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Gestational Diabetes, Atopic Dermatitis and Allergen Sensitization in Early Childhood

Rajesh Kumar, MD¹, Fengxiu Ouyang, MD, PhD², Rachel E Story, MD, MPH¹, Jacqueline A Pongratic, MD¹, Xiumei Hong, MD, PhD², Guoying Wang, MD, PhD⁴, Colleen Pearson, BA³, Kathryn Ortiz, BA³, Howard Bauchner, MD³, and Xiaobin Wang, MD ScD²

¹Division of Allergy and Immunology, Children's Memorial Hospital, Chicago, IL.

²The Mary Ann and J. Milburn Smith Child Health Research Program, Children's Memorial Hospital and Children's Memorial Research Center, Chicago, IL.

³Department of Pediatrics, Boston University School of Medicine, and Boston Medical Center, Boston, MA.

⁴Center for Population Genetics, University of Illinois at Chicago School of Public Health, Chicago, IL

Abstract

Background—The relationship between the prenatal environment, maternal-fetal interaction, and allergic disease in the offspring remains understudied.

Objective—We sought to determine whether gestational diabetes modifies the risk of early childhood atopic manifestations including atopic dermatitis and allergen sensitization.

Methods—This study includes 680 children from the Boston Birth Cohort. Mother-child dyads were recruited at birth and followed prospectively to a mean age of 3.2±2.3 years with study visits aligned with the pediatric primary care schedule. The primary outcomes were physician diagnosed atopic dermatitis on standardized medical record abstraction and allergen sensitization based on Immunocap to 7 common foods and 5 common aeroallergens (sIgE 0.10 kUA/L, Phadia). Gestational diabetes was determined by standardized medical record review. Logistic regression analysis, stratified by term/preterm status, evaluated the association of gestational diabetes with atopic dermatitis and allergen sensitization respectively, controlling for maternal pre-pregnancy BMI, fetal growth, and pertinent covariates.

Results—Of the 680 children, 488 were term and 192 were preterm (<37 weeks gestation). Overall, 4.9% of the mothers developed gestational diabetes. Among the 680 children, 34.4% developed atopic dermatitis and 51% developed allergen sensitization. In term births, gestational diabetes was significantly associated with atopic dermatitis (OR, 95%CI=7.2, 1.5-34.5) and allergen sensitization (OR, 95%CI=5.7, 1.2-28.0). Adjusting for fetal growth had little effect. The association with sensitization was driven primarily by food sensitization (OR, 95%CI=8.3, 1.6-43.3). The above associations were not observed in preterm births.

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Corresponding Author: Rajesh Kumar MD Division of Allergy and Immunology 2300 Children's Plaza #60 Children's Memorial Hospital Chicago IL 60614 PH: 773 327 3710 Fax: 773 327 3790 rkumar@childrensmemorial.org.

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Conclusions—In term births, gestational diabetes increased the risk of atopic dermatitis and early childhood allergen sensitization, independent of maternal pre-pregnancy BMI and fetal growth.

Keywords

atopic dermatitis; eczema; food allergen sensitization; gestational diabetes

Introduction

It has been suggested that alternative factors to the “hygiene hypothesis” may contribute to the allergy epidemic.¹ As per the “Barker hypothesis”, prenatal maternal-fetal interactions and early life programming may have influences on disease later in life.² Prenatal maternal-fetal interactions and early life programming may be associated with the development of asthma or allergic diseases.³⁻⁸ A number of studies suggest an association of childhood obesity with early manifestations of atopy such as sensitization.^{9,10} However, the associations of prenatal/early life factors associated with maternal obesity and prenatal metabolic factors with allergic manifestations in the child remain poorly understood.

Maternal obesity has become very common with a 20% prevalence in the US,¹¹ and is associated with the development of gestational diabetes (GDM),¹² and fetal macrosomia in the offspring.¹³ GDM and large for gestational age (LGA) have been associated with wheezing and asthma.¹⁴⁻¹⁹ LGA has been associated with atopic sensitization, serum IgE,²⁰⁻²³ and atopic dermatitis.^{24, 25} Of these inter-related variables, GDM has not to date been associated with these early allergic manifestations.

