Vitamin D Levels Are Unrelated to the Severity of Respiratory Syncytial Virus Bronchiolitis Among Hospitalized Infants

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Background. Vitamin D deficiency at birth has been reported as a risk factor for respiratory syncytial virus (RSV) lower respiratory tract infection during the first year of life. Limited data are available on whether an infant’s vitamin D status is associated with the severity of acute RSV bronchiolitis.

Methods. Infants < 1 year of age and hospitalized with their first episode of RSV bronchiolitis were enrolled into the RSV Bronchiolitis in Early Life II cohort. We investigated the relationships between vitamin D status at enrollment and the following indicators of bronchiolitis severity: duration of hospitalization, lowest oxygen saturation measured during hospitalization, and bronchiolitis severity score.

Results. Among the 145 enrolled infants, the median (quartile 1 [Q1], Q3) serum 25-OH-VitD level was 36.8 (29.8, 42.3) ng/mL, with 14 infants (9.7%) having deficient serum vitamin D levels (25-OH-VitD <20 ng/mL). Vitamin D-deficient infants were younger than infants with 25-OH-VitD ≥ 20 ng/mL (2.8 vs 4.5 months, respectively; P = .04) and were less likely to consume infant’s formula (42.9% vs 87.0%, respectively; P < .01). The following indicators of acute bronchiolitis severity did not differ between infants who were vitamin D-deficient and nondeficient: duration of hospitalization (P = .53), lowest oxygen saturation (P = .45), and bronchiolitis severity score (P = .97), even after adjusting for age, and for infant’s formula consumption.

Conclusions. Among this cohort of infants that were hospitalized for RSV bronchiolitis, vitamin D status at the time of bronchiolitis was not associated with indicators of acute bronchiolitis severity.

Key words. bronchiolitis; respiratory syncytial virus; vitamin D.

Respiratory syncytial virus (RSV) is the major cause of bronchiolitis in the first year of life, with nearly all children having serologic evidence for infection with the virus by the age of 2 years [1–3]. Most children infected with RSV experience mild disease that does not require inpatient care. However, RSV bronchiolitis remains the leading cause of hospitalizations in infants younger than 1 year of age in the United States [4, 5], and it serves as a major risk factor for future asthma, with up to 50% of hospitalized children being diagnosed with asthma by school age [6]. The subgroup of infants, which eventually requires hospitalization, suffers from a substantial clinical morbidity that is associated with significant healthcare costs in both the short and long terms.

Only supportive treatment is recommended for acute RSV bronchiolitis [7, 8], and until recently no therapy has been demonstrated to be effective in modulating the long-term outcomes of recurrent wheezing and asthma. According to a recent study, treatment of preterm infants with the monoclonal antibody palivizumab, compared with placebo, was effective in reducing the incidence of RSV-related hospitalization and was associated with fewer wheezing days during the first year of life [9]. However, palivizumab treatment is expensive and requires...
monthly injection. There is a need to identify a target for an affordable pharmacological intervention that may modulate the severity of the acute RSV bronchiolitis, save precious health resources associated with RSV-related hospitalizations, and potentially prevent the development of asthma after RSV bronchiolitis.

Vitamin D status might affect the occurrence or the severity of RSV bronchiolitis, because vitamin D has non-skeletal activities that might directly or indirectly affect bronchiolitis: eg, in utero effects on lung growth and maturation, immune system modulation, and enhancement of immunity to viral infections [10–12]. Moreover, vitamin D deficiency at birth, defined as cord blood vitamin D level below 20 ng/mL, was reported to be a risk factor for RSV lower respiratory tract infections (LRTIs) during the first year of life [13]. Although vitamin D status may alter the overall risk of RSV bronchiolitis, there are limited data on the effect of vitamin D status on the severity of the acute episode of RSV bronchiolitis [14]. This question may be even more important among the subgroup of children with bronchiolitis who require hospital-based care because these patients suffer greater morbidity and are at the highest risk of future asthma [15]. We conducted this study to investigate whether vitamin D deficiency among infants who required hospital-based care for RSV bronchiolitis is associated with the severity of the acute bronchiolitis episode.

