at school age

Each additional 100 IU of maternal intake of food-based vitamin D (the amount of vitamin D contained in an 8-ounce glass of milk) during the first trimester was associated with a 21% reduced odds of ever allergic rhinitis at school age in our adjusted model (OR 0.79, 95% CI 0.67–0.92) (Figure 2). Similarly, each additional 100IU of maternal intake of food-based vitamin D during the second trimester was associated with a 20% reduced odds of ever allergic rhinitis at school age (OR 0.80, 95% CI 0.68–0.93). There were no associations between maternal intake of supplemental vitamin D and ever allergic rhinitis at school age (OR 1.00, 95% CI 0.91–1.10 for first trimester supplemental intake, and OR 0.98, 95% CI 0.88–1.10 for second trimester supplemental intake). Adjusted models also did not show associations between serum 25(OH)D levels measured during the second trimester in mothers, in cord blood, and at school age in children with allergic rhinitis by school age.

Similarly, sensitivity analyses constrained to subjects with school age 25(OH)D levels (n=652) showed that maternal intake of food-based vitamin D during the first and second trimesters were associated with 21–22% reduced odds of ever allergic rhinitis at school age (Supplementary Table S1), with no associations between maternal supplemental or total vitamin D intake and this outcome. In this subset, maternal 25(OH)D during the second trimester was associated with 27% reduced odds of ever allergic rhinitis at school age. There were no associations between cord blood or school age 25(OH)D levels and allergic rhinitis.

No association between vitamin D and serum total IgE or environmental allergen sensitization

There were no associations between maternal vitamin D intake (food-based, supplemental, or total) and serum total IgE at school age (Supplementary Figure 1A). There were also no associations between any of the serum 25(OH)D levels (second trimester in mothers, in cord blood, and at school age in children) and serum total IgE at school age (Supplementary Figure 1B). Likewise, the adjusted models did not show associations between vitamin D measures and sensitization to environmental allergens (Figure 3).

Discussion

Main findings

We found that higher maternal intake of food-based vitamin D during the first and second trimesters of pregnancy was associated with ~20% lower risk of ever allergic rhinitis at school age. A protective association between vitamin D and childhood allergic rhinitis was not seen with prenatal intake of supplemental vitamin D or with serum 25(OH)D levels in mothers during pregnancy, during the perinatal period (cord blood), or in children during school age.

A major strength of this study is that vitamin D exposure in this prospective prebirth cohort was multiply assessed by two methods (intake and serum 25(OH)D level) and at three time points (prenatal, perinatal, and childhood). Many studies examining the relationship between

vitamin D and allergy have examined vitamin D intake or serum level individually, and typically at single time points.^{1, 2}

This study's finding of an association between food-based (but not supplemental) vitamin D intake and reduced odds of ever allergic rhinitis at school age may be due to biologically available forms of vitamin D that are present in foods but not in supplements.

Unmetabolized forms of vitamin D include cholecalciferol (vitamin D3) and ergocalciferol (vitamin D2).⁷ These must be activated into the hormone 1,25(OH)₂D for vitamin D to function in the body, or are converted to 25(OH)D, the storage form.²⁴ Vitamin D intake (by food and/or supplement) is quantified by estimating intake of unmetabolized vitamin D (e.g. combining vitamin D2 and vitamin D3 intake). This approach may reasonably reflect the vitamin D content of supplements, which are typically vitamin D2 and D3, as well as the vitamin D content of foods that are fortified with vitamin D2 and D3 (e.g. milk, breakfast foods, orange juice). However, foods from animal sources that naturally contain vitamin D (e.g. all types of meats) also contain 25(OH)D. 25(OH)D is not currently accounted for in usual measures of food-based vitamin D intake. Not accounting for 25(OH)D naturally present in animal-based foods is problematic, because the presence of this metabolite raises the vitamin D content of these particular foods.⁷ Indeed, a recent study examining USDA data showed that accounting for the 25(OH)D content of animal-based foods reduced discrepancies between vitamin D intake and serum 25(OH)D levels.⁷ It is therefore possible that this study found significant associations with food-based vitamin D intake because intake measures covaried with additional 25(OH)D in these foods.

