

High Prevalence of Vitamin D Deficiency among Inner-City African American Youth with Asthma in Washington, DC

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Objective The goal of this study was to examine the prevalence of vitamin D insufficiency and deficiency among urban African-American (AA) youth with asthma compared with control subjects without asthma.

Study design A cross-sectional case-control study was conducted at an urban pediatric medical center. Total 25-hydroxyvitamin D insufficiency (<30 ng/mL) and deficiency (<20 ng/mL) were assessed in urban self-reported AA patients, aged 6 to 20 years, with (n = 92) and without (n = 21) physician-diagnosed asthma.

Results Blood samples were available for 85 (92%) cases. The prevalence of vitamin D insufficiency and deficiency were significantly greater among cases than control subjects (73/85 [86%] vs 4/21 [19%], adjusted odds ratio = 42 [95% confidence interval: 4.4 to 399] for insufficiency and 46/85 [54%] vs 1/21 [5%], adjusted odds ratio = 20 [95% confidence interval: 1.4 to 272] for deficiency).

Conclusions Most of this sample of urban AA youth with persistent asthma were vitamin D deficient or insufficient. Given the emerging associations between low vitamin D levels and asthma, strong consideration should be given to routine vitamin D testing in urban AA youth, particularly those with asthma. (*J Pediatr* 2010; ■: ■-■).

Asthma has become considerably more prevalent and severe in the United States during the last 40 years for reasons that are not clear.^{1,2} Epidemiologic data suggest a possible inverse association between maternal intake of vitamin D during pregnancy and risk of childhood wheezing/asthma in offspring.³⁻⁵ Other studies, however, suggest that excessive intake of vitamin D may be a cause of both asthma and other atopic disorders.⁶ Either way, there is emerging evidence that low vitamin D levels are associated with more respiratory infections, especially among patients with asthma,⁷ and with increased asthma severity.⁸

Vitamin D deficiency is more common among African American (AA) individuals,⁹ especially those from urban environments¹⁰ or with obesity.¹¹ Similar epidemiologic patterns exist among youth with asthma. For example, asthma affects 83 per 1000 US children overall; however, AA youth are disproportionately affected, with a rate of 105 per 1000.¹² This population also has among the highest asthma-related morbidity and mortality rates of any U.S. racial/ethnic group.¹³

Herein, we examine the prevalence of vitamin D insufficiency and deficiency among urban AA youth with asthma compared with control subjects without asthma. We hypothesized that those with asthma would have significantly lower levels of vitamin D than those without asthma.

Methods

We conducted a cross-sectional case-control study between April 2008 and June 2009 at Children's National Medical Center (CNMC), an urban pediatric medical center in Washington, DC. All cases and control subjects were studied in the CNMC General Clinical Research Center. This study was approved by the CNMC Institutional Review Board. All participants or their guardians provided informed consent and assent.

The Asthma Severity Modifying Polymorphisms (AsthMaP) Project based at CNMC provided the case data and samples for this study. AsthMaP is a single-center cross-sectional study designed to find associations among urban environments, genetics, and asthma. AsthMaP consists of a predominantly AA convenience sample of otherwise healthy children aged 6 to 20 years, inclusive, with physician-diagnosed asthma for greater than 1 year. The control subjects were

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AA	African American
AsthMaP	Asthma Severity Modifying Polymorphisms
IQR	Interquartile range
OR	Odds ratio
SE	Standard error of the mean

made up of a convenience sample of healthy urban AA children between the ages of 6 and 9 years, inclusive, with no history of asthma enrolled in an urban bone health study in our institution. Although younger, this control group was selected for its similarity to the cases (eg, same local population, same enrollment sites, and similar prevalence of obesity). None of the case or control children studied were receiving vitamin D supplementation.