The purpose of this study was to evaluate the association between GDM and early atopic manifestations such as atopic dermatitis and allergen sensitization, accounting for maternal pre-pregnancy BMI, fetal growth and other pertinent variables in the Boston Birth Cohort, a large, multi-ethnic, inner-city cohort. Since prematurity has effects on the immunologic system²⁶⁻²⁸ and seems to have variable associations with different atopic diseases,^{15, 29-31} we were conscientious to evaluate whether these associations vary by gestational age.

Methods

Patient Population

The Boston Birth Cohort was initiated in 1998 and recruitment is ongoing at the Boston University Medical Center (BMC). It is a multi-ethnic cohort (56% black, 11% white, and 20% Hispanic) which includes subjects from a range of socio-economic strata that includes inner-city poor up to middle class subjects.

The Boston Birth Cohort was originally designed to study adverse birth outcomes, particularly preterm birth. The inclusion criteria of the parent study are as follows: Any woman admitted to the Labor and Delivery floor at BMC who delivered a singleton live infant and met our case (gestational age <37 weeks or birth weight <2,500 grams) or control (gestational age ≥ 37 weeks with birth weight ≥ 2,500 grams) criteria was eligible.³² The Children’s Memorial Hospital (CMH) Institutional Review Board (IRB), the BMC IRB, and the Massachusetts Department of Public Health approved the parent study protocol. Under a separate CMH and BMC IRB approved study protocol and consent process, all infants enrolled in the Boston Birth Cohort are eligible for the postnatal follow-up study to determine postnatal health outcomes as detailed below.

Data Collection and Measurements

Recruitment of the Birth Cohort—Mother-infant pairs were recruited 24 to 48 hours post-delivery. After obtaining signed written informed consent, we interviewed subjects using a standardized questionnaire. We also reviewed maternal and infant medical records using a standardized abstraction form to obtain clinical data including ultrasound findings, placental pathology reports, laboratory reports, pregnancy complications, labor and delivery course, and birth outcomes.

Postnatal Follow-up Study—Those individuals who sought care at the BMC for primary or specialist care were invited to participate in the postnatal follow-up study starting in 2004.²⁸ After written informed consent was obtained from the biological mother, visits were scheduled at 6-12 mo, 2 yr, 4 yr, and 6 yr in alignment with the child's pediatric primary care visit schedule. Mothers were interviewed using standardized postnatal health questionnaires. We also reviewed the study child's medical record using a standard medical record abstraction form to obtain clinical data including type and date of visits, clinical diagnosis including ICD 9 codes, and growth parameters.

Determination of Gestational Diabetes—GDM was determined by standardized review of maternal pre- and perinatal medical records. All mothers in the cohort received care in the BMC labor and delivery ward. The availability of a unified electronic medical record with ICD9 coding of diagnoses provided information on maternal prenatal and peripartum conditions.

Assessment of Maternal BMI—Maternal BMI was calculated by pre-pregnancy weight and height obtained from the maternal postpartum questionnaire interview, and categorized into underweight (<18.5), normal (18.5-24.9), overweight (25-29.9) and obesity (≥ 30) according to standard WHO definitions.³³

Assessment of Fetal Growth—Fetal growth was based on estimate of standardized birth weight. Standardized birth weight (SBWT) is defined as birth weight standardized by mean and variance in the stratum of corresponding ethnic group, sex, and gestational week in the reference population using approximately 15,000 births born at BMC during 1998-2003.³⁴ Large for gestational age (LGA) was defined as SBWT >90th percentile of the SBWT in the reference population at the same gestational week.

Assessment of Gestational Age—Gestational age was assessed based on both the first day of the last menstrual period (LMP) as recorded in the maternal medical record and early (<20 weeks) prenatal ultrasound. This approach has been used in large hospital-based preterm studies and in our ongoing funded preterm studies.

