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Winter birth in inner city asthmatic children is associated with increased food allergen sensitization risk

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To the Editor

Food allergies affect as many as 1 in 13 children in the US, (1) and estimates suggest the prevalence is increasing (2). Understanding factors which influence the development of food allergy is a particular area of interest with theories including timing of food introduction, season of birth, environmental exposures, and both excess and deficiency of vitamin D (3). Season of birth may influence the development of food allergy by several mechanisms, including infectious exposures, indoor allergen exposure, and vitamin D status during the first year of life. Vitamin D has been postulated to have a role in the allergic response primarily by means of inhibition of the inflammatory response of innate immune cells (4).

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Using previously collected serum samples and historical information from an Inner City Asthma study (5), we sought to uncover the potential role of season of birth, and because of the capability of measuring vitamin D status in the population, the potential influence of serum vitamin D on the development of food allergen sensitization in an inner city asthmatic cohort.

Four hundred twenty-four samples from the NIH-National Cooperative Inner-City Asthma Study (NCICAS) (5) were available for analysis of serum 25-hydroxyvitamin D (25[OH]D) levels.

Vitamin D was characterized as both a continuous variable and as a dichotomous variable using 20 ng/ml as a cut-off based on the distribution of vitamin D within the population. The Pearson's χ^2 -test was used for comparison of categorical data and Kruskal–Wallis for testing between quantitative and categorical data: e.g. food and environmental allergen sensitization. The relationship between food allergen sensitization and season of birth (winter – December, January, February; spring – March, April, May; summer – June, July, August; fall – September, October, November) was also examined. Season of birth was analyzed as a proxy for vitamin D levels in the first year of life (6). Because of known differences in vitamin D status and race (7), analyses were performed on the African American portion of the population since the overwhelming majority of our population was African American (n=340, Table 1). Statistical analyses were performed using R (R core Team (2013). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria).

This inner-city asthmatic population, the overwhelming majority of which were from Northern latitudes (96%), was 64% male, with a median age of 6 years (Table 1); 82% of individuals were African American and 13% Hispanic. Participants were sensitized to foods and select environmental allergens, as shown in Online Repository Table 1.

No significant relationship was detected between vitamin D status and food allergen sensitization, environmental allergen sensitization (Online Repository Table 1), environmental allergen exposure, or likelihood of clinically relevant food allergy based on established predictive values for allergic reactivity to milk, egg or peanut (data not included). A trend towards significance was noted for egg sensitization and vitamin D status ($p=0.07$, online repository Table 1), although we do not have an explanation for this trend. In models adjusting for the current Vitamin D level, a significant relationship was detected between winter birth and increased likelihood of sensitization to egg white, peanut, or soy and a trend toward significance for wheat sensitization ($p=0.06$) (Figure 1). Data was also analyzed adjusting for time of year when the blood sample was drawn, and no changes in results were observed (data not included).

Investigators have reported various associations between food allergen sensitization and either fall or winter birth. Keet, et al. recently reported a strong relationship between fall birth and an increased likelihood of developing food allergy in a Caucasian cohort of children from the NHANES database (6), and Mullins and colleagues have shown significantly higher rates of food allergy in Australian children born in fall/winter compared

to spring/summer (8). We are the first to report a positive correlation between winter birth and sensitization to egg, peanut, and soy in a predominantly African American, inner-city population.

A common hypothesis linking season of birth with the development of allergen sensitization implies vitamin D deficiency in a neonate may be responsible (9). Season of birth may impact vitamin D status during infancy, a period of time when the developing immune system may be particularly susceptible to the acquisition of allergen sensitivities. One limitation of our analysis is that samples in our cohort were taken in later childhood, after sensitization had likely occurred in the majority of individuals, and thus current vitamin D status may not have a bearing on pre-existing sensitivities. Thus we used season of birth as a proxy for vitamin D status in the first year of life which has previously been shown to be reflective of seasonal associations with food allergy (6), though this is clearly not a precise measurement. In addition to the effect of season of birth on vitamin D status, one must also consider its effects on infectious exposures (e.g. winter viruses) and indoor allergen exposures, factors we were not able to measure in the first year of life in our cohort.

Another limitation to the interpretability of vitamin D status and food allergen sensitization in our cohort may be that the majority of individuals were either vitamin D deficient or insufficient at the time of serum acquisition (online repository Figure 1) which limits interpretability based on the lack of normal controls within the population. However, we also saw no relationship of food sensitivity to Vitamin D levels when analyzed as a continuous variable (data not shown).

Our data suggests an important role between season of birth and the development of food allergen sensitization. In addition to vitamin D status, other factors may influence the development of allergen sensitivity for an infant born during winter, including exposure to winter viruses, global geographic location and indoor allergen exposure. Additional considerations during the first year of life include the influences of, breastfeeding and Caesarian birth, factors we were not able to analyze in our sample. Given the lack of food allergy history in our population and variability in vitamin D levels with other ethnicities, we caution against drawing firm conclusions with regards to the presence of clinical reactivity and vitamin D status in other ethnicities; however, this data is suggestive of a relationship which warrants further investigation. Future epidemiologic studies should prospectively measure numerous factors, including vitamin D status and the development of allergy in a diverse population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Association between Specific IgE values and season of birth for African-American participants. Each bar represents the geometric mean and vertical lines the standard error of the mean.

Table 1

Population Characteristics

	N=427
Gender: Male	64% (270)
Race: African American	82% (340)
Hispanic	13% (54)
Other	5% (21)
Age (yrs.):	6 [5 – 8]
Site: Boston	43%
Bronx	43%
Chicago	9%
Others	4%
BMI (kg/m ²) [†]	16.7 [15.5 – 18.6]
Season: Fall	25%
Winter	25%
Spring	25%
Summer	25%
25-hydroxyvitamin D (ng/mL)	18.0 [12.9 – 23.2]

[†] BMI stands for Body Mass Index

Values are percentages or medians with [interquartile Ranges]

Numbers after percents are frequencies