25-Hydroxyvitamin D Measurement

Circulating levels of 25-hydroxyvitamin D are considered the most reliable measure of overall vitamin D status.¹⁴ A direct enzyme-linked immunosorbent assay was performed on plasma (from cases) or serum (from control subjects) with the IDS 25-Hydroxy Vitamin D Direct EIA kit (Immunodiagnostic Systems Ltd., Fountain Hills, Arizona). This assay has been shown to reliably measure both 25-hydroxyvitamin D isoforms (ie, D₂ and D₃).¹⁵

Statistical Analyses

Total 25-hydroxyvitamin D insufficiency and deficiency were defined as levels <30 ng/mL (<75 nmol/L)^{16,17} and <20 ng/mL (<50 nmol/L),¹⁸ respectively. All means are reported with standard errors of the mean (SE) and medians with an interquartile range (IQR). Differences in descriptive statistics and frequencies were tested with Student's *t* tests and χ^2 testing. Two-tailed *P* values $\leq .05$ were considered significant.

Case-control associations were determined for vitamin D (insufficiency, deficiency, and absolute levels) by multinomial logistic regression analysis. Where noted, odds ratios (OR) and *P* values were corrected for age, sex, body mass index (BMI) percentile, and season of sampling. All statistical tests were performed with SPSS Statistics 17.0 (SPSS Inc., Chicago, Illinois).

Results

Cases

At the time of these analyses, there were 92 AA youth studied in AsthMaP. Of those, 58 (63%) were male, and the mean (SE) age was 11.1 (0.4) years. The mean BMI percentile for age was 69.³ A total of 83 of 92 (90%) had persistent asthma by National Institutes of Health, National Asthma Education and Prevention Program criteria.¹⁹ A detailed description of measured asthma phenotypes in these cases can be found in the [Table](#). Notable phenotypic data included a mean fractional excretion of nitric oxide = 41.5 (4.7), mean serum immunoglobulin E = 543 (98.6) IU/mL, and blood eosinophilia = 5.3% (0.4%).

Control Subjects

When compared with the cases, the control cohort (*n* = 21) had fewer males (38%; *P* = .05) and a lower mean age of 7 (0.3) years (*P* < .001). The mean BMI percentile of 60 (8) was not significantly different from that of the cases ([Table](#)).

Table. Characteristics of cases and control subjects

Variable	Cases (<i>n</i> = 92)	Control subjects (<i>n</i> = 21)	<i>P</i> value
Sex, % male	63	38.1	.05
Age, yr (SE)	11.1 (0.4)	7 (0.3)	<.001
Body mass index percentile (SE)	69 (3)	60 (8)	.22
NAEPP severity level, %			
1 - Intermittent	9		
2 - Mild persistent	23		
3 - Moderate persistent	35		
4 - Severe persistent	33		
FE _{NO} , ppb (SE)	41.5 (4.7)		
FEV ₁ change with bronchodilator, mean (SE)	9.2 (1.1)		
Post-bronchodilator FEV ₁ , mean (SE)	91.8 (1.7)		
Serum IgE, IU/mL (SE)	543 (98.6)		
Blood eosinophils, %	5.3 (0.4)		
One or more positive allergen skin prick test results	38%		

NAEPP, National Asthma Education and Prevention Program; FE_{NO}, fractional excretion of nitric oxide; FEV₁, forced expiratory volume in 1 second.

Vitamin D Insufficiency and Deficiency

Of the 85 (92%) cases with blood samples available for vitamin D testing, 73 (86%) had insufficient vitamin D levels (<30 ng/mL), and 46 of 85 (54%) had deficient levels (<20 ng/mL) ([Figure 1](#)). A typical pattern of seasonal variation in vitamin D levels can be seen in [Figure 2](#), when levels are lowest among the samples collected during the Washington, DC, winter (ie, December through February) and highest during the summer (ie, June through August) (*P* = .005). Notably, all of the samples collected during the winter (13 of 13) were in the insufficient range, with 11 (85%) in the deficient range.