Outcome Measures

Given the mean age of our subjects, we chose physician diagnosed atopic dermatitis as the primary outcome, as determined by standardized abstraction of the medical record. We also examined allergen sensitization at each recent follow-up visit, with the data from the most recent follow-up visit (mean age 3.2 years) used for this analysis. Allergen sensitization was defined as having specific IgE>0.10 kUA/L (Immunocap, Phadia) to at least one of the tested allergens, including food (egg white, milk, peanut, soy, shrimp, wheat, and walnut) and aeroallergens (*Dermatophyoides pteronyssinus* and *Dermatophyoides farinae*, German cockroach, cat, dog, and *Alternaria alternata*).

Statistical Analyses

A total of 1,262 children from the Boston Birth Cohort completed at least one postnatal follow-up visit. For the purposes of this study, only children who had specific IgE data for both food and aeroallergens were included to avoid confounding from undetected sensitization (n=680). However, their characteristics did not differ from the children who were excluded (online table #1). Children were categorized into three groups: children without atopic dermatitis and allergen sensitization (reference group), children with atopic dermatitis, and children with allergen sensitization. Of note, the outcome groups of atopic dermatitis and allergen sensitization were not mutually exclusive because 146 children had both atopic dermatitis and allergen sensitization.

To examine the association of GDM on atopic dermatitis and allergen sensitization, we performed multivariate logistic regression analysis, stratified by preterm and term status (<37 weeks for preterm and ≥37 weeks for term). We also performed a joint analysis by categorizing participants into four groups by term status and presence of GDM (with term and no GDM as a common reference group) to examine the joint association of GDM and preterm delivery on atopic outcomes.

Aside from the key determinant variables, potential confounding variables included infant and maternal factors which were retained in the model based on significance or repeated associations in prior literature. Infant factors included child's current age and sex, breastfeeding, antibiotics in the peripartum period, fetal growth, and type of delivery. Maternal factors included maternal ethnicity, family history (maternal and paternal) of atopic diseases, parity, socio-economic status (SES) as measured by highest level of maternal education achieved and maternal pre-pregnancy BMI. Of these covariates, delivery by cesarean section, maternal history of atopy, breastfeeding and SES (as determined by maternal education) were retained in the model despite lack of significance due to their prior associations with atopic disease in the literature.

Since maternal pre-pregnancy BMI, GDM, and fetal growth are inter-related variables, we included maternal pregnancy BMI (with normal BMI as the reference group) in the main model and added fetal growth in a secondary model respectively to determine if the effect of GDM on atopic phenotypes was independent of these factors.

As a secondary analysis, we carried out a nominal regression model to evaluate the effects of GDM on the outcomes of neither atopic dermatitis or sensitization, atopic dermatitis only, sensitization only, and the combined group with both sensitization and atopic dermatitis.

All analyses were carried out using statistical software SAS for Windows 8.20 (SAS Institute, NC).

Results

Baseline Characteristics of the Cohort

When we examine the mother-infant dyads in the entire cohort (n=1,262), this is a predominantly low income, minority population. Most (60.1%, n=759) mothers were African American, and 21.1% (n= 266) were Latino. The majority (81.4 %, n= 639) of mothers had an annual household income of <\$30,000. The mean age of children at follow up was 3.1 (SD 2.3) years of age with equal numbers of males and females. Prematurity was present in 28% of deliveries. The mean age of follow up of the children did not differ between term and preterm children with a mean (SD) age of follow up of 3.04 (SD 2.29) years and 3.08 (SD 2.24) years respectively. Of 1,262 births, 66 (5.3%) of the mother's had

pregnancies complicated by GDM, and 396 (31.4%) of the children developed atopic dermatitis.

When we limit our analyses to those 680 subjects who had specific IgE (sIgE) data available, 4.9% of mothers had gestational diabetes and 34.4% of infants developed atopic dermatitis. Based on sIgE, 51% were sensitized to at least one allergen (sIgE>0.1 kUA/L). If a cut point of 0.35 kUA/L is used, 44% were sensitized to at least one allergen. There was a high rate of maternal atopy in the cohort with 33.3 % of mothers having a history of an atopic disease including food allergy, atopic dermatitis, and asthma or rhinitis/hay fever.

