

## Vitamin D Deficiency Common in Critically Ill Children

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August 6, 2012 — According to 2 recent studies, two thirds of children admitted to pediatric intensive care units (PICUs) may be deficient in vitamin D, which may make them vulnerable to more severe illness. The studies were published online August 6 in *Pediatrics*.

The [first study](#) was conducted by Kate Madden, MD, an assistant in critical care medicine in the Division of Critical Care Medicine, Department of Anesthesia, Perioperative and Pain Medicine at Children's Hospital Boston and the Department of Anesthesia at Harvard Medical School in Boston, Massachusetts, and colleagues.

Dr. Madden and coauthors analyzed the vitamin D levels of 511 severely or critically ill children who were admitted to the PICU from November 2009 to November 2010 to determine the prevalence of vitamin D deficiency in severely ill children and determine factors that influence admission 25-hydroxy vitamin D (25(OH)D) levels.

Vitamin D deficiency is common in critically ill adults and is associated with sepsis and more severe critical illness, but the associations between vitamin D deficiency and pediatric critical illness have not yet been determined.

The children had 25(OH)D levels analyzed on blood that was taken as soon after PICU admission as possible, either by drawing fresh blood or by testing leftover plasma that was refrigerated in the hospital laboratory. Severity of illness was determined within the first 24 hours by using the Pediatric Risk of Mortality III score.

The median 25(OH)D level of the children studied was 22.5 ng/mL (interquartile range [IQR], 16.4 - 31.3 ng/mL), 71.2% of the patients had insufficient 25 (OH)D (<30 ng/mL), and 40.1% were 25(OH)D deficient (10 - 19.9 ng/mL in 33.1% and <10 ng/mL in 7%).

A total of 13 (2.5%) children died during hospitalization, and the median 25(OH)D level was 19.4 ng/mL (IQR, 16.6 - 31.4 ng/mL).

Serum 25(OH)D levels were considerably lower in the 51 children who had severe septic shock but were not associated with the primary reason for PICU admission. Patients with lower respiratory tract infection had the same median 25(OH)D levels (22.5 ng/mL) as patients without.

Almost half (46.6%; n = 238) of the patients were admitted with life-threatening infections, and 25(OH)D levels were not lower in this group unless they had septic shock (n = 51, 10.0%; median 25(OH)D level, 19.2 ng/mL [IQR, 12.6 - 24.8 ng/mL];  $P = .0008$ ).

In multinomial logistic regression analysis, lower admission 25(OH)D levels were associated with higher illness severity on the Sequential Organ Failure Assessment cardiovascular (CV-SOFA) tool, with a 5 ng/mL decrease in 25(OH)D corresponding to a 1.13-fold increase in odds of placing in the next higher category of CV-SOFA score (95% confidence interval [CI], 1.01 - 1.27;  $P = .03$ ). This relationship continued after adjusting for severe septic shock (OR, 1.16; 95% CI, 1.02 - 1.31;  $P = .02$ ).

Multivariate analysis found a correlation between age and race and vitamin D deficiency, with school-age children and those with dark skin being more likely to have low 25(OH)D levels.

Factors that were protective included vitamin D supplementation, formula intake, and summer season.

"We hypothesize that higher 25(OH)D levels may decrease the severity of critical illness brought on by an overwhelming insult such as infection or injury," the authors write.

"Given the high rate of vitamin D deficiency in critically ill children and the essential role of vitamin D in healthy bone development, we recommend screening critically ill children with risk factors for vitamin D deficiency and identifying effective repletion strategies," the authors write.

### Lower Levels Associated With More Severe Illness

The [second study](#) was conducted by J. Dayre McNally, MD, PhD, a pediatric intensivist in the Department of Pediatrics at Children's Hospital of Eastern Ontario and an associate investigator at Children's Hospital of Eastern Ontario Research Institute in Ottawa, Ontario, Canada, and colleagues.

The researchers conducted a secondary analysis of data collected during a prospective cohort study from 2005 to 2008 in 7 tertiary-care PICUs in Canada (Adrenal Insufficiency in Pediatric Critical Illness Study [AIP]). For this study, data from only 6 centers were studied, as 1 center declined permission.

For the 326 patients, the mean total 25(OH)D (D2 + D3) was 43.2 nmol/L (SD, 19.4). The mean 25(OH)D2 was 3.2 nmol/L (SD, 1.6), and the mean 25(OH)D3 was 40.2 nmol/L (SD, 19.5).

The prevalence of vitamin D deficiency (25(OH)D2 plus 25(OH)D3 < 50 nmol/L) among the children was 69% (95% CI, 64% - 74%). Another 23% (95% CI, 19% - 28%) had a concentration between 50 and 75 nmol/L.

Lower mean 25(OH)D levels were found in patients requiring catecholamine infusion ( $45 \pm 19$  nmol/L vs  $38.5 \pm 16$  nmol/L;  $P = .006$ ) and more than 40 mL/kg fluid bolus on the day of PICU admission ( $44.7 \pm 19.6$  nmol/L vs  $34.5 \pm 18.5$  nmol/L;  $P = .001$ ).

Patients who were mechanically ventilated had lower 25(OH)D levels compared with patients who did not require mechanical ventilation ( $47.2 \pm 19.9$  nmol/L vs  $41.7 \pm 19.1$  nmol/L;  $P = .02$ ).

25(OH)D levels were significantly lower in patients with at least 1 hypocalcemic episode compared with patients with normal or minimally reduced calcium levels ( $51.0 \pm 20.6$  nmol/L vs  $36.6 \pm 15.9$  nmol/L;  $P = .001$ ).

The researchers found no significant relationship between 25(OH)D levels and serum albumin (Spearman correlation coefficient,  $-0.08$ ;  $P = .48$ ). There was a moderate association between albumin and preexisting illness (Spearman correlation coefficient,  $0.57$ ;  $P < .001$ ).

Multivariate regression analysis showed that a 25(OH)D level less than 50 nmol/L was independently associated with a PICU stay of an additional 1.92 days (95% CI, 0.2 - 3.7;  $P = .03$ ) and an increasing illness severity, as measured by the Pediatric Risk of Mortality tool.

"[T]his study provides evidence that critically ill children commonly have 25(OH)D concentrations <50 nmol/L and that lower levels are associated with hypocalcemia, catecholamine need, significant fluid bolus administration, and longer length of stay. Subsequent prospective interventional trials are required to establish whether rapid restoration of vitamin D body stores has an impact on critical illness disease course and outcome," the authors write.

Steven A. Abrams, MD, a professor of pediatrics at Baylor College of Medicine and an attending physician in the Section of Neonatology at Texas Children's Hospital in Houston, and Jorge A. Coss-Bu, MD, an associate professor in the Section of Critical Care Medicine at Baylor College of Medicine and an attending physician at Texas Children's Hospital, commented on the studies in an [accompanying editorial](#).

These data support programs and interventions aimed at preventing vitamin D deficiency, they write, adding that, "at a minimum, comprehensive efforts to ensure that children receive at least the recommended intake of vitamin D (400 IU/day for infants, 600 IU/day for children aged > 1 year) should be developed and emphasized."

They continue, "[T]hese studies move forward and to the front concerns regarding vitamin D status in critically ill children. They do not yet tell us the best way of assessing or treating low serum 25(OH)D levels in a PICU

setting but point us to a program of public health and research on this topic, with clear identification of final outcomes and their clinical significance, focusing on both efficacy and safety of any proposed interventions."

*One study author serves as a consultant for Diasorin Inc. The other authors and editorialists have disclosed no relevant financial relationships.*

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