MATERIALS AND METHODS

Study Population

The study population included infants who were enrolled from 2009 to 2012 into the RSV Bronchiolitis in Early Life II (RBEL II) prospective cohort study that was established to investigate how specific genetic, biologic, and immunologic characteristics, along with environmental exposures, interact in children who experience severe RSV bronchiolitis early in life and impact the subsequent development of asthma.

All infants that had bronchiolitis that was severe enough to require care at St. Louis Children’s Hospital from 2009 to 2012 were screened to determine whether they met our inclusion criteria (Figure 1). Infants enrolled in the RBEL II study were 12 months of age or younger, had a positive nasopharyngeal swab result confirming infection with RSV, and had physician-documented wheezing during the acute illness. Exclusion criteria were a history of previous wheezing or a diagnosis of asthma, congenital abnormalities of the heart and lung, cystic fibrosis diagnosed in the

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![Figure 1. RSV Bronchiolitis in Early Life (RBEL) II cohort flow diagram. RSV, respiratory syncytial virus; SLCH, St. Louis Children’s Hospital.](image-url)
patient or immediate family, regular use of anti-gastroesophageal reflux medication, bronchodilators, or anti-inflammatory medications, and history of prematurity (<36 weeks). A study coordinator collected detailed information about demographic factors, risk factors for allergy or asthma, and family history of asthma from the child’s parent(s). All infants were enrolled during the winter months, the typical season for RSV bronchiolitis.

During the hospitalization, the infants were treated according to a predefined care-path: the St. Louis Children’s Hospital Bronchiolitis Pathway, a set of orders based on the American Academy of Pediatrics Guidelines for treatment of bronchiolitis [7]. All decisions regarding the treatment during the hospitalization, including the decision to use supplemental O2, and timing of discharge were decided by the primary attending physician, independent of the study.

The study was approved by the Washington University School of Medicine Institutional Review Board. Informed consent was obtained from the parents or guardians.

Outcome Measures
The primary outcome of this study was the duration of hospitalization for RSV bronchiolitis. Secondary outcomes were the lowest oxygen saturation in room air recorded during the hospitalization and the total Bronchiolitis Severity Score (BSS) [16] on the day of admission. Length of stay and the lowest oxygen saturation were measured as previously reported [17]. The BSS [16] is a clinical score that incorporates 4 parameters of bronchiolitis severity: (1) respiratory rate, (2) presence of respiratory distress evident by accessory muscle use, (3) oxygen saturation, and (4) the presence of wheezing. Each of these parameters was measured on a scale of 0 to 3: higher scores represent greater disease severity or lower oxygen saturation. The total BSS score is the sum of these 4 scores and has a scale of 0 to 12.

Although the Institute of Medicine concluded that serum 25-OH-VitD levels of at least 20 ng/mL are sufficient to maintain appropriate bone health [18], there is a lack of consensus as to the optimal serum levels of 25-OH-VitD for conditions other than bone health. In our primary analysis, we investigated the association between 25-OH-VitD level and study outcomes using 25-OH-VitD as a dichotomous value with a cutoff of 20 ng/mL, consistent with a recent study that reported that cord blood 25-OH-VitD below 20 ng/mL is a risk factor for subsequent RSV LRTIs [13]. However, previous asthma studies among older children have detected associations between respiratory outcomes and vitamin D status using serum vitamin D cutoff levels below 30 ng/mL [19–21], or when considering vitamin D as a continuous variable [22]. Due to these uncertainties in determining the appropriate vitamin D cutoffs, along with the absence of previous studies investigating the effect of serum vitamin D levels on clinical outcomes during acute RSV bronchiolitis, we performed additional analyses using 25-OH-VitD as a dichotomous value with a cutoff of 30 ng/mL, and we also considered 25-OH-VitD level as a continuous variable.