Table 1 presents epidemiological and clinical characteristics of the children who had sIgE data. The table is stratified by the three groups of children, children without atopic dermatitis or sIgE to food allergen (reference group N=245)), children with atopic dermatitis (N=234), and children with sIgE to allergen (N=347). Of note, the groups of allergen sensitization and atopic dermatitis in this table are not mutually exclusive. Instead they describe the case groups for the separate outcomes of allergen sensitization and atopic dermatitis. The control group excludes all individuals with atopic dermatitis and known sIgE sensitization.

GDM (7.3%) was more frequent among mothers of the children who developed atopic dermatitis but this only approached statistical significance. However, after the analyses are stratified by gestational age as shown in figure 1, it becomes clear that GDM increases the risk of both atopic dermatitis and allergen sensitization in term infants, but has no effect in preterm infants. As a result, all subsequent analyses are stratified by preterm / term status.

Associations of Maternal GDM with Atopic Dermatitis

Table 2 displays the results of 2 separate analyses evaluating the associations of GDM with atopic dermatitis. In the stratified analyses by preterm status, term children exposed to GDM in-utero had a 7.90 times increased risk of developing atopic dermatitis (OR, 95%CI=7.90, 1.53-40.94; p=0.01) after adjusting for maternal BMI. After further adjustment for fetal growth the effect size was slightly diminished (OR, 95%CI=5.86, 1.07-32.05, p=0.0412).

To better understand these findings, we also evaluated whether GDM and gestational age had a joint effect on the outcomes as shown in the second column of analyses in Table 2. Compared to term infants without GDM, prematurity alone was not associated with atopic dermatitis (OR=0.75, 95% CI 0.46-1.22). The combination of preterm status and GDM together was not associated with atopic dermatitis (OR=0.33, 95% CI 0.06-1.81). Again, the highest risk was found in term children born to mothers with GDM (OR=7.38, 95% CI 1.53-35.71; p=0.01). This finding was unchanged on the analysis adjusting for fetal growth (OR=6.50, 95% CI 1.30-32.57; p=0.02). This is consistent with the findings of our stratified analysis.

Associations of Maternal GDM with Allergen Sensitization

We performed similar analysis for the outcome of allergen sensitization. As shown in Table 3, in the stratified analyses, term children exposed to GDM in-utero had a 6 times increased risk of allergen sensitization (OR, 95%CI=6.05, 1.17-31.18; p=0.03). After adjustment for fetal growth the result was no longer significant, but effect size was only slightly diminished (OR, 95%CI=4.85, 0.91-25.84, p=0.06). To better understand these findings, we also evaluated whether GDM and gestational age had a joint effect on the outcomes as shown in the second column of analyses in Table 3. Compared to term infants without GDM, prematurity alone was not associated with allergen sensitization (OR=1.00, 95% CI 0.65-1.52). The combination of preterm status and GDM was not associated with allergen

sensitization (OR=0.32, 95% CI 0.07-1.39). The direction of these findings is again consistent with the findings of our stratified analysis.

Associations of Maternal GDM on Food and Environmental Allergen Sensitization in Children

Table 4 presents the results of stratified and joint analyses of the effects of GDM on food allergen sensitization and aeroallergen sensitization, respectively. In term infants, GDM was associated with greater risk of food allergen sensitization (OR=8.28, 95% CI 1.59-43.20; $p=0.01$). The association with aeroallergen sensitization (OR=5.66, 95% CI 1.01-31.63; $p=0.05$) was of borderline significance. There were no effects seen in preterm children. Again, there was no evidence of a joint effect of preterm delivery and GDM in this population.

Sensitivity analysis with a cut point of 0.35 vs. 0.1 kUA/L

In addition to using a cut point of 0.1 kUA/L, we also carried out a sensitivity analysis using a cut-off of 0.35 kUA/L as a definition of sensitization in the analyses. These results are presented in Online Tables 2 and 3, and show that the direction and significance of the effects is largely unchanged. The only exception is that the findings for aeroallergen sensitization became non-significant. Our data suggest that this study was not affected significantly by nonspecific antibody binding in the range between 0.1 kUA/L and 0.35 kUA/L.

