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Carlos A. Camargo, Jr, Tristram Ingham, Kristin Wickens, Ravi Thadhani, Karen M. Silvers, Michael J. Epton, G. Ian Town, Philip K. Pattemore, Janice A. Espinola, Julian Crane and the New Zealand Asthma and Allergy Cohort Study Group

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WHAT'S KNOWN ON THIS SUBJECT: Recent study results have suggested that higher maternal intake of vitamin D during pregnancy may lower the risk of wheezing in offspring. The relationship between cord-blood levels of 25-hydroxyvitamin D and risk of childhood respiratory outcomes is unknown.

WHAT THIS STUDY ADDS: In a population-based birth cohort with excellent 5-year follow-up, cord-blood 25-hydroxyvitamin D levels had significant inverse associations with the risk of respiratory infection and risk of childhood wheezing. In contrast, vitamin D had no association with incident asthma.

AUTHORS: Carlos A. Camargo Jr, MD, DrPH,[a,b] Tristram Ingham, MBChB,[c] Kristin Wickens, PhD,[c] Ravi Thadhani, MD, MPH,[a] Karen M. Silvers, PhD,[d] Michael J. Epton, PhD, FRACP,[d] G. Ian Town, DM,[e] Philip K. Pattemore, MD, FRACP,[d] Janice A. Espinola, MPH,[b] and Julian Crane, FRACP,[c] the New Zealand Asthma and Allergy Cohort Study Group

[a]Center for D-receptor Activation Research and [b]Department of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts; [c]Wellington Asthma Research Group, Department of Medicine, Wellington School of Medicine and Health Sciences, University of Otago, Wellington, New Zealand; [d]Canterbury Respiratory Research Group, Department of Paediatrics, Christchurch School of Medicine and Health Sciences, University of Otago, Christchurch, New Zealand; and [e]University of Canterbury, Christchurch, New Zealand

KEY WORDS
vitamin D, 25-hydroxyvitamin D, cord blood, respiratory infection, wheezing, asthma, New Zealand

ABBREVIATIONS
25(OH)D—25-hydroxyvitamin D
IQR—interquartile range
OR—odds ratio
CI—confidence interval

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Address correspondence to Carlos A. Camargo Jr, MD, DrPH, Massachusetts General Hospital, 326 Cambridge St, Suite 410, Boston, MA 02114. E-mail: ccamargo@partners.org

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abstract

OBJECTIVE: Higher maternal intake of vitamin D during pregnancy is associated with a lower risk of wheezing in offspring. The relationship between cord-blood levels of 25-hydroxyvitamin D (25[OH]D) and childhood wheezing is unknown. We hypothesized that cord-blood levels would be inversely associated with risk of respiratory infection, wheezing, and asthma.

PATIENTS AND METHODS: Cord blood from 922 newborns was tested for 25(OH)D. Parents were asked if their child had a history of respiratory infection at 3 months of age or a history of wheezing at 15 months of age and then annually thereafter. Incident asthma was defined as doctor-diagnosed asthma by the time the child was 5 years old and reported inhaler use or wheezing since the age of 4 years.

RESULTS: The median cord-blood level of 25(OH)D was 44 nmol/L (interquartile range: 29–78). Follow-up was 89% at the age of 5 years. Adjusting for the season of birth, 25(OH)D had an inverse association with risk of respiratory infection by 3 months of age (odds ratio: 1.00 [reference] for ≥75 nmol/L, 1.39 for 25–74 nmol/L, and 2.16 [95% confidence interval: 1.35–3.46] for <25 nmol/L). Likewise, cord-blood 25(OH)D levels were inversely associated with risk of wheezing by 15 months, 3 years, and 5 years of age (all $P < .05$). Additional adjustment for more than 12 potential confounders did not materially change these results. In contrast, we found no association between 25(OH)D levels and incident asthma by the age of 5 years.

