

ORIGINAL ARTICLE

Sociocultural characteristics, obesity and inflammatory biomarkers in Puerto Rican toddlers born in New York City

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Abstract

Background: In the USA, Puerto Rican children have a higher prevalence of asthma than other Latino ethnicities, and acculturation is one of hypothesized reasons for this difference. We examined associations between sociocultural characteristics and serum leptin, high-sensitivity C-reactive protein (hsCRP), and body mass index (BMI), and further, among hsCRP, leptin levels, BMI percentiles, and allergic sensitization in 2-year-old children.

Methods: IgE antibodies, leptin, and hsCRP concentrations were measured in serum from Puerto Rican toddlers (n = 143) born in New York City with a maternal history of allergy and/or asthma. Demographic and home characteristics questionnaires were administered to the mother, postpartum and two years later. Children's weight and height were measured to determine BMI percentiles.

Results: More girls (60%) had leptin levels above the median compared with boys (37%) (p = 0.0063). Leptin was positively correlated with BMI (r = 0.25; p = 0.0042). Children in daycare were more likely to be obese (40% vs. 24% p < 0.06). Maternal birthplace was significantly associated with children's leptin but not with hsCRP. Leptin levels were lower for children whose mothers were born on the US mainland (GM = 2.5 ng/ml, 95% CI [2.2–2.7]) compared with those whose mothers were born in Puerto Rico or another country (GM = 3.2 ng/ml, 95% CI [2.2–3.9], t-test p = 0.01). Mothers born in another country were more likely than those born in the US mainland or Puerto Rico to have obese children (60% vs. 26% p < 0.02). Leptin, hsCRP, and BMI percentile were not associated with sensitization to any of the measured inhalant allergens or total IgE.

Conclusion: Even at a very young age, some acculturation factors were associated with biomarkers and anthropometric measures of obesity among this Puerto Rican pediatric population. To our knowledge, this is the first study demonstrating the association of mother's birth place with child BMI and leptin as early as 24 months.

Puerto Ricans on the US mainland are a large and growing population with a disproportionate burden of chronic diseases (1). Puerto Rican (mainland and island) children have the highest asthma prevalence of any ethnic group in the United States, including Latinos (2). Based on the National Health Interview Survey for 2006–2008, for children (9.3% prevalence), current asthma prevalence is the highest among Puerto Rican Hispanics (18.4%) (3). In addition, asthma-related deaths for Puerto Ricans are the highest among all Latino groups in the United States (3).

The prevalence of overweight is among the highest in Hispanic children (4). In a prospective study of Puerto Rican children in New York City (NYC), nearly half of the 2-year-old children were overweight or at risk of being overweight (54%) (5). Together, these results highlight the magnitude of the comorbidity problems of obesity and asthma among Puerto Rican pediatric populations and underscore the need for evaluating the mechanistic associations with risk of asthma and obesity.

Research demonstrates the influence of sociodemographic factors on inflammation in chronic disease epidemiology in

adults (6). The high-sensitivity C-reactive protein (hsCRP), an acute phase protein and a sensitive marker of systemic inflammation, might be involved in the obesity–asthma link (7). The higher prevalence of asthma in Puerto Rican children could possibly be explained by sociocultural factors involving inflammatory pathways (6, 8). However, no known studies have examined the sociodemographic correlates of inflammation in relation to allergic sensitization among Puerto Rican children living in the mainland US.

A recently published study in Europe by Mustonen et al. (9) found that hsCRP was protective against allergic sensitization in 4.5-year-old children enrolled in the multicenter Protection against Allergy Study in Rural Environments (PASTURE) birth cohort study involving five countries (Austria, Finland, France, Germany, and Switzerland). Their work investigating links between hsCRP and allergen-specific IgE among children living on a farm and in rural settings in Europe is complementary to the current study conducted with inner city US children.

Thus, the current analysis builds on a birth cohort study of Puerto Rican children in NYC that has been described previously (10). Study aims were to: (i) assess the serum levels of leptin and hsCRP and BMI percentiles in early childhood; (ii) establish sociodemographic distributions for leptin, hsCRP and BMI percentile; (iii) investigate whether maternal socio-cultural factors (e.g. maternal birth place, maternal education), and home characteristics (e.g. environmental tobacco smoke, single-family vs. multifamily housing) are associated with leptin, hsCRP, and BMI; and (iv) examine whether children's leptin and hsCRP and BMI are associated with allergy (allergen-specific IgE) which is a strong predictor for atopic asthma.

