HHS Public Access

Author manuscript

Pediatr Allergy Immunol. Author manuscript; available in PMC 2022 February 11.

Published in final edited form as:

Pediatr Allergy Immunol. 2020 August ; 31(6): 695–699. doi:10.1111/pai.13241.

Associations of blood lead levels with asthma and blood eosinophils in US children

Cheryl R. Cornwell[1,2], **Kathryn B. Egan**[1], **Hatice S. Zahran**[3], **Maria C. Mirabelli**[3], **Joy Hsu**[3], **Ginger L. Chew**[1]

[1]Lead Poisoning Prevention and Environmental Health Tracking Branch, Division of Environmental Health Science and Practice, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, Georgia

[2]Oak Ridge Institute for Science and Education, Oak Ridge, Tennessee

[3]Asthma and Community Health Branch, Division of Environmental Health Science and Practice, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, Georgia

To the Editor,

US children are exposed to lead through lead-based paint, through lead-contaminated dust in older homes, and through contaminated water, air, soil, or consumer and imported products.1,2 Approximately 24 million housing units have one or more lead-based paint hazards, including 3.6 million homes with children aged ≤ 6 years.1 Epidemiologic studies have reported positive associations between lead and elevated immunoglobulin E (IgE) in children3-5; IgE is often associated with allergic asthma.6 Based on these findings, lead exposure may be a risk factor for childhood asthma. Several analyses have examined the relationship between lead and asthma in children, with inconsistent results; some reported positive associations of blood lead level (BLL) with asthma,4,7 and others observed no association.5,8 Previous studies have documented effects of lead exposure on inflammatory responses and oxidative stress as possible mechanisms for an effect of lead on asthma development.9

We investigated how BLL was related to current asthma and blood eosinophilia among children aged 1-11 years. We included eosinophils, a primary component of TH2 inflammation and an IgE-mediated allergic phenotype in many children with asthma.10 We used data from the 2001-2016 National Health and Nutritional Examination Surveys (NHANESs), nationally representative samples of the resident civilian non-institutionalized

Correspondence Cheryl Cornwell, Centers for Disease Control and Prevention, MS S106-6, Rm 06011, 4770 Buford Hwy NE, Atlanta, GA, 30341, USA. idh3@cdc.gov.

CONFLICTS OF INTEREST

The authors report no conflicts of interest.

ETHICAL APPROVAL AND INFORMED CONSENT

NHANES data collection is approved by the National Center for Health Statistics Research Ethics Review Board.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

US population.11 NHANES data collection is approved by the National Center for Health Statistics Research Ethics Review Board.

Blood lead samples were collected by trained phlebotomists using venipuncture.12 Elevated BLL was defined as BLL ≥ 5 μg/dL. BLL quartiles were also analyzed. Current asthma status was self-reported from the questions5 "Has a doctor or other health professional ever told you that [the participant] has asthma?" and "Does [the participant] still have asthma?" Blood eosinophil count was dichotomized as <500 cells/μL (no eosinophilia) versus ≥500 cells/μL (eosinophilia).

We assessed associations between each dichotomous outcome (ie, current asthma or eosinophilia) and BLL (BLL ≥ 5 μg/dL and BLL quartiles) using multivariable logistic regression models. Also, we assessed the association between eosinophils and BLL as continuous measurements using a multivariable linear regression model. All models were adjusted for sex, age group (1-5 and 6-11 years), race/ethnicity (non-Hispanic black, non-Hispanic white, Mexican American, and other), health insurance status (Medicaid, other insurance, and no coverage), season of interview (May-October and November-April), poverty income ratio (PIR) (<1.3 and ≥ 1.3), presence of household smoker, and NHANES cycle. We accounted for NHANES complex survey design in all analyses by incorporating appropriate weights, strata, and cluster.11 All statistical analyses were conducted in SAS-callable SUDAAN (RTI International, Research Triangle Park, NC, USA).

We conducted subanalyses of the association of BLL with asthma and eosinophilia stratified by age groups. We also stratified by the presence of household smoker. Our supplemental analysis assessed the association between BLL and "asthma with peripheral eosinophilia" (APE, defined as having both current asthma and blood eosinophilia) and non-APE (asthma without blood eosinophilia). Furthermore, we conducted a sensitivity analysis for missing BLL. In our study population, young children were more likely to be missing a BLL measurement. We used the WTADJUST procedure in SAS-callable SUDAAN to assess whether reweighting to adjust for item non-response would affect our results.