Secondary Analysis of Associations of GDM by Nominal Regression

We carried out a nominal regression model, re-organizing the subjects into 4 groups: controls, atopic dermatitis only, sensitization only, and individuals with both sensitization and atopic dermatitis. The results are presented in Online Table 4. The odds ratio for those with atopic dermatitis and sensitization is increased (OR= 7.15, 95% CI 1.26-40.48). The effects for atopic dermatitis only (OR= 5.56, 95% CI 0.81- 38.32) and sensitization (OR= 2.06, 95% CI 0.30-14.20) only are no longer significant though the odds ratios are in the same direction, possibly due to smaller sample size.

Discussion

In this prospective birth cohort study, we found that gestational diabetes was significantly associated with increased risk of early childhood atopic dermatitis, and sensitization to both food- and aero-allergens **in term infants** even after accounting for maternal pre-pregnancy BMI and fetal growth status. Specifically, term infants of pregnancies with GDM have a 7.57 fold increased risk of developing atopic dermatitis, and a 5.91 fold increased risk of allergen sensitization. Furthermore, only a minority of this effect seen in term infants, was accounted for by the inclusion of fetal growth as a covariate. These data suggest that, at least in term infants, prenatal metabolic risk factors increase the risk of allergic disease and sensitization in early life.

While our findings on GDM and atopic dermatitis, and sensitization to both food- and aero-allergens are novel, other findings are in general consistent with previous studies. Our findings that LGA was not associated with atopic dermatitis status is consistent with a number of other studies.^{35, 36} However, it is notable that some studies have found an association of birth weight, birth length and ponderal index with atopic sensitization and serum IgE,²⁰⁻²³ and a few others have found an association of LGA with atopic dermatitis.^{24, 25} Notably, these studies did not evaluate the role of GDM in addition to that of LGA. Furthermore, while maternal pre-pregnancy weight may influence the rates of

gestational diabetes,¹² in our analyses, the effects of GDM were independent of maternal pre-pregnancy BMI. The association of GDM with early childhood atopy mirrors some findings in a large Dutch epidemiological study of adults which found that insulin resistance may have mediated the association of obesity on allergen sensitization.¹⁰

Interestingly, we did not find any associations of GDM with atopic dermatitis and allergen sensitization in preterm infants. The direction of the effect was in an opposite direction than the term children. Thus, it is unlikely that the lack of a similar effect in preterm infants is purely due to sample size. It is unclear if this is due to the duration of exposure to the insult or susceptibility to the insult at a particular point of immunological development. The fact that the effect of GDM was only seen in the term infants is consistent with the known effects of GDM on other disorders. Specifically, only hyperglycemia in the last trimester of pregnancy has been associated with augmented fetal growth.³⁷ The differential findings between term and preterm births may also be due to non-controlled confounders such as antenatal steroids and early life feeding patterns, such as differences in duration and exclusivity of breastfeeding.

The biological mechanism by which GDM affects atopic dermatitis and allergen sensitization remains unclear. The fact that the effect of GDM was still significant despite the inclusion of LGA in the model implies that the effects are likely due to exposure to GDM in utero but unlikely to occur via the same pathway which leads to fetal macrosomia. Other pathways need to be considered. Mothers with GDM have higher levels of TNF-alpha, leptin, and visfatin as well as lower levels of adiponectin.³⁸⁻⁴⁰ Adiponectin attenuates allergic inflammation in murine models.⁴¹ Thus, it is possible that altered levels of adipokines associated with GDM may have some effect on immunological development in infancy. Future studies will need to be carried out to evaluate these questions. Also, food allergen sensitization accounted for most of the impact of GDM on sensitization. The effect on aeroallergen sensitization was at best of borderline significance, and was no longer significant when a cut-off of 0.35 kUA/L was used to define sensitization instead of 0.1 kUA/L. It has been hypothesized that atopic dermatitis may augment food allergen sensitization.¹ This hypothesis could suggest a reason for a differential effect on food and aeroallergen sensitization. This is consistent with our secondary analysis which found a larger effect of GDM in those with both atopic dermatitis and sensitization. There was less of an effect in those with atopic dermatitis only, and no clear effect on those with sensitization only. It is possible that some of the effect of GDM on sensitization may be via atopic dermatitis.