Methods

Study population

The study design for the New York City Puerto Rican Asthma Project has been described by Acosta et al. (10) In this prospective cohort study, 274 children of Puerto Rican ethnicity were born in NYC to mothers with self-reported history of inhalant allergy and/or asthma. Only 143 serum samples collected at age 2 yr were included for analyses due to: (i) loss to follow-up; (ii) insufficient amount of blood collected; and (iii) hemolysis of blood sample. Informed written consent was obtained from the women in accordance with the institutional review boards of Lincoln Hospital, Albert Einstein Medical Center and Columbia and Harvard Universities.

Sociodemographic, home and anthropometric characteristics

In the postpartum period, (child mean age = 45 ± 39 days), home visits were conducted by a team of two technicians, one of whom was bilingual (Spanish/English). The technicians administered a baseline questionnaire to the mother and assessed sociodemographics and home characteristics (Table 1). At age 2 yr, follow-up questionnaires assessing the

Table 1 Demographics, home characteristics, and Biomarkers of entire cohort and those with serum results

Characteristic	Entire Cohort (n = 274)	Subset with serum results (n = 143)
Maternal Characteristics		
Place of birth		
Mainland United States	203 (74%)	101 (71%)
Puerto Rico	55 (20%)	30 (21%)
Other	16 (6%)	12 (8%)
Currently employed outside of the home (at age 2 yr)	91 (49%)*	64 (45%)
Education level		
Less than college	153 (56%)	88 (62%)
At least some college	121 (44%)	55 (38%)
Child Characteristics		
Gender of the child		
Male	139 (51%)	76 (53%)
BMI category (at age 2 yr)*		
Not obese or overweight		69 (53%)
Overweight		23 (18%)
Obese		37 (29%)
		(n = 129)
Leptin (Mean $\pm$ s.d.) (ng/ml)	–	2.66 $\pm$ 1.7
High-Sensitive C-reactive Protein (Mean $\pm$ s.d.) (ng/ml)	–	0.29 $\pm$ 7.5
Breastfeeding duration		
Never	79 (33%)	49 (35%)
Some, but less than 1 month	65 (27%)	35 (25%)
2 months	23 (10%)	13 (9%)
3 months	27 (11%)	15 (11%)
4 months	13 (5%)	9 (6%)
5 months	7 (3%)	4 (3%)
6 months	16 (7%)	11 (8%)
More than 6 months	12 (5%)	5 (4%)
	(n = 242)	(n = 141)
Child ever fed formula		
Yes	238 (98%)	138 (98%)
	(n = 242)	(n = 141)
Grandmother helped take care of baby (at birth): Yes	104 (38%)	51 (36%)
Home Environment Characteristics		
Household Environmental Tobacco Smoke (ETS) at birth	123 (45%)	66 (46%)
	(n = 272)	(n = 142)
Household (ETS) at age 2 yr†	86 (46%)*	66 (46%)
		(n = 142)
Lived in a multi-family apartment (at age 2 yr): Yes	172 (77%)	87 (79%)
	(n = 224)	(n = 110)
Lived in a high-rise multi-family apartment (at age 2 yr): Yes	135 (60%)	65 (59%)Z
	(n = 224)	(n = 110)
Child had siblings (at birth)		
Yes	182 (66%)	103 (72%)
Pet dog (at age 2 yr)		
Yes	15 (8%)*	12 (8%)

Table 1. (Continued).

Characteristic	Entire Cohort (n = 274)	Subset with serum results (n = 143)
Pet cat (at age 2 yr)		
Yes	20 (11%)*	13 (9%)
Reported frequency of cockroach sightings (at age 2 yr)		
Never or monthly	86 (46%)*	60 (42%)
Daily or weekly	99 (54%)*	83 (58%)
Reported frequency of mouse sightings (at age 2 yr)		
Never or monthly	146 (79%)*	113 (79%)
Daily or weekly	39 (21%)*	30 (21%)

*For these questions, n = 185 due to loss-to-follow-up by age 2 yr.

†Reported as someone who lives in the home is a smoker.

above characteristics were administered to the mothers. Height and weight of the child were measured. Blood samples were collected in the home or in the pediatric blood drawing unit of Columbia University Medical Center according to the preference of the mother.

