

IgE antibodies and urinary trimethylarsine oxide accounted for 1–7 % population attributable risks for eczema in adults: USA NHANES 2005–2006

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Abstract Population attributable risks from serum IgE and dust mite allergen concentrations and environmental chemicals for eczema are unclear. Therefore, it was aimed to examine serum IgE and allergen concentrations and environmental chemicals for eczema in adults and to calculate population attributable risks in a national and population-based setting. Data retrieved from the National Health and Nutrition Examination Survey, 2005–2006, was analyzed. Information on demographics and self-reported ever eczema was obtained by household interview. Bloods and urines (sub-sample) were also collected during the interview. Adults aged 20–85 were included. Statistical analyses were using chi-square test, *t* test, survey-weighted logistic regression modeling, and population attributable risk (PAR) estimation. Of all the included American adults ($n=4979$), 310 (6.2 %) reported ever eczema. Moreover, more eczema cases were observed in female adults but fewer cases in people born in Mexico. There were no significant associations observed between commonly known biomarkers (including vitamin D) and eczema or between dust mite allergens and eczema. Serum D. Farinae (PAR 1.0 %), D. Pteronyssinus (PAR 1.1 %), cat (PAR 1.8 %), dog (PAR 1.6 %), and mouse (PAR 3.2 %) IgE antibodies were associated with eczema. Adults with ever eczema were found to have higher levels of urinary trimethylarsine oxide concentrations

(PAR 7.0 %) but not other speciated arsenic concentrations. There were no clear associations between other environmental chemicals including heavy metals, phthalates, phenols, parabens, pesticides, nitrate, perchlorate, polycyclic hydrocarbons and eczema as well. Elimination of environmental risks might help delay or stop eczema up to 7 % in the adult population.

Keywords Eczema · Population attributable risk · Arsenic · IgE · Allergen · Chemical

Introduction

The prevalence of eczema in United States of America (USA) is about 10.7 %, and up to 17.1 % reported at least one of four eczematous symptoms (Hanifin et al. 2007). In addition, there has also been observed geographic variations (Darsow et al. 2004). Even within the same country, such as the UK, the rates from different age groups could also vary across sub-regions (Shiue 2012). While the genetic influence could only be minimal (Esparza-Gordillo et al. 2010), social, health, and environmental influences could be of greater concerns for the individual and society. Typically, eczema remitted from age 1 to 7 years but became more persistent from the age of 15 years, especially in those who were atopic. One UK cohort study with 23 years of follow-up found that the prevalence of eczema rose in women from age 15 to 23 years and adults with eczema had higher IgE (Burr et al. 2013). There has been abundant literature on eczema among children. However, such information in adults was relatively less. Therefore, it was aimed to identify environmental attributes by studying serum IgE antibodies, house dust, mite allergens, and different sets of urinary chemicals to eczema and to estimate their population attributable risks in a national and population-based setting.

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Methods

Study sample

United States National Health and Nutrition Examination Surveys (NHANES) has been a national, population-based, multi-year, cross-sectional study. The sampling method was a complex, multistage probability sampling design that was used to select a sample representative of the civilian noninstitutionalized household population of the US (for more details, please refer to http://www.cdc.gov/nchs/data/series/sr_01/sr01_056.pdf). It started from selecting counties or small groups of contiguous counties and then went down to a block or group of blocks containing a cluster of households. After identifying eligible households within segments, individuals within households were invited for surveying. Information on demographics, self-reported ever medical conditions, and self-reported eczema (has a doctor or other health professional ever told you/SP that you have/SP s/he has eczema?) was obtained by household interview using questionnaires. In the current analysis, the 2005–2006 cohort (more details via http://www.cdc.gov/nchs/nhanes/search/nhanes05_06.aspx), being the most recent with all the relevant information (demographics, self-reported health conditions, serum measurements including vitamin D, IgE antibodies and dust mite allergens and urinary concentrations) for the current analysis, was selected and included for the statistical analysis. Informed consents were obtained from participants.