A particular strength of the Boston Birth Cohort is that it is a prospectively followed cohort with large numbers of inner-city minority subjects, and detailed and extensive phenotyping of pre- and peri-natal clinical data, including postnatal atopic phenotypes. However, our study has the following limitations: first, the data used to evaluate pre-pregnancy BMI was derived from self reported height and weight. This could lead to a systematic lowering of maternal BMI's since individuals tend to underreport weight by up to 5 pounds.^{42, 43} While it is possible that this may lead to some residual confounding, the effect size for GDM was not diminished by the inclusion of maternal BMI in the final analysis. Second, despite the large number of children included in this report, the number of children born to mothers with GDM is relatively small. The smaller numbers in this group resulted in larger confidence intervals for our effects. Replication in even larger cohorts would be important. Another limitation is the duration of follow-up. The mean age of the children at follow-up was 3.2 years of age. While some children may not have developed the outcomes of interest by the time of follow up, studies such as the Multi-center Allergy Study suggest that most children who develop eczema will do so within the first 2 years of life.⁴⁴ Also, other birth cohorts also found a significant number children to be sensitized within the first two years of

life.⁴⁵⁻⁴⁷ Other questions may arise around the choice of a cut point of 0.1 kUA/L as evidence of sensitization. We obtained very similar findings in a sensitivity analysis with a cut point of 0.35 kUA/L, suggesting that our findings were not a function of nonspecific binding of the assay between 0.1 kUA/L and 0.35 kUA/L. Finally, caution should be exercised when generalizing our study findings to other populations since there was a high proportion of African-American and Latino subjects in our cohort, and most individuals were living in the inner city.

In summary, we found an association between GDM, a prevalent risk factor in inner-city populations, and the development of atopic dermatitis and sensitization to allergens, specifically food allergens, in the offspring. This is of great interest since the allergy and the obesity /metabolic syndrome epidemics are co-incident in westernized societies. Our findings suggest that there may be an early life link between these two epidemics. If replicated, our findings may open a new area for future investigation and offer a new potential for early prediction and prevention of allergic diseases.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations used

BBC	Boston birth cohort
BMI	body mass index
BMC	Boston University Medical Center
FGR	fetal growth restriction
IUGR	intrauterine growth restriction
GDM	gestational diabetes
LGA	large for gestational age
LMP	last menstrual period
SBWT	standardized birth weight
sIgE	specific IgE
SES	socio-economic status

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Clinical Implications: Gestational diabetes may predispose to both allergen sensitization and atopic dermatitis in the offspring. Children affected by gestational diabetes may be at high risk for these atopic conditions.

Capsule Summary: In a prospective, inner-city birth cohort study of 680 children, Kumar et al found that gestational diabetes was associated with an increased risk of atopic dermatitis and allergen sensitization in the offspring, independent of maternal pre-pregnancy BMI.

Figure 1. Prevalence of atopic dermatitis and food allergen sensitization in children with and without GDM stratified by term / preterm Status

Term children are represented by the solid bars. Preterm children are represented by the striped bars. The black solid and striped bars represent the prevalence of atopic dermatitis in term and preterm children respectively. The grey solid and striped bars represent the prevalence of allergen sensitization in term and preterm children respectively.

Table 1Description of infant/ perinatal factors and maternal factors by atopic dermatitis and any sensitization^f