High-sensitivity C-reactive protein and leptin

Serum CRP samples were analyzed by high-sensitivity latex-enhanced nephelometry on a BMII Nephelometer (Dade Behring, Newark, DE). The lower limit of detection was 0.10 mg/l. Serum concentrations of leptin were determined using 96-well microplate commercially available enzyme immunoassay (ELISA) (Alpco Diagnostics, Windham, NH) procedure. The assay sensitivity was 0.1 ng/ml, and the intra-assay % CV was 3.5.

Allergic sensitization

Allergic sensitization was assessed by measuring total and allergen-specific IgE antibodies to dust mite, cockroach, mouse, and cat in serum using the ImmunoCAP method (Phadia, Uppsala, Sweden).

Statistical analysis

The three outcome variables in this observational study were child BMI percentile, serum leptin, and serum hsCRP at age 24 months. Basic descriptive statistics were computed for all predictors and the outcome variables. BMI *z* scores (equivalent-for-age BMI percentile) were computed according to age- and sex-specific reference values from National Center for Health Statistics/Centers for Disease Control and Prevention (CDC) 2000 growth curves. Children were also classified as overweight corresponding to a BMI $\geq$ 85th percentile but less than 95th percentile; or obese (BMI $\geq$ 95th percentile) (11).

Serum biomarkers (leptin and hsCRP) were natural log-transformed to achieve normality before their use in linear and logistic regression models. Values below the detection limit

were assigned half the limit of detection. Pearson correlation and linear regression models were used to assess associations among continuous variables (e.g. BMI percentile, leptin, and hsCRP). CRP concentrations were evaluated utilizing the CDC/American Heart Association (AHA) cut point of >3 mg/l, representing high-risk category for cardiovascular disease in adults. (12) Leptin and hsCRP were also dichotomized at the median for categorical analysis. For categorical variables, chi-square tests for trend were also used. Allergic sensitization was defined as any allergen-specific IgE $\geq$ 0.35 IU/ml. Total IgE (most of which would be comprised of food-specific IgE at this young age) was treated as a continuous variable in the analyses.

Results

Sociocultural, demographic, and home characteristics are shown in Table 1. The parent cohort and the biomarkers sample did not differ significantly on the sociocultural, demographic, and home characteristics. The majority of mothers were US mainland born, of Puerto Rican ethnicity. Many of the children either attended daycare or had a grandmother helping to take care of them. Many of the mothers with a college degree worked outside the home. Most of the mothers did not breastfeed. The majority of the children lived in multifamily housing and had siblings that lived with them at birth. Using CDC growth charts to assess weight status, 29% of children were obese ($\geq$ 95th percentile) and 18% were overweight ($\geq$ 85th to $<$ 95th percentile). At age 2 yr, median BMI percentile was 81.4 (25th percentile = 42.5; 75th percentile = 95.8). There was no gender difference noted in this distribution at age 2 yr.

Geometric mean (GM) serum leptin and hsCRP concentrations were 2.66 ng/ml (geometric standard deviation (GSD) = 1.7) and 0.29 mg/l (GSD = 7.5), respectively. (Table 1) Sixteen percent (n = 23) of the children had hsCRP levels above 3 mg/l, defined by the CDC/AHA reference for adults (12).

BMI percentile was positively correlated with leptin ($r = 0.25$; $p = 0.0042$). BMI was not significantly associated with hsCRP when treated as categorical (Table 2) or continuous variables. More girls had leptin levels above the median than did boys (60% vs. 37% ($p < 0.0063$), but gender was not a significant factor in hsCRP levels (Table 2). Leptin levels were not significantly associated with hsCRP ($r = -0.03$, $p = 0.70$).

Mothers born in another country were more likely than those born in the US mainland or Puerto Rico, to have obese children (Table 2) and overweight children (OR = 3.8, 95% CI [1.0–14.6]) Maternal birthplace was significantly associated with the children's leptin but not with hsCRP levels. The leptin levels were significantly lower for children whose mothers were born on the US mainland (GM = 2.5 ng/ml, 95% CI [2.2–2.7]) compared with those whose mothers were born in Puerto Rico or another country (GM = 3.2 ng/ml, 95% CI [2.2–3.9], t -test $p = 0.01$). Much of this difference was attributed to the 12 children whose mothers were born in a country other than the US mainland or Puerto Rico (GM = 3.6 ng/ml, 95% CI [2.3–5.8]).

