Low Vitamin D Tied to COVID-19 Severity

Vitamin D deficiency linked with ICU admission, greater mortality

by Nancy Walsh, Contributing Writer, MedPage Today September 12, 2020

Patients hospitalized with COVID-19 who were vitamin D deficient experienced worse outcomes than those with normal levels of the vitamin, a researcher reported.

Low levels of 25-hydroxyvitamin D [25(OH)D] in hospitalized COVID-19 patients were inversely associated with the development of acute respiratory distress syndrome (ARDS) requiring admission to the ICU (OR 1.06, 95% CI 1.01-1.12, P=0.038), according to Luigi Gennari, MD, of the University of Siena in Italy, at the [American Society for Bone and Mineral Research](#) virtual meeting.

Levels of 25(OH)D below 20 ng/mL also were associated with higher mortality among these patients (OR 1.18, 95% CI 1.02-1.37, P=0.029), according to Gennari and colleagues.

"The clinical consequences of infection with the SARS COVID-19 virus vary from benign to fatal," Gennari said. While many patients are asymptomatic, others have mild symptoms, and some have a severe life-threatening disease mainly characterized by interstitial pneumonia that can progress to ARDS and death from respiratory failure, as well as other complications.

Vitamin D is an important regulator of immune function and modulates the inflammatory response to infection. "Indeed, vitamin D through its receptor may be implicated in the regulation of many pathways that seem to be involved in the progression and severity of COVID-19 by turning down the cytokine storm, protecting the integrity of the epithelial barrier, and limiting the prothrombotic state commonly seen in severe COVID-19 cases," he stated.

In addition, vitamin D is an important regulator of the renin-angiotensin system, whose dysregulation has been implicated in the pathogenesis of ARDS.

Several lines of evidence suggest that 25(OH)D deficiency may be a risk factor of severe COVID-19 infection. For instance, certain demographic groups known to be at high risk for vitamin D deficiency such as Blacks, the elderly, nursing home residents, and individuals with obesity or diabetes, are at high risk of COVID-19 infection and mortality. A recent study suggested that patients with inadequate vitamin D levels had nearly double the risk of testing positive for COVID-19.

Previous studies also have shown that low 25(OH)D status is associated with increased risks for respiratory tract infection in general, and that vitamin D supplementation decreases the risk of respiratory tract infections, especially for those with low 25(OH)D levels.

"Italy is generally considered one of the European countries with the highest levels of 25(OH)D deficiency, particularly in the winter. COVID-19 mortality rates have been particularly high in our country but declined in the summer months when vitamin D deficiency is lower," Gennari said.

To examine the potential relationship between levels of 25(OH)D levels and COVID-19 outcomes, Gennari's group enrolled 103 patients with severely symptomatic COVID-19 who were admitted to the San Luca Hospital COVID-19 unit in Milan from March 9 to April 30, 2020. They were compared with 52 individuals with asymptomatic or only mildly symptomatic COVID-19 and 206 age- and sex-matched controls who had undergone measurements of 25(OH)D levels during a routine health check-up. Participants' mean age was 66. Older age, male sex, and severely symptomatic COVID-19 had significantly lower levels of 25(OH)D than those with mild disease or controls.

Vitamin D levels also were inversely associated with interleukin (IL)-6 and C-reactive protein levels, both of which are associated with inflammatory status, and IL-6 has been suggested as a possible marker of COVID-19 severity.

At the time of hospital admission, 25(OH)D levels were lower in the severely symptomatic group, at 18.2 ng/mL, than in the mildly symptomatic group, at 30.3 ng/mL, and in controls, at 25.4 ng/mL (*P*<0.0001 for both comparisons).

Subsequently, 54 of the symptomatic patients were admitted to the ICU because of the development of ARDS. Those patients had lower levels of 25(OH)D, at 14.4 ng/mL, and also had higher IL-6 levels, at 49.6 pg/mL, than patients not requiring admission to the ICU, whose levels were 22.4 ng/mL (*P*=0.0001) and 28.8 pg/mL (*P*=0.016), respectively. They also more often were male and had at least one comorbidity.

A total of 19 patients died, all from ARDS. Compared with the patients who survived, those who died had lower levels of 25(OH)D (13.2 vs 19.3 ng/mL, *P*=0.03) and higher levels of IL-6 (61 vs 34.9 pg/mL, *P*=0.02).

"Interestingly, the inverse association with ICU admission and mortality was independent of IL-6 levels and the presence of major comorbidities," he observed.

"Thus, notwithstanding the limitation of a small sample size, our results support the need for intervention trials aimed at exploring whether vitamin D supplementation may limit the risk of respiratory failure in patients with COVID-19, and suggest that the correction of vitamin D deficiency might be of relevance for reducing the clinical burden during future outbreaks of SARS COVID-19," he concluded.

Disclosures
Gennari disclosed no relevant relationships with industry.

Primary Source
American Society for Bone and Mineral Research
Source Reference: Gennari L, et al "Vitamin D deficiency is independently associated with COVID-19 severity and mortality" ASBMR 2020; Abstract 1023.