There were 14 751 children aged 1-11 years with a BLL measurement in NHANES from 2001 to 2016 (Table 1). Descriptive statistics (eg, geometric mean) and subanalyses are shown in Tables S1-S5. The adjusted prevalence ratio (aPR) estimate for BLL ≥ 5 μg/dL with current asthma (aPR = 1.09; 95% CI = 0.76-1.59) was not statistically significant (Table 2). Similarly, there was no association between current asthma, APE, and non-APE when BLL was modeled as quartiles (first quartile as referent; Tables 2 and S5). BLL in the third and fourth quartiles was associated with eosinophilia (aPR_{Q3} = 1.21; 95% CI = 1.02-1.44; aPR_{Q4} = 1.39; 95% CI = 1.15-1.68). We also observed a positive association between continuous BLL and eosinophil count (β = 0.01; 95% CI = 0.002-0.01); every 1 μg/dL increase in blood lead corresponded to a 0.01-unit increase in eosinophils (1000 cells/μL), controlling for other covariates.

We found no associations of BLL with current asthma or eosinophilia in analyses stratified by age groups of younger (1-5 years) and older (6-11 years) children (Table 3). When evaluating smaller age strata (Table S3), BLL was associated with asthma only among

children 1-2 years with a BLL in the second quartile. BLL was also associated with eosinophilia among children 6-8 and 9-11 years in the highest BLL quartile. There was no association between BLL and asthma among households with no smoker, and an elevated, but non-statistically significant, association among households with a smoker (aPR = 1.45; 95% CI = 0.89-2.36) for the highest BLL quartile (Table S4). Eosinophilia was more prevalent among children with BLL in the highest quartiles among both households with and without a smoker.

In this nationally representative sample, we investigated whether BLL was associated with current asthma or blood eosinophilia in children aged 1-11 years participating in NHANES from 2001 to 2016. Overall, no association was observed between BLL and current asthma. However, BLL in the highest quartiles was associated with eosinophilia and we found a positive association between continuous BLL and eosinophil count. Consistent with our finding of an association between BLL and eosinophils, experimental studies have shown lead exposure can promote TH2 inflammatory responses associated with allergic diseases.9,13

We did not observe an association between BLL and asthma. BLL is a marker of lead exposure from the past few months. Therefore, children with current asthma may have had past remote lead exposures that were not detected through NHANES's cross-sectional design. Among previous US studies on BLL and asthma, several have similarly reported no associations.5,8 A cohort study of young children (n = 4634) found no association between BLL ≥ 5 μg/dL or BLL ≥ 10 μg/dL and asthma for black children, and an elevated, but non-statistically significant, association among white children.8 This study showed black children had a higher risk of asthma regardless of BLL than white children with a BLL ≥ 5 μg/dL. Unlike our findings, a few studies, primarily from non-US populations, have reported positive associations between pediatric BLL and asthma.4,7,14 International variation in lead exposure sources and levels could explain differences between these studies and ours. Few studies exist on BLL and eosinophils. An Egyptian study found children with a BLL ≥ 10 μg/dL had a higher frequency of eosinophilia, total IgE, and increased asthma severity.14

To our knowledge, our investigation is the largest study of BLL, asthma, and eosinophilia in US children to date (N = 14 751). Our results were nationally representative, and we controlled for relevant demographic and socioeconomic factors. Our study limitations included the NHANES cross-sectional study design in which asthma is self-reported from a household reference person. Diagnosing asthma in younger children is difficult15; misclassification bias was possible. The availability of variables collected by NHANES limited our ability to analyze asthma by endotypes or assess potential confounders (eg, indoor housing characteristics and possible take-home exposure of lead from children's parent's/caregiver's occupations). About 27% of all children aged 1-11 years who participated in NHANES from 2001 to 2016 were missing BLL measurements. However, reweighting for non-response to phlebotomy in a sensitivity analysis did not affect our results. We found no association between BLL and asthma, despite experimental or smaller epidemiologic studies suggesting a relationship. We did find a significant relationship between BLL and eosinophils, but its clinical significance is uncertain. Additional information about how lead exposure relates to asthma endotypes could improve our

understanding of how lead exposure might affect the development and exacerbation of asthma among children.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