Table 2 Leptin, hsCRP, and Obesity stratified by characteristics of children (n = 143)

Characteristic	N	Leptin > Median	hsCRP > Median	Obesity (BMI ≥ 95th percentile)
Gender of the child				
Male	76	28 (37%)*	27 (36%)	18 (28%)
Female	67	40 (60%)*	28 (42%)	19 (30%)
Maternal birthplace				
Mainland USA	101	43 (43%)	40 (40%)	26 (28%)*
Puerto Rico	30	17 (57%)	10 (33%)	5 (19%)*
Other	12	8 (67%)	5 (42%)	6 (60%)*
Child in daycare at 24 months				
Yes	43	22 (51%)	14 (33%)	21 (24%)
No	100	46 (46%)	41 (41%)	16 (40%)
Obese [†]				
Yes	37	20 (54%)	19 (51%)	n/a
No	92	42 (46%)	31 (34%)	
Overweight [†]				
Yes	23	12 (52%)	8 (35%)	n/a
No	69	30 (44%)	23 (33%)	

*Chi-square test for trend $p < 0.05$.[†]n < 143 due to some missing measurements of either height or weight.**Table 3** Multiple linear regression model for continuous measurements of leptin (n = 143, $r^2 = 0.11$)

Characteristic	Parameter estimates (p-values) (Leptin)
Gender of the child	
Male	Referent
Female	$\beta = 0.28$ (p = 0.002)
Maternal birthplace	
Mainland USA	Referent
Puerto Rico or Other	$\beta = 0.22$ (p = 0.023)
Child in daycare at 24 months	
No	Referent
Yes	$\beta = 0.06$ (p = 0.528)

Leptin concentration (treated as a continuous variable) was associated with BMI (OR = 2.4; CI = 1.6–4.9; $p = 0.02$), but the association of leptin with overweight did not reach statistical significance (OR = 2.5; CI = 0.9–7.0; $p = 0.09$). Children in daycare were more likely to be obese (40% vs. 24% $p < 0.06$) measured with BMI distributions; however, no association between daycare and leptin level was observed. Neither leptin nor hsCRP was associated with self-reported household-level ETS exposure. In the adjusted linear regression model, the effect of gender and place of birth was almost equal in magnitude even after adjusting for daycare attendance (Table 3). None of the adjusted models (using children's characteristics) for hsCRP or BMI percentile were statistically significant.

Of the 142 children that had serum available for IgE, leptin, and hsCRP assessment, only 17 were sensitized to at least one of the indoor allergens (dust mite, cat, cockroach, or mouse).

Leptin and hsCRP levels were not significantly associated with any sensitization to the measured inhalant allergens or total IgE.

Discussion

To our knowledge, this is the first study evaluating the physical and sociocultural correlates of leptin and C-reactive concentrations in 2-year-old children at risk of asthma development. In this study, maternal acculturation specifically mother's birth place was associated with child BMI and leptin as early as 24 months of age. Children born to mothers born in Puerto Rico or another country (for example, Virgin Islands, Mexico, Dominican Republic) had higher levels of leptin than those born to mothers from the Mainland US. Mothers born in another country were more likely than those born in the US (mainland or Puerto Rico) to have obese children – evaluated on the basis of BMI. These findings are timely given that researchers have called for more in-depth evaluation of the relationship of maternal acculturation with obesity in early childhood (13, 14). CRP concentrations did not vary by gender, family income level, education, or maternal acculturation, although family income was found to be previously associated with elevated hsCRP levels in the NHANES data for 8–16 yr old children (8).

In some studies, acculturation is related to increased nutritional risk, (13) but in others, it is also related to protective factors (15). A study of low-income Puerto Rican women from Hartford, Connecticut revealed a statistically significant increase in BMI with length of time in the US, and these differences were even greater among women born in Puerto Rico (16). Studies have documented a socioeconomic (SES) gradient in dietary choices (17). Research with Hispanic children living in disadvantaged communities suggests that acculturation might involve increased consumption of fast food, soda, and trans fats. (18) Notably, the dietary risk factors for early childhood obesity are sweetened beverages and fruit juice consumption (19).

We believe this is the first study demonstrating the association of mother's birth place with child BMI and leptin as early as 24 months of age. Understanding the unique influences on leptin is essential because this adipokine could have a role in the pathogenesis of asthma (20). The findings for the intergenerational effect on BMI and leptin are intriguing, and it is possible that maternal birth place may act through epigenetic mechanisms such as leptin methylation pattern which could be involved by regulating the expression of important epiobesigenic genes. (21) Three main findings deserve further consideration in this context.

