

Letter to the Editor

Serum 25-hydroxyvitamin D levels are lower in urban African American subjects with chronic rhinosinusitis*To the Editor:*

In addition to its traditional role in the endocrine system, vitamin D decreases the risk of many chronic illnesses, including cancer, autoimmunity, infection, and cardiovascular disease.¹ This vitamin has also been implicated in the development of atopic diseases, such as asthma, allergic rhinitis, and anaphylaxis.²⁻⁴ Because these diseases share clinical and biologic features with chronic rhinosinusitis (CRS), we sought to determine whether serum vitamin D levels might be associated with CRS.

We measured serum 25(OH)-vitamin D (25[OH]D) levels in our clinical laboratory by using samples from African American and white adults with and without severe CRS (Table I). Subjects were recruited through our institution's otolaryngology clinic located in an urban, tertiary care, academic hospital in Chicago through an ongoing study of the genetics of CRS. We attempted to enroll all subjects meeting entry criteria (see below). The institutional review board approved this study, and informed consent was obtained. Definition of cases met consensus diagnostic criteria, including clinical symptoms, nasal endoscopy, and stage IV disease on computed tomographic analysis graded by using the Harvard criteria (ie, pansinusitis).⁵ Control subjects had normal imaging study results. Data were stratified by factors known to affect serum 25(OH)D, including sex, race, season, and body mass index.⁶ Comparisons of groups were performed by using nonparametric analysis (Kruskal-Wallis test).⁷

We found that white female control subjects had higher serum 25(OH)D levels than African American female control subjects ($P < .018$), and a similar nonsignificant trend between white and African American male subjects was seen, which is consistent with reported variation by ethnicity. There were no significant differences in 25(OH)D levels between white subjects with and without CRS in either sex ($P > .05$ for all).

Levels in African American subjects with CRS were significantly lower than those in race- and sex-matched control subjects (male subjects with CRS, 15.4 ± 2.1 ng/mL; male control subjects, 26 ± 2.6 ng/mL [$P \leq .015$]; female subjects with CRS, 13.5 ± 2.0 ng/mL; female control subjects, 20.8 ± 2.6 ng/mL [$P \leq .018$; Table I). Of note, the mean values for all African American groups were less than accepted normative values (see below).

Samples obtained in June through September (summer) were compared with those obtained in November through April (winter); we eliminated "transition" months for clarity. There was a trend toward lower 25(OH)D levels in the winter in all groups. African American subjects with CRS had significantly lower 25(OH)D levels in the winter compared with those seen in control subjects (male subjects with CRS, 22.3 ± 3.3 ng/mL; male control subjects, 26.8 ± 4 ng/mL [$P \leq .05$]; female subjects with CRS, 8.5 ± 0.96 ng/mL; female control subjects, 17.4 ± 2.5 ng/mL [$P \leq .006$]; Fig 1); there were similar trends in summer months, although these did not meet statistical significance (Fig 1). However, it should be noted that the numbers in some of the comparisons by season were not robust. There were no

TABLE I. Age, race, sex, and serum vitamin D levels

	Age (y)	BMI (kg/m ²)	Serum 25(OH)D (ng/mL)
White subjects			
Female			
CRS (n = 19)	53 $\pm$ 3.4	28 $\pm$ 1.3	30.1 $\pm$ 2.4
Control (n = 16)	42.3 $\pm$ 3.7	28 $\pm$ 1.5	30.8 $\pm$ 3.7
P value	.037	.942	.728
Male			
CRS (n = 37)	49 $\pm$ 2	28 $\pm$ 0.74	40.2 $\pm$ 2.3
Control (n = 17)	54 $\pm$ 4	28 $\pm$ 1.6	29.4 $\pm$ 2.3
P value	.27	.45	.904
African American subjects			
Female			
CRS (n = 23)	50 $\pm$ 2.9	31 $\pm$ 1.1	13.5 $\pm$ 2.0
Control (n = 28)	46 $\pm$ 3.3	31 $\pm$ 1.0	20.8 $\pm$ 2.6
P value	.25	.77	.018
Male			
CRS (n = 7)	55 $\pm$ 6.7	34 $\pm$ 4.9	15.4 $\pm$ 2.1
Control (n = 7)	60 $\pm$ 4.6	25 $\pm$ 1.4	26 $\pm$ 2.6
P value	.56	.064	.015

BMI, Body mass index.

Data are presented as means $\pm$ SEMs.

differences between white subjects with CRS and control subjects ($P > .05$ for all). Demographic factors were similar across comparisons (age and body mass index), except white female subjects with CRS were older than control subjects (53 ± 3.4 vs 42 ± 3.7 years, $P \leq .037$; Table I).