CONCLUSIONS: Cord-blood levels of 25(OH)D had inverse associations with risk of respiratory infection and childhood wheezing but no association with incident asthma. *Pediatrics* 2011;127:e180–e187

Asthma researchers have documented the prevalence of childhood wheezing around the world.[1] Although this knowledge is helpful for understanding respiratory health, all that wheezes is not asthma,[2] and asthma itself is a heterogeneous condition.[3,4] Nevertheless, because an asthma diagnosis in young children remains a major clinical challenge,[5] epidemiologic studies of children in this age group often focus on childhood wheezing.

In 2006, Camargo et al[6,7] reported a strong inverse association between maternal intake of vitamin D during pregnancy and the risk of recurrent wheezing in offspring. Similar findings from other birth cohorts[8–10] have led to speculation that vitamin D deficiency is responsible for the global asthma epidemic.[11] Another possibility[12] is that vitamin D deficiency increases the risk of respiratory infections[13] that then provoke wheezing, a nonspecific finding that might be confused with incident asthma. Indeed, recent laboratory studies have linked vitamin D with favorable changes in innate immunity,[14] an important host defense against microbial pathogens,[15,16] particularly among infants.[17]

To further examine the role of vitamin D in childhood respiratory health, we examined cord-blood levels of 25-hydroxyvitamin D (25[OHD]) in 922 children in New Zealand. We sought to determine the relationship between vitamin D status at birth and the risk of respiratory infection during the first months of life. We also examined the relation of vitamin D with several wheeze outcomes, including incident asthma by the age of 5 years.

MATERIALS AND METHODS

Study Design and Subjects

The New Zealand Asthma and Allergy Cohort Study is a prospective birth cohort comprising 1105 infants recruited in Wellington (41°S latitude) and Christchurch (43°S latitude) between 1997 and 2001. Briefly, expectant mothers were recruited by a random sample of midwives, health professionals who provide almost all maternity care in New Zealand. The only exclusion criterion was the inability to speak sufficient English to complete the baseline questionnaire. At birth, midwives or study nurses collected the newborn's anthropometric details and cord blood, when available. Study nurses administered questionnaires shortly after birth, at 3 and 15 months, and then annually between the ages of 2 and 5 years; the interviews were face-to-face at birth, 3 months, and 15 months and then by telephone thereafter. Full details of recruitment and follow-up have been presented elsewhere.[18] Ethics committee approval for the study was obtained from the Wellington and Canterbury Regional ethics committees, and informed consent was obtained from each mother.

Cord-Blood 25(OH)D

The primary exposure for this analysis is a cord-blood level of 25(OH)D. Cord blood was available from 922 participants (83% of the original cohort), and this sample was representative of the overall study population (data not shown). The cord-blood samples were promptly refrigerated at −4°C and then transferred, within 24 hours, to −80°C freezers for long-term storage. Levels of 25(OH)D were measured in duplicate using the Diasorin (Stillwater, MN) LIAISON automated chemiluminescence immunoassay. The assay has an intra-assay coefficient of variation of 9% and an interassay coefficient of variation of 11%. On the basis of the definitions of vitamin D status from the Canadian Paediatric Society,[19] 25(OH)D levels were categorized as 75 or more (reference group), 25 to 74.9, and less than 25 nmol/L.

Outcomes

The primary outcomes for this analysis were respiratory infection, cumulative wheeze, and asthma. We defined respiratory infection by 3 months of age as a positive response to a series of questions ("Has [child's name] had any of the following?") about colds, cough, whooping cough, chest infections, and ear infections during the first 3 months of life. To further examine infection, we expanded the definition to any infection by including any positive response to a series of questions about vomiting, diarrhea, eye infection, urine infection, skin infection, German measles, mumps, measles, chicken pox, and other viral infection.

We also examined the cumulative incidence of wheeze at ages 15 months, 3 years, and 5 years. We assessed wheeze status by using the same question across all visits (3 and 15 months and 2, 3, 4, and 5 years): "Has he/she ever had wheezing or whistling in the chest at any time?"[1] The question was modified at follow-up visits to cover the period since the previous visit (ie, parents were instructed that "the answers apply to what has happened since our last telephone questionnaire"). Parental report of wheezing has been shown to be a sensitive and specific outcome when using physician assessment as the criterion standard.[20]

Parental report of doctor-diagnosed asthma was collected at all visits; however, given the uncertainty about this diagnosis in early childhood,[5] these data were integrated into the variable "incident asthma by 5 years of age," which was defined as any previous report of doctor-diagnosed asthma by the age of 5 years plus either a history of inhaler use or wheeze since the age of 4 years. The inhaler question was, "Has he/she used any inhaled medicines (such as a puffer or nebulizer)

for asthma, cough, or breathing problems?"