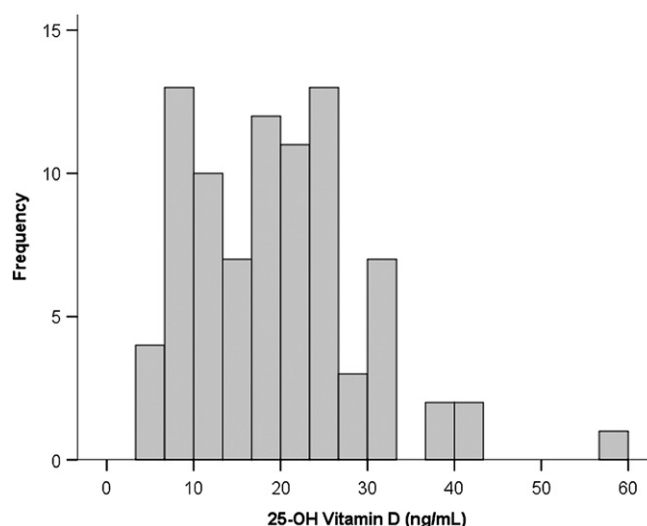


Figure 1. Histogram of plasma vitamin D levels among urban African American youth with asthma. Of the 85 children represented in this graph, 73 (86%) had insufficient vitamin D levels (<30 ng/mL) including 46 (54% of the cohort) with deficient levels (<20 ng/mL).

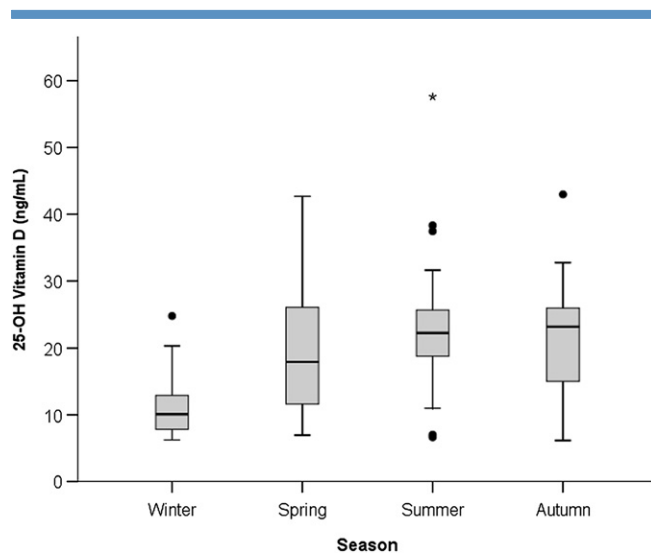


Figure 2. Seasonal variation in plasma vitamin D levels among urban African American youth with asthma. Seasons in Washington, DC, are denoted as winter (December through February), spring (March through May), summer (June through August), and autumn (September through November). Data are presented as medians (*black bars*) and interquartile ranges (*gray boxes*) ($P = .005$ by analysis of variance).

After adjusting for age, sex, BMI percentile, and season of sampling, the median vitamin D level of those with asthma (18.5 [IQR: 11.3, 25.1]) was significantly lower than that of the control subjects without asthma (40.4 [IQR: 34.6, 49.5], $P = .002$). Furthermore, the prevalence of vitamin D insufficiency was significantly greater among cases than control subjects (73 of 85 [86%] vs 4 of 21 [19%], adjusted odds ratio [OR] = 42 [95% confidence interval {95% CI}: 4.4 to 399]). A similar association was observed for vitamin D deficiency: 46 of 85 (54%) vs 1 of 21 (5%), adjusted OR = 20 (95% CI: 1.4 to 272).

Subgroup analysis was undertaken for all children 9 years old and younger to explore potential confounding caused by the age difference between the cases and control subjects. There were 29 cases that met this age criterion in addition to all 21 control subjects. With identical methods as used in the overall analyses, the subgroup analysis results were similar to those for the overall cohort: Median vitamin D level Cases vs. Control subjects = 23.1 (IQR: 18.0, 26.3) versus 40.4 (IQR: 34.6, 49.5), $P = .026$; prevalence of vitamin D insufficiency Cases vs. Control subjects = 24 of 29 (83%) versus 4 of 21 (19%), adjusted OR = 65 (95% CI: 3.9 to 1090); vitamin D deficiency Cases vs. Control subjects = 10 of 29 (35%) versus 1 of 21 (5%), adjusted OR = 41 (95% CI: 1.6 to 1059).