Biomarkers and biomonitoring

Bloods were collected in participants aged 1 and above to measure biomarkers including vitamin D, vitamin C, serum folate (vitamin B12), serum cotinine (a marker of smoking status), proteins, cholesterol, hepatitis C, glucose, and parathyroid hormone with detectable level and normal and abnormal values identified, respectively. Laboratory Procedure Manuals for each of these biomarkers mentioned above could be found publicly online: http://www.cdc.gov/nchs/nhanes/nhanes2005-2006/lab_methods_05_06.htm. Blood pressure (BP) was measured on all examinees 8 years and older at the household interview and for three times (more details via: http://www.cdc.gov/nchs/nhanes/nhanes2009-2010/BPX_F.htm). The standard measuring protocol can be found here: http://www.cdc.gov/nchs/nhanes/nhanes20092010/BPX_F.htm#Protocol_and_Procedure. Participants with any of the following on both arms were excluded from the exam according to the standard protocol: rashes, gauze dressings, casts, edema, paralysis, tubes, open sores or wounds, withered arms, a-v shunts, and radical mastectomy or if BP cuff does not fit on the arm. The measurements took three times, and in the present study, we took the the second time BP measurement when humans could be at the stable state in

the analysis. People with ≥ 140 mmHg systolic BP and ≥ 90 mmHg diastolic BP were classified as high BP.

On the other hand, urines were only collected in a representative subsample, being one third of the whole cohort (more details, please refer to http://www.cdc.gov/nchs/data/nhanes/nhanes_subsample_notes.pdf), to measure environmental chemical concentrations in urines among people aged 6 and above. Therefore, subsample weights are to be applied in the statistical modeling. Urine specimens were processed, stored under appropriate frozen (-20°C) conditions, and shipped to the Division of Environmental Health Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention for analysis. Urine specimens were processed, stored, and shipped to Division of Laboratory Sciences, National Center for Environmental Health, National Centers for Disease Control and Prevention, Atlanta, Georgia.

Liquid samples are introduced into the inductively coupled plasma-mass spectrometry, a multi-element analytical technique, through a nebulizer and spray chamber carried by a flowing argon stream to detect heavy metals (Date and Gray 1989; Mulligan et al. 1990). High-performance liquid chromatography-electrospray ionization-tandem mass spectrometry was used for the quantitative detection in urine of phthalate metabolites (Silva et al. 2007; Westgard et al. 1981). A sensitive method for measuring BPA, BP-3, triclosan, parabens, and pesticides was developed to use on-line solid phase extraction coupled to HPLC and tandem mass spectrometry (Ye et al. 2006). With the use of isotopically labeled internal standards, the detection limits in 100 μL of urine are 0.1–2.3 ng/mL, sufficient for measuring urinary levels of phenols in non-occupationally exposed subjects. Arsenic is measured through the use of inductively coupled-plasma dynamic reaction cell-mass spectrometry (for more details, please refer to http://www.cdc.gov/nchs/nhanes/2005-2006/UAS_D.htm).

To detect and measure metabolites of hydrocarbons (more details via http://www.cdc.gov/nchs/data/nhanes/nhanes_11_12/PAH_G_met.pdf), the procedure involved enzymatic hydrolysis of glucuronidated/sulfated OH-polyaromatic hydrocarbon metabolites in urine, extraction, derivatization, and analysis using isotope dilution capillary gas chromatography tandem mass spectrometry (GC-MS/MS). Ion transitions specific to each analyte and carbon-13 labeled internal standards are monitored, and the abundances of each ion are measured. Also, according to the NHANES website (more details via http://www.cdc.gov/nchs/nhanes/2011-2012/PERNT_G.htm), ion chromatography coupled with electrospray tandem mass spectrometry was used to detect and measure the amount. Chromatographic separation is achieved using an IonPac AS16 column with sodium hydroxide as the eluent. The eluent from the column is ionized using an electrospray interface to generate and transmit negative ions into the mass

spectrometer. Comparison of relative response factors (ratio of native analyte to stable isotope labeled internal standard) with known standard concentrations yields individual analyte concentrations. The lower detection limits were 0.05 ng/mL for urinary perchlorate, 700 ng/mL for urinary nitrate, and 20 ng/mL for urinary thiocyanate. In cases, where the result was below the limit of detection, the value for that variable is the detection limit divided by the square root of two.