The study's finding of a protective effect of maternal vitamin D intake from food sources but not from supplemental vitamin D intake or 25(OH)D levels may also be due to nutrients that accompany vitamin D in vitamin D-containing foods. These nutrients may reduce the odds of allergic rhinitis either directly or in synergy with vitamin D. Many studies in nutritional epidemiology have focused on specific nutrients and their association with asthma and allergy outcomes, with unresolved questions about whether individual nutrients are responsible for the associations observed, or whether they are markers of other nutrients or overall dietary pattern.^{25, 26} Foods are a rich mixture of many nutrients, and consistent with the concept of "food synergy"²⁶, there may be interactive effects on allergic diathesis between vitamin D and other nutrients in vitamin D-containing foods. This study's finding of a protective effect of vitamin D from food sources could be because the vitamin D content of vitamin D-containing foods is a marker of the beneficial food synergy in these foods.

Comparison with other studies

Consistent with this study, Erkkola and colleagues reported an inverse relationship between maternal food-based intake of vitamin D during late pregnancy and allergic rhinitis in 5-year-old children. The subjects of this Finnish cohort had HLA-DQB1-conferred susceptibility for Type 1 diabetes.²⁷ A relative strength of our study is that subjects were unselected for any disease or condition, which supports the generalizability of this study's findings. An additional relative strength of our study is minimal recall bias-- mothers completed FFQs during the first and second trimesters, before any outcomes in their children occurred. In contrast, Erkkola et al. retrospectively assessed food intake during pregnancy by

asking mothers of these diabetes susceptible children after delivery to recall their diet during the eighth month of pregnancy. Additionally, our examination of maternal intake of vitamin D occurred at two points during pregnancy. Maternal diet changes during pregnancy,^{10, 28} and this is particularly important to consider when examining vitamin D because maternal intake of vitamin D-rich foods varies between trimesters. For example, intake of skim or reduced fat dairy foods increases by 22%, of whole dairy foods by 15%, and of red and processed meats by 11% between the first and second trimesters of pregnancy.¹⁰ In our study, the inverse association between food-based vitamin D intake and ever allergic rhinitis at school age was present during both the first and second trimesters.

In contrast to this study's findings and those of Erkkola et al., Maslova et al. found no association between vitamin D intake during the second trimester and childhood allergic rhinitis at age 7 years in the Danish Birth Cohort Study.⁵ Mothers in our study had higher levels of vitamin D exposure than those in the Danish study-- the median second trimester vitamin D intake by mothers in our prebirth cohort was 31% higher, with 80% higher median food-based intake and 19% higher median supplemental intake. The relatively higher vitamin D exposures in our study may have enabled detection of associations between maternal vitamin D intake and childhood allergic rhinitis.

We had hypothesized that there would be an association between vitamin D exposure and allergic rhinitis because a growing body of literature supports that vitamin D has immunomodulatory functions relevant to allergic disease.¹⁻³ However, it was unclear from prior studies which mode of vitamin D exposure in early life would have greatest effect. This study's results support that maternal food-based vitamin D intake during the first and second trimesters of pregnancy are exposures of high interest. This is consistent with the fact that early pregnancy is a formative period of fetal immune system development, with early forms of many cells involved in allergy developing and potentially influenced during this period. For example, during the first trimester, early dendritic and macrophage cells develop, positive and negative T cell selection occurs, immunoglobulin isotypes develop, and IgE production begins.¹⁻³ As maternal vitamin D is bioavailable to the fetus during this time,¹ maternal intake of vitamin D during early pregnancy could modulate the fetal immune system toward or away from allergic disorders in childhood.

Null findings

Although higher maternal intake of food-based vitamin D during pregnancy was associated with lower odds of ever allergic rhinitis at school age, there were no associations between serum 25(OH)D levels and this outcome (Figure 2). This was the case whether the serum level was assayed from mothers during the second trimester, cord blood, or the children at school age. Previous studies examining maternal,²⁹ cord blood³⁰⁻³² or childhood serum levels of 25(OH)D³³⁻³⁵ in many different populations (Danish, Australian, German, and Asian) have similarly reported no association with allergic rhinitis. The distinct association between vitamin D intake (as compared to serum 25(OH)D levels) with the development in allergic rhinitis may be because 25(OH)D levels fluctuate between measurement and season⁵, while vitamin D intake assessment (via food frequency questionnaire) reflects long-term diet and may be a more accurate measure of vitamin D exposure.¹