The pathogenesis of CRS is not understood. However, there is ample evidence that chronic inflammation is a histopathologic finding in these patients, often similar to that seen in allergic rhinitis and asthma, 2 diseases in which recent evidence supports a role for vitamin D. Nutritional studies in pregnancy indicate that increasing maternal consumption of vitamin D decreases the risk of asthma,³ suggesting that *in utero* exposure might create a protective program for the developing immune system. These and other data support the role of vitamin D in the development of asthma.⁸ Anaphylaxis, measured in proxy based on prescription of Epipens (Dey Laboratories, Napa, Calif), varies with geographic latitude, with higher levels found in areas with less sun exposure.⁹ The prevalence of allergic rhinitis was associated with serum 25(OH)D levels in a population database study.⁴ Because CRS is known to be associated with asthma and atopy and has similar inflammatory cellular profiles, these studies are consistent with a role for vitamin D in chronic sinus disease.

Vitamin D is also known to have a number of immunologic effects, including those on T cells, dendritic cells, and macrophages.^{10,11} CRS is characterized by severe mucosal inflammation, and thus deficiency might lead to an increase in inflammation, as seen in CRS. Indeed, administration of vitamin D to subjects with steroid-resistant asthma has been reported to enhance subsequent steroid responsiveness, a finding with implications for CRS, a disease in which steroids are an important therapy.¹² The mechanism might be related to the ability of vitamin D to promote IL-10 production by regulatory T cells, to regulate glucocorticoid receptor expression, or both.¹² Deficits

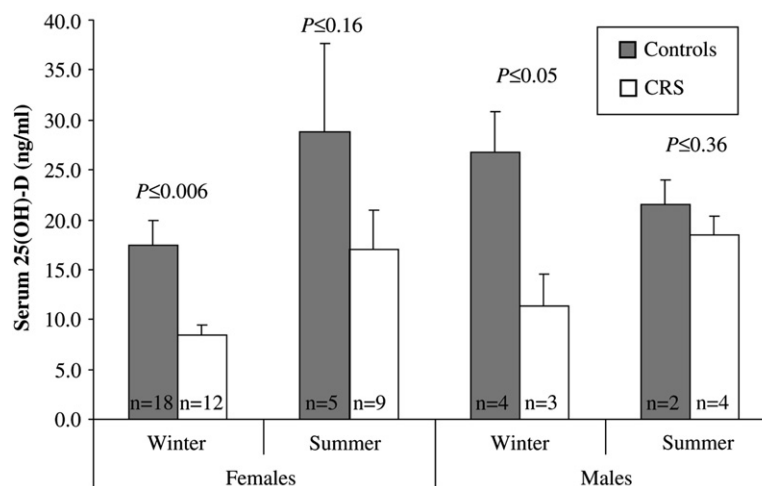


FIG 1. Effect of season on mean serum vitamin D levels in urban African Americans with CRS and control subjects. Summer was defined as June through September, and winter was defined as November through April, corresponding to seasons in Chicago. Data are presented as means $\pm$ SEMs.

in these pathways might partially explain decreased checks on immune responses, allowing for the abundant inflammation seen in CRS.

Some have speculated that lower 25(OH)D levels might be associated with increased susceptibility to viral infections, such as influenza. This suggestion is consistent with the clinical observation that rhinosinusitis exacerbations are more prevalent in the winter and are often virally induced. Thus deficiency of vitamin D in the winter months might partially account for the observed clinical worsening of CRS symptoms during this season, and this supports the role of vitamin D in the pathogenesis of this disease.

Although there are no carefully controlled studies of the epidemiology of CRS including race, sex, or geographic differences, analysis of International Classification of Diseases, Ninth Revision, codes in Olmsted County, Minnesota, revealed that 67.7% of patients given diagnoses of CRS were female in 2000.¹³ Minnesota is located in a northern latitude, and therefore these findings are consistent with other data relating sun exposure and vitamin D levels to atopic disease. Aging has been noted to affect serum vitamin D levels,¹⁴ although we found no age differences between groups in our African American subjects that would affect our results.

Our results suggest an ethnic difference in CRS disease profile. Two factors that might affect our results include small sample size and location of recruitment (outpatient clinic at an urban academic medical center vs population-based recruitment). It should be noted that a reference range for normal serum 25(OH)D levels is controversial; hypovitaminosis D is generally accepted as less than 30 ng/mL or, alternatively, a level that results in an increased parathyroid hormone level, testing of which was cost prohibitive for this study. All of our African American subjects showed levels markedly less than this threshold, an observation with important implications for a variety of diseases. Because we only examined patients with severe disease, we do not know whether serum 25(OH)D levels correlate with CRS disease severity or clinical symptoms. Further study of this phenomenon might provide novel hypotheses for the development of CRS and, perhaps, ideas for new therapeutic interventions.

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