CDC DISCLAIMER

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

REFERENCES

1. Dignam T, Kaufmann RB, LeStourgeon L, Brown MJ. Control of lead sources in the United States, 1970–2017: public health progress and current challenges to eliminating lead exposure. J Public Health Manag Pract. 2019;25 Suppl 1, Lead Poisoning Prevention:S13–S22.
2. Brink LL, Talbott EO, Sharma RK, et al. Do US ambient air lead levels have a significant impact on childhood blood lead levels: results of a national study. J Environ Public Health. 2013;2013:278042. [PubMed: 23983719]
3. Sun L, Hu J, Zhao Z, Li L, Cheng H. Influence of exposure to environmental lead on serum immunoglobulin in preschool children. Environ Res. 2003;92(2):124–128. [PubMed: 12854692]
4. Wang IJ, Karmaus WJJ, Yang CC. Lead exposure, IgE, and the risk of asthma in children. J Expo Sci Environ Epidemiol. 2017;27(5):478–483. [PubMed: 28401896]
5. Wells EM, Bonfield TL, Dearborn DG, Jackson LW. The relationship of blood lead with immunoglobulin E, eosinophils, and asthma among children: NHANES 2005–2006. Int J Hyg Environ Health. 2014;217(2–3):196–204. [PubMed: 23726529]
6. Wenzel SE. Asthma phenotypes: the evolution from clinical to molecular approaches. Nat Med. 2012;18(5):716–725. [PubMed: 22561835]
7. Pugh Smith P, Nriagu JO. Lead poisoning and asthma among low-income and African-American children in Saginaw. Michigan. Enviro Res 2011;111(1):81–86.
8. Joseph CLM, Havstad S, Ownby DR, et al. Blood lead level and risk of asthma. Environ Health Perspect. 2005;113(7):900–904. [PubMed: 16002380]
9. Farkhondeh T, Samarghandian S, Sadighara P. Lead exposure and asthma: an overview of observational and experimental studies. Toxin Rev. 2015;34(1):6–10.
10. Licari A, Castagnoli R, Brambilla I, et al. Asthma endotyping and biomarkers in childhood asthma. Pediatr Allergy Immunol Pulmonol. 2018;31(2):44–55. [PubMed: 30069422]
11. Johnson CL, Paulose-Ram R, Ogden CL, et al. National Health and Nutrition Examination Survey: Analytic guidelines: 1999–2010. In: (NCHS) NCfHS, ed. Vol Series 2. 2013.
12. NCHS (National Center for Health Statistics). National Health and Nutrition Examination Survey (NHANES). Laboratory Procedures Manual, 2009
13. Lawrence DA, McCabe MJ Jr. Immunomodulation by metals. Int Immunopharmacol. 2002;2(2–3):293–302. [PubMed: 11811932]
14. Mohammed AA, Mohamed FY, el El-Okda S, Ahmed AB. Blood lead levels and childhood asthma. Indian Pediatr. 2015;52(4):303–306. [PubMed: 25929627]
15. NIH (National Institutes of Health). Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma-Summary Report, 2007

TABLE 1

Select characteristics of children aged 1-11 years by current asthma, eosinophilia, and blood lead level (BLL): NHANES from 2001 to 2016

	Survey respondents	Current asthma		Eosinophils ≥ 500 cells/μL		BLL ≥ 5 μg/dL	
Characteristic	**n**[a]	**%**[b] **(95% CI)**	***P*-value**[c]	**%**[b] **(95% CI)**	***P*-value**[c]	**%**[b] **(95% CI)**	***P*-value**[c]
Total	14 751	8.9 (8.3-9.4)		14.5 (13.7-15.3)		1.8 (1.4-2.2)	
Sex							
Male	7526	10.2 (9.3-11.1)	<.001	17.4 (16.2-18.6)	<.001	2.0 (1.5-2.5)	<.05
Female	7225	7.4 (6.7-8.2)		11.4 (10.5-12.4)		1.6 (1.3-2.0)	
Age group							
1-5 y	6751	7.3 (6.6-8.2)	<.001	13.3 (12.3-14.3)	.004	3.1 (2.5-3.8)	<.001
6-11 y	8000	9.9 (9.2-10.7)		15.3 (14.3-16.4)		0.9 (0.6-1.2)	
Race/ethnicity							
Non-Hispanic black	3934	15.1 (13.7-16.5)	<.001	15.8 (14.6-17.0)	.001	4.8 (3.5-6.6)	<.001
Non-Hispanic white	4064	7.7 (6.9-8.6)		13.3 (12.1-14.7)		1.3 (1.0-1.7)	
Mexican American	4099	6.0 (5.1-7.0)		14.3 (13.0-15.7)		1.1 (0.8-1.5)	
Other	2654	10.2 (8.8-11.8)		17.5 (15.7-19.3)		1.4 (0.8-2.4)	
Health insurance							
Medicaid	5736	12.0 (10.9-13.3)	<.001	15.3 (14.2-16.6)	.23	2.8 (2.2-3.7)	<.001
Other insurance	7400	8.1 (7.5-8.7)		14.2 (13.2-15.3)		1.2 (0.9-1.6)	
No coverage	1556	4.1 (3.1-5.4)		13.7 (11.8-15.9)		2.1 (1.4-3.2)	
Season of interview							
May 1-October 31	7612	8.3 (7.7-9.0)	.04	14.2 (13.2-15.3)	.37	2.3 (1.7-3.0)	<.001
November 1-April 30	7139	9.6 (8.6-10.6)		14.8 (13.8-16.0)		1.1 (0.9-1.4)	
Education, household reference person							
<High school	4453	8.6 (7.5-9.9)	.70	15.0 (13.5-16.7)	.55	3.6 (2.6-5.0)	<.001
≥High school	9864	8.9 (8.2-9.6)		14.5 (13.6-15.4)		1.2 (1.0-1.5)	
Poverty income ratio (PIR)							
<1.3	6895	10.7 (9.6-11.9)	<.001	15.7 (14.5-16.9)	.02	3.4 (2.7-4.3)	<.001
≥1.3	6988	7.8 (7.1-8.6)		13.8 (12.7-14.9)		0.7 (0.5-1.0)	
Household smoker							
Yes	2236	10.6 (9.2-12.3)	.02	14.9 (12.9-17.1)	.70	4.6 (3.5-6.0)	<.001