Although there was an inverse association between maternal intake of food-based vitamin D during pregnancy with ever allergic rhinitis at school age, there was no association between vitamin D by any measure and serum total IgE or environmental allergen sensitization (Supplementary Figure 1, Figure 3). As environmental allergen sensitization and serum total IgE are intermediate phenotypes of allergic rhinitis and allergy, it may seem counterintuitive that vitamin D intake was not also associated with these outcomes, but these null findings can be explained in several ways. First, allergic rhinitis results from environmental allergen sensitization that leads to naso-ocular symptoms upon exposure to the corresponding allergen.³⁶ But environmental sensitization may not necessarily lead to symptoms of allergic rhinitis, so these outcomes are never in complete agreement. Indeed, in the 616 children who had serum total and allergen specific IgE levels measured in the cohort, 26% were sensitized to an environmental allergen but did not report allergic rhinitis. Vitamin D intake may be associated with risk for sensitization that leads to an allergic phenotype, but not with sensitization only. Second, environmental sensitization was based on allergen specific IgE levels to 8 common indoor and outdoor environmental allergens. The inclusion of more environmental allergens in our sensitization assessment may have changed the outcome. Third, tests for association between vitamin D and allergen sensitization were restricted to the 616 children for whom serum total and allergen-specific IgE levels were available, while the full school age cohort (n=1277) was used for the primary analysis of allergic rhinitis. That said, a previous study examining 18,224 subjects similarly found no association between serum 25(OH)D levels and allergen sensitization, and power was not likely a limitation in that large study.³⁷ As context, results of studies examining the relationship between early-life vitamin D exposure and serum IgE levels have been very inconsistent, with studies showing inverse,^{38–40} non-linear,³⁰ and null^{31, 37, 41, 42} relationships.

Limitations

In an effort to address the limitations of previous studies, where single measures of vitamin D exposure were typically employed,^{1, 2, 7} vitamin D exposure was measured by two methods (food intake questionnaire and serum 25(OH)D level) and at three time intervals (prenatal, perinatal, school age) in this study. Our focus on multiple exposures may raise concern regarding multiple testing, but this is strongly counterbalanced by the benefit of having multiple measures of vitamin D in a single cohort, as single measures of vitamin D exposure incompletely capture its potential effects.^{1, 2, 7}

Conclusions

In conclusion, we performed a multifaceted assessment of vitamin D exposure during early life in a prebirth cohort of mothers and children unselected for any disease. Weak to moderate correlations between maternal vitamin D intake during pregnancy and serum 25(OH)D levels during the prenatal, perinatal, and childhood periods were observed. Food-based, but not supplemental, vitamin D intake by mothers during the first and second trimesters was associated with 20% reduced odds of ever allergic rhinitis at school age. There were no associations between any other measure of vitamin D and allergic rhinitis; likewise, all measures of vitamin D were not associated with serum total IgE level or environmental allergen sensitization at school age. This study's results provide further

motivation for randomized trials examining vitamin D intake during pregnancy and their effects on childhood asthma and allergy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations/Acronyms

25(OH)D	serum 25-hydroxyvitamin D
FFQ	Food frequency questionnaire
sIgE	specific IgE

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Key Messages

- Higher maternal intake of food-based vitamin D during pregnancy was associated with reduced odds of ever allergic rhinitis at school age.
- Supplemental vitamin D intake and serum 25(OH)D levels during the prenatal, perinatal, or childhood periods) were not associated with ever allergic rhinitis at school age.
- Inclusion of foods containing vitamin D in maternal diets during pregnancy may have beneficial effects on childhood allergic rhinitis.

Figure 1. Correlation between vitamin D measures obtained during the prenatal, perinatal, and childhood periods in Project Viva participants
A: Spearman rank correlation coefficients are shown for tests of correlation between total maternal vitamin D intake during the first and second trimesters, maternal serum 25(OH)D level during the second trimester, cord blood 25(OH)D level, and child serum 25(OH)D level at school age. **B:** Spearman rank correlation coefficients are shown for tests of correlation between maternal intake of vitamin D analyzed by source, including food, supplemental, and total intakes during the first and second trimesters. Color scale and eccentricity of the shapes correspond to numerical values of Spearman rank correlation coefficients. All Spearman rank correlation coefficients in this figure were statistically significant (at P value ranging from $< 2.2 \times 10^{-16}$ to 0.0009), except for the three correlation coefficients marked with *.