Vitamin D Measurements
Baseline serum samples at enrollment, once the infants presented to the hospital with acute bronchiolitis, were available from 145 RBEL II participants. The 25-OH-VitD levels were measured in these serum samples at Heartland Assays, LLC (Ames, IA) using the DiaSorin platform as previously described [23].

Statistical Considerations and Data Analysis
A logarithmic transformation was applied to the measures of immunoglobulin E and eosinophil counts to improve normality of the data. Results are presented as mean ± standard deviation (SD) in untransformed units or percents. Analyses of demographic data among the vitamin D-deficient and nondeficient groups were performed using two-sided t tests for continuous outcomes and the χ² test for categorical outcomes. The associations between vitamin D level as a continuous variable and the study outcomes were investigated using linear regression. Estimates of the mean and standard error (SE) of duration of hospitalization, BSS, and lowest oxygen saturation were obtained from an analysis of covariance model after adjusting for covariates that differed between the vitamin D-deficient and nondeficient groups at a significance level of <.05. A P value of less than .05 was considered statistically significant. Results were analyzed using SAS version 9.3 (SAS Institute Inc.).

RESULTS
Characteristics of Study Populations
Serum samples for vitamin D measurements were available from 145 (87%) of the 167 infants enrolled in the RBEL II cohort. The mean (SD) age of the infants was 4.3 (±2.9) months, 61% were males, 46% were white, and 42% were African American. Other demographic and clinical characteristics of the study population are presented in Table 1. The mean (±SD) duration of hospitalization for RSV bronchiolitis was 72.9 ± 49.8 hours, the mean lowest oxygen saturation was 90.6% ± 5.2%, and the mean BSS was 7.6 ± 2.1.

The 22 infants who did not have serum samples available at baseline were more likely to be female, have a

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Table 1. The mean (±SD) duration of hospitalization for RSV bronchiolitis was 72.9 ± 49.8 hours, the mean lowest oxygen saturation was 90.6% ± 5.2%, and the mean BSS was 7.6 ± 2.1.
mother with asthma, and had a different distribution of season at birth compared with the 145 infants who had serum samples available for vitamin D measurement, (Supplementary Table S1). Other demographics did not differ between these 2 groups.

Baseline Vitamin D Levels Among the Study Population
Median serum 25-OH-VitD (Q1, Q3) was 36.8 (29.8, 42.3) ng/mL. Fourteen infants (9.7%) had serum 25-OH-VitD < 20 ng/mL (ie, vitamin D deficiency), and 23 infants (15.8%) had serum 25-OH-VitD between 20 and 29.9 ng/mL. The distribution of vitamin D levels among the study population is presented in Figure 2.

Associations Between Baseline Participant Characteristics and Baseline Vitamin D Levels
Vitamin D-deficient infants were younger compared with participants with vitamin D levels of 20 ng/mL and above (2.8 [± 2.5] vs 4.5 [± 2.9] months, respectively; $P = .04$). Vitamin D levels were lower among infants who were breast fed at time of enrollment and were higher among infants who reported any formula feeding