Covariates

The most important potential confounder was season of birth because of its known associations with both serum 25(OH)D levels[21] and respiratory infections.[13] Other potential confounding variables included study site (Wellington and Christchurch), maternal age at birth, parental history of asthma, gestational age, birth weight, child's gender, child's ethnicity, any smoking during pregnancy, any passive smoke exposure to the child at 3 months of age, number of children younger than 16 years in household at the time the child was 3 months old, endotoxin on the bedroom floor at the time the child was 3 months old, damp musty smell in any room of home at the time the child was 3 months old, and duration of exclusive breastfeeding. The child's ethnicity was assessed with the question, "Which ethnic group or groups does [child's name] belong to?" For analytic purposes, a child's ethnicity was assigned by using the following prioritization: Māori, non-Māori Pacific Islander, other, then European. Full details of endotoxin sampling and analysis have been presented elsewhere.[22] Socioeconomic status was assessed by using the New Zealand Deprivation Index based on the child's home address at 3 months of age[23]; the index ranges from 1 (affluent) to 10 (poor).

Atopy was measured at the age of 15 months by using the Quintest system (Bayer Corporation, West Haven, CT) for skin-prick tests. The following allergens were included: *Dermatophagoides pteronyssinus*, cat, dog, rye grass, cow's milk, egg white, peanut, *Aspergillus*, cockroach, a positive histamine control (10 mg/mL), and a negative control. A reaction was considered positive if there was an allergen-to-histamine wheal ratio of more than 0.5 after subtraction of the negative control mean wheal size. Atopy was defined as a positive reaction to any allergen.

Data Analysis

We performed all analyses by using Stata 10.0 (Stata Corp, College Station, TX). The cohort was described according to vitamin D status at birth. We tabulated means (SD), medians (interquartile range [IQR]), and proportions. We tested for trend across vitamin D for each of the characteristics by using linear regression or the Kruskal-Wallis test for continuous variables and a nonparametric test for trend based on Wilcoxon-Mann-Whitney test for categorical variables.

We used multivariable logistic regression models to test the association between cord-blood 25(OH)D level and infection outcomes at 3 months of age. We assessed the confounding effect of covariates by examining the association of 25(OH)D levels with outcomes before and after adding the covariates to the model. We also evaluated potential intermediate factors (birth weight and atopy) in this manner. We calculated *P* for trend across vitamin D categories by using median vitamin D values within each group. Multivariable logistic regression models also were used to evaluate the relationships between serum 25(OH)D concentrations (per 10 nmol/L) with wheeze outcomes and incident asthma. Results of all logistic regression models are reported as odds ratios (ORs) with 95% confidence intervals (CIs). We examined effect modification of the 25(OH)D–asthma association by stratifying the cohort according to atopy status and formally testing the interaction term (continuous 25[OH]D × atopy status). Reanalysis of all clinical outcomes that excluded children with any missing covariates yielded similar results (data not shown). A 2-tailed *P* value of $<.05$ was considered statistically significant.

RESULTS

Among 922 newborns with cord-blood 25(OH)D concentrations recorded, 470 (51%) were recruited by midwives in Wellington and 452 (49%) in Christchurch. The median gestational age of the newborns was 40 weeks (IQR: 39–41), and the mean birth weight was 3.6 kg (SD: 0.5). Mean maternal age at birth was 30 years (SD: 5). Half of the newborns were male, and 71% were of European ethnicity.

