

## Vitamin D Levels and Cardiopulmonary Status in Infants with Acute Bronchiolitis: Tip of the Iceberg?

We read with interest the recent article assessing the association of vitamin D deficiency (VDD) with cardiopulmonary status in infants with acute bronchiolitis [1]. They have concluded that low vitamin D levels were associated with clinical severity and impaired cardiopulmonary status in infants with acute bronchiolitis [1]. We have the following comment on their study [1].

VDD is common in infants with respiratory tract infections and those with respiratory syncytial virus (RSV) bronchiolitis [2]. However, there are many studies in which the association between vitamin D levels and disease severity was not detected [2]. Vo, et al. [2] have suggested that bioavailable 25-OHD deficiency is associated with length of hospital stay and admission to the pediatric intensive care unit (PICU) [2]. Contribution of comorbidities such as age, prematurity, congenital heart disease, chromosomal abnormalities, chronic lung disease, or immunodeficiency to the severity of the infection should also be considered [3]. In particular, age was associated with non-invasive ventilation (NIV) failure, length of hospital stay, and disease severity [3]. We think it would be useful to consider other factors when commenting on the relationship between vitamin D levels and the severity of bronchiolitis.

Another issue we want to draw attention to is that the NIV was used with a high frequency of 25% in this study [1], but the details about the NIV methods are lacking. A meta-analysis of 15 studies [4] showed that high-flow nasal oxygen therapy is beneficial and safe, with similar failure rates with continuous positive airway pressure. Secondly, bi-level positive pressure ventilation has been reported to be associated with longer PICU stay and prolonged ventilation needs [5]. Although NIV is widely used for bronchiolitis, there is no consensus on what the indications are, what the correct method is, what the failure criteria are, and how the weaning should be done.

We feel that further studies are needed to determine the exact role of vitamin D level and cardiorespiratory status in infants with respiratory infection.

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### AUTHORS' REPLY

We thank the readers for their thoughtful comments. We agree that the role of vitamin D as a biomarker for severity in acute bronchiolitis has been previously reported with controversial results. We think the differences in the prevalence of vitamin D deficiency (VDD), and vitamin D level cut-off points used to define VDD across studies could be the main reason for these conflicting results. Thus, the low incidence of VDD in studies showing no correlation between the severity of disease and vitamin D [1,2] is a significant limitation to consider when interpreting their results. Conversely, studies with larger sizes and higher rates of VDD [3,4] had conclusions similar to ours [1]. We also agree with the comment about the relevance of age and prematurity on the severity of acute bronchiolitis. Thus, as a significant limitation, we discussed the possible influence of age and prematurity as confounding factors on our results, which should not be fully considered until further studies determine the exact role of vitamin D in this setting.

The high rate of NIV in our series could be explained by the low median age (1 month) and the high rate of prematurity (20%) in our population, which are apparent risk factors for a need for ventilation in acute bronchiolitis. We used NIV in the presence of respiratory acidosis or moderate-severe respiratory distress. In the meta-analysis cited [5], HFNC was not superior to CPAP in these situations. In addition, it has not shown differences in treatment or intubation failure rates; and it does not analyze the differences between HFNC and BIPAP, which was the modality used in all the children in our series. The more extended stay in the PICU in patients with BIPAP may be due to a longer duration in days of BIPAP and the severity of bronchiolitis since they also found a significant association in the level of pH and pCO<sub>2</sub>, and prematurity as a comorbidity in the BiPAP group [6]. Although there are many studies investigating the role of vitamin D as a risk factor for severe acute bronchiolitis, addition of more data to the literature could help clarify this controversial issue, especially in the association between different cardiac variables and VDD in this setting.

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