### Table 1. Baseline Characteristics of the RBEL II Cohort *

<table>
<thead>
<tr>
<th>All Participants (n = 145)</th>
<th>Baseline Covariates Based on 25-OH-VitD Level Cutoff of 20 ng/mL</th>
<th>Baseline Covariates Based on 25-OH-VitD Level Cutoff of 30 ng/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at enrollment (months)*</td>
<td>Age at enrollment (months)</td>
<td>&lt; 20 ng/mL (n = 14)</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>Gender (male)</td>
<td>60.7%</td>
</tr>
<tr>
<td>Race</td>
<td>Race</td>
<td>42.1%</td>
</tr>
<tr>
<td>African American</td>
<td>White</td>
<td>46.2%</td>
</tr>
<tr>
<td>Other/multiple</td>
<td>Other/multiple</td>
<td>11.7%</td>
</tr>
<tr>
<td>Birth weight (kg)†</td>
<td>Birth weight (kg)</td>
<td>3.3 (0.5)</td>
</tr>
<tr>
<td>Birth length (cm) ‡</td>
<td>Birth length (cm)</td>
<td>50.4 (2.9)</td>
</tr>
<tr>
<td>Length of pregnancy (wks) ‡</td>
<td>Length of pregnancy (wks)</td>
<td>38.6 (1.4)</td>
</tr>
<tr>
<td>Season at Birth</td>
<td>Season at Birth</td>
<td>29 (20.0%)</td>
</tr>
<tr>
<td>Winter (December–February)</td>
<td>Winter (December–February)</td>
<td>31 (21.4%)</td>
</tr>
<tr>
<td>Spring (March–May)</td>
<td>Spring (March–May)</td>
<td>38 (26.2%)</td>
</tr>
<tr>
<td>Summer (June–August)</td>
<td>Summer (June–August)</td>
<td>47 (32.4%)</td>
</tr>
<tr>
<td>Fall (September–November)</td>
<td>Fall (September–November)</td>
<td>13.3%</td>
</tr>
<tr>
<td>Current eczema</td>
<td>Current eczema</td>
<td>23.4%</td>
</tr>
<tr>
<td>Paternal asthma</td>
<td>Paternal asthma</td>
<td>28.8%</td>
</tr>
<tr>
<td>Maternal smoking during pregnancy</td>
<td>Maternal smoking during pregnancy</td>
<td>22.8%</td>
</tr>
<tr>
<td>Total IgE level (IU/mL)†</td>
<td>Total IgE level (IU/mL)</td>
<td>24.1 (95.2)</td>
</tr>
<tr>
<td>Blood eosinophils (%)‡</td>
<td>Blood eosinophils (%)</td>
<td>1.7 (1.8)</td>
</tr>
<tr>
<td>Diet</td>
<td>Diet</td>
<td>85 (58.6)</td>
</tr>
<tr>
<td>Current breast feeding</td>
<td>Current breast feeding</td>
<td>120 (82.8)</td>
</tr>
<tr>
<td>Ever fed with formula</td>
<td>Ever fed with formula</td>
<td>23 (15.9)</td>
</tr>
<tr>
<td>Ever fed with solid food</td>
<td>Ever fed with solid food</td>
<td>23 (15.9)</td>
</tr>
</tbody>
</table>

Abbreviations: Ig, immunoglobulin; RBEL II, RSV Bronchiolitis in Early Life II; SD, standard deviation.
*Data are expressed as proportion of children in each vitamin D range except as noted.
†Data represent the mean (SD) of this covariate.
‡Significance level for differences in means was calculated after logarithmic transformation to improve normality of the data.
Vitamin D levels were not different between infants who consumed solid foods compared with infants who did not consume solid foods (Table 1 and Supplementary Table S2). Other baseline characteristics did not differ between the vitamin D-deficient and nondeficient infants. Once using a 25-OH-VitD cutoff level of 30 ng/mL, birth length and feeding history were the only baseline characteristics that were different between the groups once using a 25-OH-VitD cutoff level of 30 ng/mL. (Table 1).

Clinical Indicators of Acute Bronchiolitis Severity According to Vitamin D Levels

The mean (SE) duration of hospitalization, adjusted for age at enrollment and for formula consumption, did not differ between vitamin D-deficient infants and infants with vitamin D levels ≥20 ng/mL (64.5 [13.9] hours vs 73.8 [4.3] hours; \(P = .53\)). The secondary outcomes of total BSS and the lowest oxygen saturation also did not differ between these 2 groups (Table 2).

Infants with a 25-OH-VitD level <30 ng/mL did not differ in the primary or secondary outcomes compared to those with a 25-OH-VitD level ≥30 ng/mL. (Table 2). Finally, vitamin D level as a continuous variable was not associated with any of the clinical indicators of bronchiolitis severity (Table 3).