Follow-up data were available for 882 (96%) children at 3 months of age and 823 (89%) at 5 years of age. The 40 mothers who dropped out before the 3-month visit were younger than those who remained in the cohort (mean maternal age: 27 vs 30 years; $P < .001$). The 2 groups did not differ, however, according to the newborns' vitamin D status, gestational age, gender, and birth weight (data not shown). Similar results were obtained from a comparison of children with ($n = 823$) and without ($n = 99$) follow-up to the age of 5 years (data not shown). Family history of asthma was obtained at the 3-month visit, and results were consistent with those of previous surveillance studies in New Zealand[1]; asthma was reported by 26% of the mothers and 21% of the fathers.

The median cord-blood level of 25(OH)D was 44 nmol/L (IQR: 29–78). As shown in Table 1, higher levels of 25(OH)D were reported among children of slightly older mothers and of European ethnicity. Low levels were more common among children born in winter, of lower socioeconomic status, and with paternal history of asthma, maternal smoking during pregnancy, and early exposure to passive smoke. Additional baseline associations have been presented elsewhere.[24] With regard to po-

TABLE 1 Characteristics of 922 Participants According to Cord-Blood Levels of 25(OH)D

Characteristic	Serum 25(OH)D Concentration			*P* for Trend[a]
	≥75 nmol/L	25–74 nmol/L	<25 nmol/L	
25(OH)D, median (IQR), nmol/L	100 (87–124)	41 (34–53)	19 (14–22)	—
n	251	491	180	
Season of birth, %				
Spring (September to November)	19	36	33	
Summer (December to February)	40	12	4	
Fall (March to May)	33	19	9	
Winter (June to August)	9	33	53	<.001
Study site, %				
Wellington	53	52	46	
Christchurch	47	48	54	.18
Parents and household				
Maternal age at birth, mean (SD), y	31 (5)	30 (5)	29 (5)	<.001
New Zealand Deprivation Index, mean (SD)	4.4 (2.8)	4.8 (2.9)	5.3 (3.0)	.002
Maternal history of asthma, %	25	26	27	.72
Paternal history of asthma, %	15	23	25	.009
Newborn and home environment				
Gestational age at birth, median (IQR), wk	40 (39–41)	40 (39–40)	40 (39–41)	.01
Male, %	51	52	46	.38
Child's ethnicity, %				
European	83	74	63	<.001
Māori	12	16	16	
Pacific Islander	3	6	12	
Other	3	5	8	
Any smoking during pregnancy, %	17	21	26	.03
Any passive smoke exposure at 3 mo of age, %	26	35	38	.008
No. of children aged <16 y in the household when the child was 3 mo old, mean (SD)	0.8 (0.9)	0.7 (0.9)	0.8 (1.0)	.97
Endotoxin on the bedroom floor when the child was 3 mo old, mean (SD), log EU/g	9.1 (2.1)	9.1 (2.1)	9.2 (1.9)	.60
Damp, musty smell in any room when the child was 3 mo old, %	41	37	41	.99
Duration of exclusive breastfeeding, mean (SD), mo	2.2 (2.0)	2.0 (2.0)	1.8 (1.9)	.06
Potential intermediate factors				
Birth weight, mean (SD), kg	3.6 (0.5)	3.6 (0.5)	3.6 (0.5)	.27
Skin-prick test positivity at 15 mo of age, %	26	32	23	.64

[a] *P* for trend is based on linear regression or the Kruskal-Wallis test for continuous variables and a nonparametric test for trend based on the Wilcoxon-Mann-Whitney test for categorical variables (for season of birth, we tested winter trend; for ethnicity, we tested European trend).

tential intermediate factors in the causal pathway between vitamin D and childhood respiratory outcomes, we did not detect any association between vitamin D status and either birth weight or atopy status at 15 months of age.

Table 2 demonstrates an inverse association between cord-blood 25(OH)D level and risk of infection outcomes at 3 months of age. Newborns with 25(OH)D levels less than 25 nmol/L were twice as likely to develop respiratory infection compared with those with levels of 75 nmol/L or higher (adjusted OR: 2.04). Expanding the outcome to risk of any infection, children born with a 25(OH)D level less than 25 nmol/L remained at increased risk (adjusted OR: 2.36). Because 94% of the children had experienced at least 1 respiratory infection by 15 months of age, it was not possible to examine the association between cord-blood 25(OH)D and the risk of infection beyond 3 months of age.