First, results suggest that maternal birth place influences BMI and leptin levels at child age 2 yr. We examined the possibility that sociocultural factors might also impact pro-inflammatory hsCRP levels, but none was significant.

Second, attending day care was positively associated with obesity measured by BMI, but not with leptin, and not with other home characteristics. Research shows a strong correlation between a child's size (height, weight, and BMI) and the ecological factors present in the family's environment (22). The extent to which day care influence functions through biologic or sociocultural parameters needs to be further examined given that

the majority of the early life stages during immune system development are under non-parental childcare (child care center, someone else's home, and child's own home by non-parent) (23).

Third, the serum leptin levels in children correlated with gender, and BMI percentile confirming earlier findings for older children (24). Girls had higher leptin levels than boys, consistent with reports for children age 5 and older (25). Earlier studies have shown a positive (25), negative, or no association (27) between maternal acculturation and their children's obesity.

We expected to find an association for leptin with hsCRP and hsCRP with BMI; however, there was no such association found in the current cohort. In NHANES III, overweight children had higher hsCRP, suggesting low-grade systemic inflammation. (28) However, the small sample size may have limited our ability to examine whether such an association exists (i.e. Type II Beta errors). The small sample is not as large as some European studies. Recruiting and maintaining a large sample of low-income inner city children is extremely difficult. Nonetheless, our small cohort of 2-year-old Puerto Rican children is among the largest in the United States, and even with some beta errors, our data suggest associations that are biologically plausible, and namely, leptin is associated with BMI.

In the current study, one-third of the children were partially breastfed through the first 2 months of age; however, we did not see an effect of any exposure to breastfeeding on obesity and inflammation unlike other studies (27). Maternal smoking in this study sample was significantly higher among those born on the mainland compared with those born elsewhere. (10) ETS exposure was, however, not related to inflammation and was not associated with the biomarkers or anthropometric measures of obesity. We acknowledge possible exposure misclassification because this assessment was based upon self-report of any household members smoking in the home. In our analysis, children living in multifamily housing (compared with single-family houses/duplexes) were not more likely to have higher leptin levels or elevated BMI measures.

We used total IgE as a proxy for overall allergy (much of the total IgE would be comprised of food-specific IgE at this young age), but we did not observe any relationships with leptin, hsCRP, or BMI percentile. Also, our results do not support a significant role for current levels of leptin or hsCRP in association with current sensitization (at age 2 yr) to any of the measured allergens in the 2-year-old children, but the small

sample size ($n = 17$ allergic children) could have precluded seeing an association if one truly existed. For example, European researchers observed a protective effect of hsCRP on inhalant allergy among a cohort of rural children ($n = 652$) age 4.5 yr (9). Furthermore, some researchers using BMI for categorizing obesity have found obesity to be related to allergy symptoms or to higher serum IgE levels (29), whereas others have not (30). In contrast to our findings, hsCRP levels in NHANES 2005–2006 were found to be associated with total IgE levels and atopy (29).

Major strengths of this study include the geographic focus and the recruitment of a high-risk sample of US children with probably similar environmental exposures and shared seasonal variations. However, the study's inclusion criterion (Puerto Rican children born in NYC with maternal history of allergy and/or asthma) limits the generalization of the findings to similar low-income women and children with a high proportion of Puerto Rican families living in the urban Northeast. We underscore that a number of associations identified in this study such as gender and body weight have also been reported with older children of other ethnic groups. These findings should be interpreted with caution because they may partly reflect differences in statistical power.

In conclusion, this study contributes uniquely to the literature by suggesting that the influence of maternal birth place on child BMI and leptin may begin as early as age 24 months. Most of the studies evaluating the roles of acculturation and obesity in early childhood have been conducted by research groups that only measured anthropometric parameters and did not measure biomarkers. Furthermore, those other studies did not evaluate the potential roles of home environmental characteristics. Future research should examine the mechanisms through which maternal birth place may affect proximal determinants of energy balance through caregiving practices and the home vs. day care environment. In light of the obesity epidemic which will likely continue to contribute to higher levels of inflammation in US children, these findings are important due to large and persistent disparities in childhood asthma, for which obesity is a major risk factor.

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