Statistical analysis

There were 7 steps in analysis in the present study. In the first step, demographic characteristics of the included American adults were described by using Chi-square test and *t* test. In the second step, associations of biomarkers (including vitamin D, HDL cholesterol, total cholesterol, vitamin C, c-reactive protein, Apolipoprotein, fasting glucose, serum folate/vitamin B12, parathyroid hormone, and serum cotinine) and eczema were investigated by using survey-weighted logistic regression modeling. In the third step, associations of serum IgE antibodies (for more details, please refer to http://wwwn.cdc.gov/nchs/nhanes/2005-2006/AL_IGE_D.htm) and eczema were examined by using *t* test and survey-weighted logistic regression modeling. In the third step, associations of common indoor allergens (for more details, please refer to http://wwwn.cdc.gov/nchs/nhanes/2005-2006/ALDUST_D.htm) and eczema were analyzed as well. The allergen dust collection procedure could be found here http://www.cdc.gov/nchs/data/nhanes/nhanes_05_06/allergen_manual_06.pdf. Finally, the associations of different sets of urinary environmental chemicals and eczema were correlated. Serum IgE antibodies, indoor allergens, and urinary chemical concentrations were log-transformed in the statistical analyses since they were highly skewed. All statistical effects were presented with odds ratios (OR), with $P < 0.05$ considered statistically significant. The statistical software STATA version 13.0 (STATA, College Station, Texas, USA) was used to conduct all the analyses. Population attributable risks from significant associations were calculated based on the formula introduced by Fleiss (Fleiss 1979). Since this study is only a secondary data analysis based on extracting data from the US NHANES website, no further ethics approval was required.

Results

Of all the included American adults ($n=4979$), 310 (6.2 %) reported ever eczema. Moreover, more eczema cases were observed in female adults but fewer cases in people born in Mexico. Characteristics of adult participants could be found in Table 1. There were no significant associations observed between commonly known biomarkers (including vitamin D, vitamin C, serum folate (vitamin B12), serum cotinine,

proteins, cholesterol, hepatitis C, glucose, and parathyroid hormone) and eczema (data not shown).

Table 2 presents the associations of serum IgE antibodies and eczema. It was observed that serum *D. Farinae* (PAR 1.0 %), *D. Pteronyssinus* (PAR 1.1 %), cat (PAR 1.8 %), dog (PAR 1.6 %), and mouse (PAR 3.2 %) IgE antibodies were significantly associated with eczema. There were no strong associations observed between dust mite allergens and eczema (see Table 3). Moreover, adults with ever eczema were found to have higher levels of urinary trimethylarsine oxide concentrations (PAR 7.0 %; see Table 4) but not other speciated arsenic concentrations. There were no clear associations between other environmental chemicals including heavy metals, phthalates, phenols, parabens, pesticides, nitrate, perchlorate, and polycyclic hydrocarbons and eczema as well (data not shown).

Discussion

Previous research

Being exposed to pets might have a higher risk of eczema. For example, in the large International Study of Asthma and Allergies in Childhood study across numerous countries (Solis-Soto et al. 2013), the OR for children was 1.2 (95 % CI 1.0–1.5). However, according to an earlier systematic review looking at literature between 1950 and 2006, no such association was confirmed in populations across age groups (Langan et al. 2007). A recent systematic review looking at studies between 2012 and 2013 across different age groups found that exposure to dog might be actually protective for eczema (Madhok et al. 2015). These conflicting results might be due to different age groups and study designs. In the present study, American adults with eczema were found to have higher levels of cat, dog, and mouse IgE antibodies. A similar finding in Scotland using a small sample in the early times had already observed higher levels of serum cat IgE antibody in adults with eczema. Research looking into the relationships of specific IgE antibodies and eczema in adults is limited. Therefore, it is difficult to make comparisons.

Arsenic might have a role in eczema, in particular in women (Vahter et al. 2007), although very few studies have been reporting this. There might be a safe net level to be set—3 mg/kg maximum (Cosmetic Ingredient Review Expert Panel 2007). Interestingly, in the present study, trimethylarsine oxide had a risk effect on eczema in adults while dimethylarsinic acid had a protective effect. Other speciated arsenics did not seem to have effects on eczema in adults. The current analysis might be the first to provide such evidence. Future research looking to the differences among speciated arsenics and finding out the mechanisms, if