Fig 1 shows the unadjusted association between cord-blood 25(OH)D concentration and the 2 major wheeze outcomes at 5 years of age: cumulative wheeze and incident asthma. The smoothed line represents the probability of the outcome for each observed 25(OH)D level. Vitamin D had an inverse linear association with wheeze but no association with incident asthma. Adjusting for season, the OR for cumulative wheeze increased across categories of 25(OH)D (1.00 [reference] for ≥75 nmol/L, 1.63 [95% CI: 1.17–2.26] for 25–74 nmol/L, and 2.15 [95% CI: 1.39–3.33] for <25 nmol/L). In contrast, cord-blood 25(OH)D levels had no association with incident asthma (1.00 [reference], 1.19 [95% CI: 0.78–1.83], and 0.94 [95% CI: 0.53–1.64], respectively).

To further explore the association between vitamin D and risk of wheeze outcomes, we examined cord-blood 25(OH)D as a continuous variable in a series of logistic regression models (Table 3). Controlling for numerous characteristics, every 10 nmol/L increase in cord-blood 25(OH)D lowered cumulative risk of wheeze by the age of 5 years (adjusted OR: 0.95). Table 3 also demonstrates that there was no association between cord-blood 25(OH)D and incident asthma by the age of 5 years in any model. To further examine this null finding, we stratified the asthma outcome according to atopy status at the age of 15 months. In all models, cord-blood 25(OH)D levels had no association with either atopic or nonatopic asthma (all $P > .20$).

DISCUSSION

In a population-based cohort of 922 apparently healthy New Zealand children, we found low cord-blood levels of 25(OH)D; 1 in 5 children started life with less than 25 nmol/L. These low levels were associated with a higher risk of respiratory infection during the first months of life and a higher risk of cumulative wheeze throughout early childhood. In contrast, vitamin D status at birth was not associated with incident asthma.

TABLE 2 Association Between Cord-Blood Levels of 25(OH)D and the Risk of Infection by the Age of 3 Months

Outcome	25(OH)D Concentration, OR (95% CI)			*P* for Trend[a]
	≥75 nmol/L	25–74 nmol/L	<25 nmol/L	
Respiratory infection ($N = 553$ cases)				
Unadjusted	1.00 (reference)	1.22 (0.89–1.67)	1.80 (1.19–2.74)	.02
Multivariable model 1	1.00 (reference)	1.39 (0.98–1.99)	2.16 (1.35–3.46)	.004
Multivariable model 2	1.00 (reference)	1.35 (0.88–2.08)	2.04 (1.13–3.67)	.03
Any infection ($N = 697$ cases)				
Unadjusted	1.00 (reference)	1.27 (0.88–1.83)	1.84 (1.11–3.07)	.03
Multivariable model 1	1.00 (reference)	1.47 (0.98–2.22)	2.21 (1.26–3.90)	.008
Multivariable model 2	1.00 (reference)	1.49 (0.92–2.43)	2.36 (1.17–4.73)	.02

Model 1 adjusted for season of birth; model 2 adjusted for season of birth plus 14 potential confounders (study site, maternal age at birth, New Zealand Deprivation Index, maternal history of asthma, paternal history of asthma, gestational age, gender, child's ethnicity, any smoking during pregnancy, any passive smoke exposure at 3 months of age, number of children younger 16 years in household at the time the child was 3 months old, endotoxin on bedroom floor at the time the child was 3 months old [in quartiles], damp musty smell in any room of home at the time the child was 3 months old, and duration of exclusive breastfeeding).

[a] *P* for trend is from logistic regression models using a variable comprising the median value within each vitamin D group.