Discussion

Most of this sample of urban AA youth with persistent asthma in Washington, DC, were vitamin D deficient or insufficient. However, vitamin D deficiency has been docu-

mented in many populations around the world regardless of sun exposure.^{20,21}

Vitamin D deficiency is more common in AA individuals than in other races.^{11,20,22} One study of preadolescent AA children in the Pittsburgh area found that 71% had vitamin D levels below 30 ng/mL during the winter and early spring, including almost 50% with levels below 20 ng/mL.²³ There are multiple factors that contribute to this, including dark skin,²⁴ low vitamin D intake,^{25,26} urban environments,¹⁰ and high rates of poverty²⁷ and obesity.¹¹ In addition, latitude is an important consideration. The effect of the relatively northern latitude of Washington, DC, can be seen in the seasonal variation in vitamin D levels among our cases (ie, levels lowest during winter months). As expected, the overall distribution of vitamin D levels among our asthma cases was considerably lower than that of a recently reported Costa Rican (ie, equatorial) cohort of children with asthma in which only 28% of levels were <30 ng/mL.⁸

Traditionally, the principal role of vitamin D was believed to be regulation of calcium and phosphorus homeostasis and bone formation and resorption. More recently, vitamin D has been implicated in wound healing and immunomodulation.^{28,29} In fact, vitamin D deficiency has been linked to a variety of non-bone-related diseases, including cancer, depression, and autoimmune inflammatory states.³⁰⁻³³ More recently, epidemiologic data show protective associations between maternal intake of vitamin D during pregnancy and risk of childhood wheeze,^{3,4} asthma, and allergic rhinitis.⁵ An inverse association between vitamin D and susceptibility to respiratory viruses is strongly suspected^{7,34} and may underlie the recent observation that higher levels of vitamin D are associated with less risk of asthma-related hospitalizations.⁸ Nevertheless, the role of vitamin D in airway inflammatory diseases such as asthma remains unclear.^{4,6}

The normal circulating vitamin D levels used by clinical laboratories were derived from healthy population distributions with the purpose of sustaining bone health.³⁵ These levels are likely lower than optimal levels because of sun deprivation in most northern populations.³⁶ Authoritative groups disagree on blood levels that define insufficiency with respect to linear growth and bone mass. Data to determine sufficient levels for lung health and other outcomes are lacking. As a result, we have analyzed our vitamin D levels with both definitions of vitamin D deficiency and insufficiency,^{16,17,37} as well as a continuous variable.

Our study may be limited by the comparability of case and control vitamin D levels in 2 ways. First, because only plasma or serum was available for cases and control subjects, respectively, we could not compare identical sample types. However, simultaneous plasma and serum 25-hydroxyvitamin D levels measured by a similar chemiluminescent assay were reported to be equivalent.³⁸ Second, there was the possibility of confounding because of the age difference between the case and control cohorts. This was not supported by a subgroup analysis in the youngest children (≤ 9 years) that showed similar results to the findings in the complete groups. Additionally, the generalizability of our control data may be questioned because

the median 25-hydroxyvitamin D level of the control subjects was slightly more than 40 ng/mL. This is higher than that reported for a nationally-representative sample of similarly-aged AA children whose levels were predominantly between 10 and 30 ng/mL.³⁹ It is unclear why this difference exists.

Despite finding statistically significant results, our study was limited by small sample sizes, which likely account for the large confidence intervals reported. In addition, this was a cross-sectional analysis so no conclusions regarding causation can be drawn. Furthermore, the small number of cases and tight vitamin D level distribution resulted in insufficient power to detect statistically significant associations between vitamin D levels and asthma severity. Therefore it remains unclear whether the low vitamin D levels are a contributing factor to asthma or a result of having asthma (eg, children with asthma may be outside less frequently than healthy children). Clinical trials of vitamin D supplementation among urban AA youth with asthma that control for confounding factors such as adiposity, physical activity, ultraviolet exposure, and baseline vitamin D status would help clarify this issue.

The public health implications of very low vitamin D levels among urban AA youth with asthma extend beyond traditional bone health associations and the possible indication of poor overall nutrition. Emerging associations between low vitamin D levels and asthma, obesity, and immunodeficiency necessitate strong consideration for routine vitamin D testing in urban AA youth, particularly those with asthma. ■

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