Characteristic	Survey respondents n[a]	Current asthma %[b] (95% CI)	*P*-value[c]	Eosinophils ≥ 500 cells/μL %[b] (95% CI)	*P*-value[c]	BLL ≥ 5 μg/dL %[b] (95% CI)	*P*-value[c]
No	12 386	8.6 (8.0-9.2)		14.4 (13.6-15.3)		1.3 (1.0-1.6)	
Survey cycle							
2001-2002	1942	9.0 (7.5-10.6)	.93	12.8 (11.1-14.8)	.03	4.4 (2.9-6.5)	<.001
2003-2004	1767	8.4 (6.7-10.4)		15.1 (12.5-18.1)		3.1 (1.7-5.4)	
2005-2006	1902	9.5 (8.2-11.0)		12.9 (10.9-15.3)		2.0 (1.2-3.3)	
2007-2008	1828	8.5 (7.5-9.7)		13.7 (12.0-15.6)		1.7[d] (0.9-3.0)	
2009-2010	1845	8.5 (7.2-10.0)		13.4 (11.8-15.3)		1.0 (0.7-1.5)	
2011-2012	1761	9.6 (7.8-11.8)		16.4 (14.0-19.1)		1.0[d] (0.5-2.0)	
2013-2014	1893	8.6 (7.3-10.1)		14.3 (12.0-17.0)		0.3[d] (0.1-0.8)	
2015-2016	1813	8.7 (7.0-10.8)		17.3 (15.5-19.2)		0.7[d] (0.3-1.6)	

[a] Number and percent of missing values: current asthma (n = 51, 0.3%), eosinophils (n = 69, 0.5%), health insurance (n = 59, 0.4%), household reference person education (n = 434, 2.9%), poverty income ratio (n = 868, 5.9%), household smoker (n = 129, 0.9%).

[b] Percentages listed are weighted row percentages.

[c] Chi-square *P*-value.

[d] Relative standard error of estimate > 30, statistic is potentially unreliable.

TABLE 2

Adjusted prevalence ratios (aPRs) of asthma and eosinophils for US children aged 1-11 years by blood lead level (BLL) and other select covariates: NHANES from 2001 to 2016 (n = 14 751)[a]