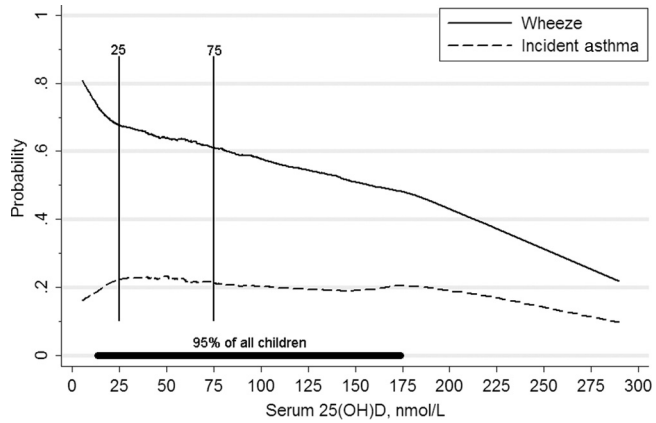

FIGURE 1
Unadjusted associations of cord-blood 25(OH)D levels with probabilities of cumulative wheeze or incident asthma by 5 years of age. The graph was smoothed by carrying out weighted regression of outcomes on vitamin D. The vertical lines denote serum 25(OH)D benchmarks.

Although most studies of the nonskeletal effects of vitamin D have focused on adults,[21] there is growing interest in these effects on the developing fetus and child.[19,25,26] At all ages, vitamin D status is determined largely from ultraviolet B ray exposure. Vitamin D also is available from dietary sources, which are more important at higher latitudes at which ultraviolet B ray exposure is inadequate for skin synthesis of vitamin D during winter. Indeed, vitamin D insufficiency is common among children at higher latitudes, such as the United States[27] and New Zealand.[28] The diverse sources of vitamin D, which involve environmental conditions and complex behaviors, complicate vitamin D research. Fortunately, serum 25(OH)D levels provide an excellent measure of overall vitamin D status.[19,21,25,26]

In early 2006, Camargo et al[6,7] reported that higher maternal intake of vitamin D during pregnancy might lower the risk of recurrent wheeze in offspring. The authors recognized that dietary intake provided an approximation of true vitamin D status. They also recognized that wheeze outcomes provide a fragile platform from which to draw causal inferences about asthma. Shortly thereafter, Scottish investigators confirmed the wheeze finding but reported no association between maternal vitamin D intake and doctor-diagnosed asthma at 5 years of age.[8] In 2009, Finnish investigators[9] reported an inverse association between maternal vitamin D intake and incident asthma but only for vitamin D from foods, not from supplements. Most recently, Japanese investigators[10] reported an inverse association between maternal vitamin D intake and infantile wheezing. Because all 4 cohort studies[7–10] were based on maternal intake, rather than serum 25(OH)D levels in either the mother or child, it remained possible that serum 25(OH)D levels might still implicate vitamin D deficiency as an important cause of asthma. Our findings do not support this hypothesis. Although vitamin D may affect incident asthma risk in later childhood (or adulthood), most asthma begins by the age of 5 years.[29] On a positive note, our null findings for risk of atopy at 15 months of age and incident asthma by 5 years of age may reassure clinicians concerned that even small increases in vitamin D intake may increase the risk of allergic diseases.[30,31]

The inverse association between cord-blood 25(OH)D levels and respiratory infections is novel and provides a compelling explanation for the wheeze findings. Although it is unclear how a single cord-blood level could explain wheeze risk a few years later (Table 3), vitamin D status during pregnancy might alter the developing immune system in utero or in the first months of exposure outside the womb. Another possibility is that the childhood associations reflect a correlation between cord-blood levels and serum levels in later years. In other words, mothers may "transmit" behavioral factors (eg, time spent outdoors) and nonbehavioral factors (eg, skin pigmentation) to their growing children. In such

TABLE 3 Association Between Cord-Blood 25(OH)D Levels (per 10 nmol/L Increase) and Risk of Wheeze Outcomes