	No atopic dermatitis/ No any sensitization (n=245)	Atopic dermatitis (n=234)	Any sensitization (n=347)
Infant / Peri-natal Factors			
	mean (SD)		
Age (years)	2.9 (2.2)	3.6 (2.3)	3.5 (2.3)
	N (%)		
Gender			
female	135(55.1)	107(45.7)	166(47.8)
male	110(44.9)	127(54.3)	181(52.2)
Fetal growth			
normal	175(71.4)	177(76.0)	279(80.6)
FGR	49(20.0)	29(12.4)	37(10.7)
LGA	21(8.6)	27(11.6)	30(8.7)
Preterm	75(30.6)	56(23.9)	97(28.0)
Delivery by cesarean section	73(29.9)	70(30.2)	114(33.8)
Peripartum antibiotics use	115(50.4)	77(36.2)	120(38.7)
Breast or bottle feed			
Breast feeding	79(69.9)	72(84.7)	112(79.4)
Bottle only	34(30.1)	13(15.3)	29(20.6)
Maternal Factors			
	N (%)		
GDM	10(4.1)	17(7.3)	16(4.6)
Race			
black	169(69.0)	173(73.9)	260(74.9)
Other	76(31.0)	61(26.1)	87(25.1)
Parity			
0	87(35.5)	100(42.7)	159(45.8)
1	158(64.5)	134(57.3)	188(54.2)
Family history of atopic diseases, yes	94(38.7)	81(35.1)	120(34.8)
Maternal prepregnancy BMI (kg/m ²)			
<18.5	12(4.9)	4(1.7)	13(3.7)
18.5 to <25	108(44.1)	102(43.6)	145(41.8)
25 to <30	64(26.1)	70(29.9)	117(33.7)
30	61(24.9)	58(24.8)	72(20.7)
Household income			
<\$30,000	125(80.1)	116(83.5)	173(86.1)
\$30,000	31(19.9)	23(16.5)	28(13.9)
Education			

	No atopic dermatitis/ No any sensitization (n=245)	Atopic dermatitis (n=234)	Any sensitization (n=347)
Infant / Peri-natal Factors			
<high school	75(31.0)	74(32.2)	110(32.3)
high school	88(36.4)	78(33.9)	124(36.4)
>high school	79(32.6)	78(33.9)	107(31.4)

¹The groups of food allergen sensitization and atopic dermatitis in this table are not mutually exclusive. Instead they describe the case groups for each analysis. Maternal history of atopic diseases included food allergy, atopic dermatitis, asthma, and hay fever. Fetal growth restriction (FGR) is defined as SBWT <10th percentile of the SBWT in the reference population at the same gestational week.

Large for gestational age (LGA): is defined as SBWT >90th percentile of the SBWT in the reference population at the same gestational week.

Standardized birth weight (SBWT) is defined as birth weight standardized by mean and variance in the stratum of corresponding ethnic group, sex, and gestational week in the reference population using around 15,000 births born at BMC during 1998-2003.

Table 2

Association of maternal GDM with atopic dermatitis

Atopic dermatitis (AD) including adjustment for maternal BMI									
Stratified analysis							Joint analysis		
Term/ Preterm Status	Total N	AD N	(%)	OR	(95% CI)	P value	OR	(95% CI)	P value
Term									
No GDM	330	164	49.7	1.00			1.00		
GDM	18	14	77.8	7.90	1.53,40.94	0.0138	7.38	1.53,35.71	0.0129
Preterm									
No GDM	122	53	43.4	1.00			0.75	0.46,1.22	0.2415
GDM	9	3	33.3	0.60	0.10,3.65	0.5821	0.33	0.06,1.81	0.1997

Atopic dermatitis (AD) including adjustment for maternal BMI and fetal growth									
Stratified analysis							Joint analysis		
Term/ Preterm Status	Total N	AD N	(%)	OR	(95% CI)	P value	OR	(95% CI)	P value
Term									
No GDM	330	164	49.7	1.00			1.00		
GDM	18	14	77.8	5.86	1.07,32.05	0.0412	6.50	1.30,32.57	0.0228
Preterm									
No GDM	122	53	43.4	1.00			0.68	0.41,1.11	0.1232
GDM	9	3	33.3	0.74	0.11,4.91	0.7554	0.27	0.05,1.52	0.1361

Basic model is adjusted for children's age, sex, maternal race (black/other), maternal education (<high school, high school, >high school), breast-feeding (breast/bottle feeding), peripartum antibiotics use (yes, no), family (paternal or maternal) history of atopic diseases (including food allergy, atopic dermatitis, asthma, and hay fever), parity (0, >=1), delivery by cesarean section, prepregnancy BMI (<18.5, 18.5 to <25, 25 to <30 and >=30).

Fetal growth was characterized by use of standardized birth weight. Standardized birth weight (SBWT) is defined as birth weight standardized by mean and variance in the stratum of corresponding ethnic group, sex, and gestational week in the reference population using around 15,000 births born at BMC during 1998-2003.