**DISCUSSION**

The findings of our study suggest that vitamin D deficiency was infrequent among a cohort of infants hospitalized with RSV bronchiolitis; and when present, vitamin D deficiency was more often seen in younger infants and infants who do not consume infant’s formula. Moreover, among this cohort of patients that required hospital-based care for RSV bronchiolitis, vitamin D status at the time of bronchiolitis was not associated with indicators of acute bronchiolitis severity.

Previous reports have provided mechanistic rationale to support the hypothesis that vitamin D might modulate the occurrence or severity of acute RSV bronchiolitis through its antiviral activities. Vitamin D can augment the innate immune system activity by inducing antimicrobial peptides, mainly cathelicidin in epithelial cells, and by augmenting superoxide generation from monocytes and cytotoxic activity of natural killer cells [24]. Epidemiologic data in children support the biologic plausibility of these mechanistic hypotheses by showing that maternal serum vitamin D levels measured during pregnancy [25] or infant vitamin D levels in cord blood [26, 13] are inversely associated with the risk of respiratory tract infections in infancy. The main difference between our current study and these previous studies [25, 26, 13] is the timing of the vitamin D measurement: our study measured vitamin D at the time of bronchiolitis (which was mandated to occur during the first year of life), whereas most previous studies [26, 13] measured vitamin D in cord blood, which is a reflection of maternal vitamin D status during late pregnancy and subsequently the in utero vitamin D status of the fetus.

### Table 2. Clinical Indicators of Bronchiolitis Severity Based on Baseline Serum Vitamin D Level

<table>
<thead>
<tr>
<th>Vitamin D Level Cutoff</th>
<th>Participants</th>
<th>Clinical Indicators Based on 25-OH-VitD Level</th>
<th>Clinical Indicators Based on 25-OH-VitD Level Cutoff of 30 ng/mL Participants</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20 ng/mL (n = 14)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 20 ng/mL (n = 131)</td>
<td></td>
<td>Duration of hospitalization (hours)</td>
<td>Duration of hospitalization (hours)</td>
<td>.53</td>
</tr>
<tr>
<td></td>
<td></td>
<td>64.5 (13.9)</td>
<td>73.8 (4.3)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lowest oxygen saturation recorded on room air (%)</td>
<td>91.7 (1.5)</td>
<td>.45</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BSS*</td>
<td>7.6 (0.6)</td>
<td>.97</td>
</tr>
<tr>
<td>≥ 30 ng/mL (n = 37)</td>
<td></td>
<td></td>
<td></td>
<td>.72</td>
</tr>
<tr>
<td>≥ 30 ng/mL (n = 108)</td>
<td></td>
<td></td>
<td></td>
<td>.27</td>
</tr>
</tbody>
</table>

*Data were analyzed using a linear regression methodology.

### Table 3. Associations Between Serum Vitamin D Level, Analyzed as a Continuous Variable, and Bronchiolitis Severity

<table>
<thead>
<tr>
<th>Vitamin D Level Cutoff</th>
<th>Participants</th>
<th>Bronchiolitis Severity Score</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted</td>
<td></td>
<td>0.010</td>
<td>.54</td>
</tr>
<tr>
<td>Adjusted for age</td>
<td>0.008</td>
<td>0.022</td>
<td>.54</td>
</tr>
<tr>
<td>Adjusted for birth length</td>
<td>0.009</td>
<td>0.023</td>
<td>.57</td>
</tr>
<tr>
<td>Adjusted for any formula consumption</td>
<td>0.011</td>
<td>0.024</td>
<td>.52</td>
</tr>
</tbody>
</table>

*Data were analyzed using a linear regression methodology.
As suggested by animal models, vitamin D is important for the development of the fetal lungs [27], and therefore it might serve as a protective factor against the development of viral LRTI. However, until recently, only limited data were available on the association between serum vitamin D levels and the severity of the acute bronchiolitis once it has already occurred. Mansbach et al [14] studied 82 infants presenting to the emergency department (ED) with viral bronchiolitis (62 with confirmed RSV infection) and found no association between serum vitamin D levels and subsequent hospitalization for at least 24 hours. Our study’s findings substantially extend the findings of Mansbach et al [14], by providing greater confidence in the absence of significant relationship between vitamin D status and RSV bronchiolitis severity by virtue of its greater sample size, bronchiolitis only due to RSV, and the use of a continuous measure for duration of hospitalization. Together, the results of these 2 studies suggest that, at least among hospitalized children, vitamin D status is not associated with bronchiolitis severity.