Table 1 Demographic characteristics for eczema in American adults aged 20–85

	Eczema (<i>n</i> =310, 6.2 %)	Non-Eczema (<i>n</i> =4662, 93.8 %)	OR (95 % CI)*	<i>P</i> value
Age	46.4±18.9	48.4±19.1	0.99 (0.99–1.00)	0.063
Sex				
Male	126 (5.3 %)	2259 (94.7 %)	1.00	
Female	184 (7.1 %)	2403 (92.9 %)	1.48 (1.12–1.94)	0.008
Birthplace				
Within USA	278 (7.2 %)	3596 (92.8 %)	1.00	
In Mexico	5 (0.8 %)	642 (99.2 %)	0.17 (0.06–0.50)	0.003
Elsewhere	26 (5.8 %)	420 (94.2 %)	0.79 (0.44–1.40)	0.389
Body mass index				
<18.5	3 (3.8 %)	76 (96.2 %)	0.30 (0.06–1.55)	0.138
18.5–24.9	97 (7.2 %)	1252 (92.8 %)	1.00	
25–29.9	83 (5.2 %)	1519 (94.8 %)	0.72 (0.43–1.18)	0.176
30+	127 (6.5 %)	1815 (93.5 %)	0.89 (0.66–1.18)	0.380
Family PIR				
0–4.99	222 (5.8 %)	3595 (94.4 %)	0.85 (0.60–1.20)	0.326
5+	88 (7.6 %)	1067 (92.4 %)	1.00	

*Adjusted for all the study variables listed in the table and survey weighting

at all, would be needed. On the other hand, consistent with previous studies (Silverberg and Simpson 2014; Silverberg and Hanifin 2013; Silverberg et al. 2013) using different surveys in USA, it was observed that people (both children and

adults) born outside of USA were less diagnosed with eczema. This might be due to the different early living environments. Unfortunately, it is not possible to examine within the current limited dataset.

Table 2 Associations of serum IgE concentrations and eczema in American adults aged 20–85

	Eczema (<i>n</i> =310, 6.2 %)	Non-Eczema (<i>n</i> =4662, 93.8 %)	OR (95 %CI)**	PAR
Total IgE	214.2±740.7	160.3±456.0	1.06 (0.99–1.15)	-
D. FarinaeIgE	2.9±8.9	1.9±12.7	1.17 (1.02–1.34)	1.0 % (0.1–2.1 %)
D. PteronyssinusIgE	3.3±10.5	2.0±13.0	1.18 (1.04–1.33)	1.1 % (2.5–2.0 %)
Cat IgE	1.6±6.5	0.9±7.0	1.29 (1.15–1.44)	1.8 % (0.9–2.7 %)
Dog IgE	0.6±1.4	0.5±2.5	1.26 (1.15–1.39)	1.6 % (0.9–2.4 %)
Cockroach IgE	0.6±3.2	0.7±3.6	1.00 (0.78–1.27)	-
AlternariaIgE	0.6±1.7	0.6±2.3	1.08 (0.91–1.29)	-
Peanut IgE	0.3±0.3	0.4±2.8	0.85 (0.60–1.20)	-
Egg IgE	0.3±0.2	0.3±± 0.4	1.30 (0.75–2.26)	-
Milk IgE	0.3±0.2	0.3±0.8	0.97 (0.55–1.72)	-
Ragweed IgE	0.8±2.0	1.0±6.8	1.12 (0.97–1.29)	-
Rye grass IgE	2.0±6.4	2.5±13.5	1.10 (0.97–1.24)	-
Bermuda grass IgE	1.0±4.0	1.5±9.5	1.04 (0.89–1.22)	-
Oak IgE	0.9±3.8	0.8±5.6	1.12 (0.91–1.38)	-
Birch IgE	1.2±6.5	1.1±9.7	1.09 (0.83–1.42)	-
Shrimp IgE	0.5±2.7	0.5±3.1	1.09 (0.86–1.38)	-
AspergillusIgE	0.4±0.9	0.3±0.7	1.27 (0.95–1.70)	-
Thistle IgE	0.4±1.2	0.6±3.4	0.95 (0.81–1.13)	-
Mouse IgE	0.4±1.7	0.3±1.0	1.54 (1.16–2.06)	3.2 % (1.0–6.2 %)
Rat IgE	0.4±1.7	0.3±1.0	0.74 (0.35–1.54)	-

*Adjusted for age, sex, birthplace, and survey weighting

Table 3 Associations of allergens in household dust and eczema in American adults aged 20–85