Fetal growth restriction (FGR) is defined as SBWT <10th percentile of the SBWT in the reference population at the same gestational week.

Large for gestational age (LGA): is defined as SBWT >90th percentile of the SBWT in the reference population at the same gestational week.

Table 3

Association of maternal GDM with allergen sensitization in children

Sensitization including adjustment for maternal BMI									
Stratified analysis					Joint analysis				
Term/ Preterm Status	Total N	Sensitization N	(%)	OR	P value	OR	(95% CI)	P value	
Term									
No GDM	403	237	58.8		1.00	1.00			
GDM	17	13	76.5	6.05	1.17,31.18	0.031	5.81	1.18,28.61	0.0304
Preterm									
No GDM	163	94	57.7	1.00		1.01	0.65,1.52		0.9957
GDM	9	3	33.3	0.33	0.07,1.60	0.1614	0.32	0.07,1.39	0.1281

Sensitization including adjustment for maternal BMI and fetal growth									
Stratified analysis					Joint analysis				
Term/ Preterm Status	Total N	Cases N	(%)	OR	P value	OR	(95% CI)	P value	
Term									
No GDM	403	237	58.8	1.00		1.00			
GDM	17	13	76.5	4.85	0.91,25.84	0.0643	5.29	1.04,26.77	0.0441
Preterm									
No GDM	163	94	57.7	1.00		0.90	0.59,1.39		0.6404
GDM	9	3	33.3	0.37	0.07,1.88	0.2300	0.26	0.06,1.17	0.0788

Basic model is adjusted for children's age, sex, maternal race (black/other), maternal education (<high school, high school, >high school), breast-feeding (breast/bottle feeding), peripartum antibiotics use, family (maternal or paternal) history of atopic diseases (including food allergy, atopic dermatitis, asthma, and hay fever), parity (0,>=1), delivery by cesarean section, prepregnancy BMI (<18.5, 18.5 to <25, 25 to <30 and >= 30).

Fetal growth was characterized by use of standardized birth weight. Standardized birth weight (SBWT) is defined as birth weight standardized by mean and variance in the stratum of corresponding ethnic group, sex, and gestational week in the reference population using around 15,000 births born at BMC during 1998-2003.

Fetal growth restriction (FGR) is defined as SBWT <10th percentile of the SBWT in the reference population at the same gestational week.

Large for gestational age (LGA): is defined as SBWT >90th percentile of the SBWT in the reference population at the same gestational week.

Table 4

Evaluation of association of maternal GDM with food allergen and aeroallergen sensitization in children

		Food Sensitization								
		Stratified analysis					Joint analysis			
Term/ Preterm Status	Total N	Cases N	(%)							
Term										
No GDM	349	183	52.4	1.00			1.00			
GDM	17	13	76.5	8.28	1.59,43.20	0.0121	7.72	1.56,38.16	0.0122	
Preterm										
No GDM	131	62	47.3	1.00			0.90	0.57,1.45	0.6650	
GDM	8	2	25.0	0.26	0.04,1.64	0.1513	0.30	0.05,1.62	0.1618	
Aeroallergen sensitization										
		Stratified analysis					Joint analysis			
Term/ Preterm Status	Total N	Cases N	(%)							
Term										
No GDM	313	147	47.0	1.00			1.00			
GDM	13	9	69.2	5.66	1.01,31.63	0.0484	5.34	0.98,29.09	0.0530	
Preterm										
No GDM	132	63	47.7	1.00			0.86	0.53,1.40	0.5408	
GDM	8	2	25.0	0.38	0.07,2.19	0.2810	0.29	0.05,1.64	0.1625	

Adjusted for children's age, sex, maternal race (black/others), maternal education (<high school, high school, >high school), breast-feeding (breast/bottle feeding), peripartum antibiotics use, family (maternal or paternal) history of atopic diseases (including food allergy, atopic dermatitis, asthma, and hay fever), parity (0, >=1), delivery by cesarean section, prepregnancy BMI (<18.5, 18.5 to <25, 25 to <30 and >= 30).