	Current asthma aPR (95% CI)	Eosinophils ≥500 cells/μL aPR (95% CI)
BLL		
<5 μg/dL	referent	referent
≥5 μg/dL	1.09 (0.76-1.59)	1.19 (0.89-1.59)
BLL quartiles		
Q1 (<0.68 μg/dL)	referent	referent
Q2 (0.68-1.05 μg/dL)	0.89 (0.71-1.10)	1.05 (0.87-1.27)
Q3 (1.05-1.71 μg/dL)	0.94 (0.76-1.17)	1.21 (1.02-1.44)
Q4 (>1.71 μg/dL)	0.90 (0.69-1.17)	1.39 (1.15-1.68)
Sex		
Female	referent	referent
Male	1.38 (1.20-1.59)	1.51 (1.36-1.67)
Age group		
6-11 y	referent	referent
1-5 y	0.73 (0.64-0.83)	0.85 (0.77-0.94)
Race/ethnicity		
Non-Hispanic white	referent	referent
Non-Hispanic black	1.60 (1.35-1.89)	1.16 (1.01-1.34)
Mexican American	0.72 (0.57-0.92)	1.05 (0.91-1.21)
Other	1.23 (0.99-1.53)	1.27 (1.10-1.47)
Health insurance		
Other insurance	referent	referent
Medicaid	1.28 (1.08-1.53)	0.97 (0.85-1.11)
No coverage	0.49 (0.37-0.67)	0.96 (0.80-1.14)
Season of interview		
November 1-April 30	referent	referent
May 1-October 31	0.86 (0.75-0.99)	0.98 (0.88-1.08)
Poverty income ratio (PIR)		
≥1.3	referent	referent
<1.3	1.20 (0.98-1.46)	1.12 (0.99-1.27)
Household smoker		
No	referent	referent
Yes	1.02 (0.84-1.25)	1.05 (0.89-1.25)

[a]Number and percent of missing values: current asthma (n = 51, 0.3%), eosinophils (n = 69, 0.5%), health insurance (n = 59, 0.4%), poverty income ratio (n = 868, 5.9%), household smoker (n = 129, 0.9%).

TABLE 3

Age-stratified adjusted prevalence ratios of asthma and eosinophils for US children by blood lead level (BLL) and other select covariates: NHANES from 2001 to 2016

	1- to 5-year-olds (n = 6751)[a]		6- to 11-year-olds (n = 8000)[b]	
	Asthma aPR (95% CI)	**Eosinophils ≥500 cells/μL aPR (95% CI)**	**Asthma aPR (95% CI)**	**Eosinophils ≥500 cells/μL aPR (95% CI)**
BLL				
<5 μg/dL	referent	referent	referent	referent
≥5 μg/dL	1.13 (0.74-1.71)	1.11 (0.78-1.57)	0.74[c] (0.36-1.51)	1.26 (0.85-1.89)
Sex				
Female	referent	referent	referent	referent
Male	1.58 (1.29-1.95)	1.77 (1.52-2.05)	1.29 (1.09-1.51)	1.38 (1.20-1.58)
Race/ethnicity				
Non-Hispanic white	referent	referent	referent	referent
Non-Hispanic black	1.88 (1.45-2.43)	1.19 (0.95-1.50)	1.47 (1.20-1.78)	1.14 (0.98-1.34)
Mexican American	0.62 (0.45-0.85)	0.95 (0.78-1.14)	0.78 (0.58-1.05)	1.12 (0.94-1.33)
Other	1.14 (0.82-1.58)	1.35 (1.09-1.67)	1.29 (0.99-1.68)	1.23 (1.03-1.47)
Health insurance				
Other insurance	referent	referent	referent	referent
Medicaid	1.19 (0.92-1.52)	1.08 (0.91-1.28)	1.35 (1.07-1.69)	0.91 (0.77-1.07)
No coverage	0.66 (0.41-1.06)	1.07 (0.80-1.43)	0.42 (0.29-0.62)	0.90 (0.72-1.13)
Season of interview				
November 1-April 30	referent	referent	referent	referent
May 1-October 31	0.92 (0.75-1.14)	1.01 (0.87-1.17)	0.84 (0.71-1.01)	0.96 (0.84-1.10)
Poverty income ratio (PIR)				
≥1.3	referent	referent	referent	referent
<1.3	1.42 (1.04-1.94)	1.06 (0.88-1.27)	1.09 (0.87-1.36)	1.15 (0.99-1.34)
Household smoker				
No	referent	referent	referent	referent
Yes	1.11 (0.87-1.41)	1.10 (0.87-1.40)	0.99 (0.76-1.29)	1.03 (0.83-1.28)

[a]Number and percent of missing values for 1- to 5-year-olds: current asthma (n = 28, 0.4%), eosinophils (n = 46, 0.7%), health insurance (n = 27, 0.4%), poverty income ratio (n = 423, 6.3%), household smoker (n = 61, 0.9%).

[b]Number and percent of missing values for 6- to 11-year-olds: current asthma (n = 23, 0.3%), eosinophils (n = 23, 0.3%), health insurance (n = 32, 0.4%), poverty income ratio (n = 445, 5.6%), household smoker (n = 68, 0.9%).

[c]Relative standard error of estimate is >30, statistic is potentially unreliable.