Outcome	OR (95% CI)	*P*
Wheeze by 15 mo of age ($N = 331$ cases)		
Unadjusted	0.97 (0.94–1.01)	.13
Multivariable model 1	0.96 (0.92–1.00)	.03
Multivariable model 2	0.98 (0.93–1.02)	.30
Wheeze by 3 y of age ($N = 472$ cases)		
Unadjusted	0.96 (0.92–0.99)	.001
Multivariable model 1	0.94 (0.91–0.98)	.002
Multivariable model 2	0.96 (0.91–1.00)	.04
Wheeze by 5 y of age ($N = 533$ cases)		
Unadjusted	0.94 (0.91–0.97)	.001
Multivariable model 1	0.93 (0.90–0.97)	<.001
Multivariable model 2	0.95 (0.91–0.99)	.02
Incident asthma by 5 y of age ($N = 181$ cases)		
Unadjusted	0.98 (0.94–1.02)	.37
Multivariable model 1	0.99 (0.94–1.04)	.76
Multivariable model 2	1.03 (0.97–1.10)	.27

Model 1 adjusted for season of birth; model 2 adjusted for season of birth plus 13 potential confounders (study site, maternal age at birth, New Zealand Deprivation Index, maternal history of asthma, paternal history of asthma, gestational age, gender, child's ethnicity, any smoking during pregnancy, any passive smoke exposure at 3 months of age, number of children younger than 16 years in household at the time the child was 3 months old, endotoxin on bedroom floor at the time the child was 3 months old [in quartiles], and duration of exclusive breastfeeding).

a scenario, the cord-blood level may provide a reasonably accurate rank ordering of vitamin D status in early childhood. These possibilities merit further study.

The inverse association between cord-blood 25(OH)D levels and respiratory infections is consistent with a growing literature on vitamin D and innate immunity.[14,32] For example, laboratory studies[33] have showed that activated vitamin D induces cathelicidin (an endogenous antimicrobial peptide) in bronchial epithelial cells. The in vivo effects of ultraviolet B ray exposure or oral vitamin D supplementation on airway levels of cathelicidin have not been established, but results of recent experimental studies[34,35] indicate that both approaches raise skin levels of cathelicidin. Thus, even if vitamin D is unrelated to the etiology of most asthma, interventions to improve vitamin D status may provide a simple, safe, and inexpensive way to reduce the respiratory infections that cause most asthma exacerbations.[12] Indeed, results of recent studies have indicated that asthmatic children with higher levels of serum 25(OH)D are less likely to develop severe exacerbations[36] and that serum 25(OH)D levels have a particularly strong association with upper respiratory infection among people with asthma.[37] A recent randomized controlled trial[38] of vitamin D supplementation versus placebo in Japanese school children showed that vitamin D supplementation lowered the risk of seasonal influenza.

Our study has potential limitations. With regard to the exposure, it would have been interesting to track serum 25(OH)D levels earlier in pregnancy and later in childhood. The half-life of serum 25(OH)D is ~2 to 3 weeks,[39] which suggests that the measured levels reflect maternal-fetal status during the final months of pregnancy (and first months of life). Although we cannot rule out major changes in vitamin D intake during follow-up, the lack of vitamin D–fortified foods and the rarity of supplement use in New Zealand argue against this. Major changes in sun-related behaviors are more likely, despite heightened awareness of the carcinogenic effect of sun exposure.[40] In future studies, we plan to track serum 25(OH)D levels during pregnancy and childhood to help address this methodologic issue.

Another limitation is the imprecision of the primary outcomes. Because they were captured from interviews with mothers, rather than actual medical evaluations, it is likely, for example, that the different components of "respiratory infection" were misclassified. For that reason, we focused on the global outcome of respiratory infection and even expanded it to include any possible infection. It should be noted that we found consistent inverse associations between cord-blood 25(OH)D level and most of the individual components (data not shown). Likewise, we found a consistent lack of association between cord-blood 25(OH)D level and incident asthma regardless of how we defined the asthma outcome.

CONCLUSIONS

Low cord-blood levels of 25(OH)D were common in these newborns and were associated with higher risk of respiratory infections by the age of 3 months. Furthermore, cord-blood 25(OH)D levels were inversely associated with wheeze throughout early childhood but had no association with incident asthma. Although vitamin D is unlikely to explain the current asthma epidemic, its antimicrobial effects[14,32] might prove helpful in reducing asthma exacerbations and, thereby, assist with asthma control. Our observational data support the initiation of randomized controlled trials of vitamin D supplementation during pregnancy and early childhood to better define the effect of vitamin D on childhood respiratory health.

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