	Eczema (<i>n</i> =310, 6.2 %)	Non-Eczema (<i>n</i> =4662, 93.8 %)	OR (95 %CI)**
Total dust weight (mg)	947.5±667.6	952.9±629.1	0.93 (0.59–1.48)
Sieved dust weight (mg)	655.6±549.0	654.6±501.6	0.95 (0.66–1.38)
Fungus alternaria alternate (ng/mL)	0.2±0.2	0.2±0.4	0.96 (0.69–1.34)
Aspergillusfumigatus (ng/mL)	7487.5±10634.3	6926.5±7276.9	1.12 (0.86–1.45)
German Cockroach Blattellagermanica 1 (U/mL)	0.1±0.2	0.1±0.4	0.89 (0.74–1.08)
German Cockroach Blattellagermanica 2 (U/mL)	10.3±6.5	10.0±6.8	0.97 (0.75–1.24)
Dog allergen Canisfamiliaris 1 (ng/mL)	587.8±1460.6	580.4±2301.1	1.01 (0.96–1.06)
Dust mite Dermatophagoides farina 1 (ng/mL)	34.8±114.4	49.4±212.0	0.95 (0.85–1.05)
Dust mite Dermatophagoidespteronysinus 1 (ng/mL)	74.2±427.5	53.6±261.8	1.00 (0.90–1.10)
Cat allergen felisdomesticus 1 (ng/mL)	1417.3±4931.6	1234.6±5691.6	1.00 (0.94–1.06)
Mouse urinary protein (ng/mL)	7.5±29.7	15.1±157.0	0.97 (0.84–1.12)
Rat urinary protein (ng/mL)	18.9±265.5	0.7±12.9	0.94 (0.71–1.26)
Endotoxin dust (EU/mL)	1389.8±2880.7	2180.0±10104.4	0.93 (0.83–1.06)

*Adjusted for age, sex, birthplace, and survey weighting

Strengths and limitations

The present study has a few strengths. First, it was conducted in a large study sample from across USA with different ethnicities and socioeconomic levels. Second, this is for the first time to estimate population attributable risks for eczema in adults. However, there are also a few limitations worthy of being noted. First, only commonly known and detectable biomarkers, serum IgE antibodies, dust mite allergens, and environmental chemicals were included in the current dataset. In other words, other uncommon elements emerging from the environment that could also be linked with eczema were unable to be analyzed and would need future research to identify. Second, study variables on other environmental exposures including dampness in the home environment (McNally et al. 2001; Simoni et al. 2005) and air pollution (Lee et al. 2007) were not available in the current limited

dataset. Moreover, the causation cannot be drawn due to the study design being cross-sectional in nature. Future research keeping the strengths and overcoming the limitations mentioned above and with a longitudinal or experimental monitoring would be suggested.

Conclusion

The prevalence of eczema in American adults aged 20–85 was 6.2 %, being half of it among American youth aged 0–19. Elimination of environmental risks might help delay or stop eczema up to 7 % in the adult population. Future research further looking for other potential environmental risk attributes should be encouraged in order to remove any environmental risks early in life and consequently prolong quality of human life.

Table 4 Associations of urinary arsenic concentrations and eczema in American adults aged 20–85

(μg/L)	Eczema	Non-Eczema	OR (95 %CI)*	<i>P</i> value	PAR
Total arsenic	14.9±26.2	25.1±71.5	0.76 (0.58–1.00)	0.051	-
Arsenous acid	0.9±0.4	0.9±0.6	0.85 (0.17–4.31)	0.836	-
Arsenic acid	0.9±1.3	0.7±0.3	1.27 (0.72–2.25)	0.382	-
Arsenobetaine	7.7±23.1	14.0±57.4	0.81 (0.64–1.03)	0.085	-
Arsenocholine	0.4±0.1	0.5±0.3	0.08 (0.003–2.46)	0.139	-
Dimethylarsonic acid	5.5±13.5	5.9±9.1	0.69 (0.51–0.95)	0.025	-
Monomethylarsonic acid	1.2±2.3	1.0±1.0	1.04 (0.71–1.50)	0.842	-
Trimethylarsine Oxide	0.8±0.6	0.7±0.82	2.22 (1.67–2.95)	<0.001	7.0 % (4.0–10.8 %)

*Adjusted for urinary creatinine, age, sex, birthplace, and survey weighting

Note: OR 1.87 (95 %CI 1.36–2.56) and PAR 5.1 % (2.2–8.8 %) for trimethylarsine oxide after additionally adjusted for dimethylarsonic acid

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Conflict of interest None.

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