Figure 2. Associations between vitamin D measures (obtained during the prenatal, perinatal, and childhood periods) and ever allergic rhinitis at school age

The unit of exposure for intake was 100IU/day (the amount of vitamin D contained in an 8 ounce serving of milk) and the unit for serum 25(OH)D level was 25 nmol/L. Models were adjusted for potential confounders, including maternal education, pre-pregnancy BMI, smoking during pregnancy, parity at enrollment, parental allergy, and child sex, ethnicity, season of birth, breastfeeding history, and BMI at school age. A forest plot is shown for results from the adjusted models.

Figure 3. Associations between vitamin D measures (obtained during the prenatal, perinatal, and childhood periods) and environmental allergen sensitization at school age

The unit of exposure for intake was 100IU/day (the amount of vitamin D contained in an 8 ounce serving of milk) and the unit for serum 25(OH)D level was 25 nmol/L. Environmental allergen sensitization was based on allergen specific IgE level ≥ 0.35 kU/L to any of the environmental allergens tested. Models were adjusted for potential confounders, including maternal education, pre-pregnancy BMI, smoking during pregnancy, parity at enrollment, parental allergy, and child sex, ethnicity, season of birth, breastfeeding history, and BMI at school age. A forest plot is shown for results from the adjusted models.

Table 1

Parental and child characteristics among participants from the Project Viva pre-birth cohort

Characteristic	Participants with school age data (N=1248)	Participants with school age data AND sIgE levels measured (N=616)
Mean (SD) or N (%)		
Parental Characteristics		
Maternal education college graduate	858 (69.1%)	407 (66.5%)
Maternal smoking during pregnancy	119 (9.6%)	61 (9.9%)
Maternal pre-pregnancy BMI, kg/m ²	24.7 (5.3)	25.1 (5.3)
Maternal allergy	492 (39.6%)	241 (39.4%)
Maternal asthma	157 (12.7%)	84 (13.7%)
Maternal allergic rhinitis	358 (28.8%)	167 (27.3%)
Maternal atopic dermatitis	162 (13.0%)	72 (11.8%)
Paternal allergy	425 (34.7%)	200 (33.2%)
Paternal asthma	145 (12.0%)	71 (12.0%)
Paternal allergic rhinitis	318 (26.8%)	154 (26.5%)
Paternal atopic dermatitis	74 (6.1%)	29 (4.9%)
Household income \$70,000	718 (63.3%)	359 (64.2%)
Parity at enrollment	0.74 (0.89)	0.86 (0.95)
Child characteristics		
Sex- female	619 (49.6%)	302 (49.0%)
Season of birth		
Fall	267 (21.4%)	142 (23.1%)
Winter	322 (25.8%)	155 (25.2%)
Spring	324 (26.0%)	154 (25.0%)
Summer	335 (26.8%)	165 (26.8%)
Ethnicity		
Caucasian	810 (65.0%)	383 (62.4%)
African American	198 (15.9%)	121 (19.7%)
Hispanic	51 (4.1%)	30 (4.9%)
Asian	40 (3.2%)	13 (2.1%)
>1 race or other	147 (11.8%)	67 (10.9%)
Breastfed 6 months	649 (55.9%)	319 (55.5%)
Age at school age visit, years	7.9 (0.8)	7.8 (0.7)
BMI at school age, kg/m ²	17.3 (3.1)	17.3 (3.3)
Maternal Vitamin D intake during pregnancy[*]		
First trimester		
Food – IU/day	218.1 (112.0)	218.5 (114.8)
Supplement –IU/day	282.1 (173.7)	274.5 (178.3)
Total –IU/day	500.1 (207.6)	493.0 (215.8)

Characteristic	Participants with school age data (N=1248)	Participants with school age data AND sIgE levels measured (N=616)
Mean (SD) or N (%)		
Second trimester		
Food – IU/day	231.6 (112.0)	232.7 (115.9)
Supplement – IU/day	369.3 (142.3)	367.5 (147.1)
Total –IU/day	600.9 (184.3)	600.2 (189.5)
Serum vitamin D (25(OH)D) levels		
Maternal, second trimester – nmol/L	59.0 (21.4)	59.6 (21.9)
Cord blood– nmol/L	46.4 (18.0)	45.8 (18.1)
Child at school age– nmol/L	67.5 (19.1)	67.4 (19.1)
Child sensitization and allergic rhinitis		
Total IgE – kU/L		48.5 (2–3284) **
Environmental allergen sensitization		259 (42.0%)
Allergic rhinitis	291 (23.4%)	145 (23.8%)

* energy adjusted nutrients using the nutrient residual method.

** geometric mean (range) provided