Our study has the advantage of including a homogenous cohort consisting of otherwise healthy and not premature infants who experience acute RSV bronchiolitis. Moreover, our research question was investigated among a subgroup of patients that have the most severe disease because all of them required hospital-based care. These children experience the greatest morbidity and have the highest risk for subsequent asthma [15]. However, this group of hospitalized patients has relatively limited variability in their disease severity because hospitalized children are the children with the most severe disease, which represent a minority of all cases of RSV bronchiolitis [28]. Therefore, we cannot exclude the possibility that vitamin D status might be associated with bronchiolitis severity among nonhospitalized patients. However, this result seems unlikely because 2 previous studies that compared vitamin D levels between young children that were hospitalized with viral LRTI and age-matched controls determined that vitamin D status was not a risk factor for hospitalization due to viral LRTI [29, 30].

One potential explanation for the absence of an association between vitamin D status and RSV bronchiolitis severity in our study is the relatively low prevalence of non-sufficient vitamin D levels, because 37 infants (26%) were insufficient (vitamin D below 30 ng/mL) and 14 infants (10%) were vitamin D-deficient (vitamin D below 20 ng/mL). Belderbos et al [13] reported an association between vitamin D deficiency at birth and the risk for RSV LRTIs during the first year of life, among European infants, with an estimated prevalence of vitamin D deficiency at 27%. However, vitamin D levels in his cohort were measured in cord blood, and they were a reflection of maternal vitamin D status. Overall, the prevalence of vitamin D deficiency seems to be age-related, because vitamin D deficiency in the United States is less common among preschool aged children compared with adolescents and young adults [31]. The prevalence of vitamin D deficiency in our study (10%) is consistent with the prevalence of this condition in infants and toddlers in the United States, as demonstrated by a recent study among 380 US children aged 8–24 months that estimated the prevalence of vitamin D deficiency as 12% [32]. This result suggests that vitamin D deficiency alone is not a significant risk factor for the development of severe RSV bronchiolitis.

In addition, a study [14] among US infants presenting to the ED with viral bronchiolitis reported a median (Q1, Q3) vitamin D level of 34 ng/mL (28, 40), which is very comparable to the median vitamin D level (36.8 [29.8, 42.3] ng/mL) documented in our study. The relatively lower prevalence of vitamin D deficiency among infants and toddlers in the United States might be related to routine vitamin D supplementation among this age group as recommended by the American Academy of Pediatrics [33], maternal sources, and to the presence of vitamin D supplements in many foods. We acknowledge that the relatively low prevalence of vitamin D deficiency among our cohort is a potential limitation, because we cannot entirely exclude the unlikely possibility that different results might be noted in a population where the prevalence of vitamin D deficiency is higher.

In summary, our results indicate that, among infants who required hospital-based care for acute RSV bronchiolitis, vitamin D status was not associated with the severity of bronchiolitis. These results need to be confirmed in additional larger cohorts with greater variability of bronchiolitis severity (including hospitalized and nonhospitalized infants). In addition, further studies are needed to determine whether vitamin D status, and its potential association with RSV bronchiolitis, is a risk factor for subsequent respiratory outcomes such as recurrent wheezing and asthma.

Acknowledgments

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Potential conflicts of interest. M. C. was the Primary Investigator of the NHLBI-funded vitamin D add-on therapy that enhances corticosteroid responsiveness in asthma; L. B. B. was Co-Investigator in the NHLBI-funded Vitamin D Antenatal Asthma Reduction Trial. All
authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References