

Maternal Asthma, its Control and Severity in Pregnancy, and the Incidence of Atopic Dermatitis and Allergic Rhinitis in the Offspring

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Objective To evaluate the relationship between maternal asthma, its level of control and severity during pregnancy, and atopic dermatitis (AD) and allergic rhinitis (AR) incidence in children.

Study design A cohort of 26 265 singletons born to mothers with and without asthma (1990–2002) was constituted by use of 3 Quebec databases. Mothers with asthma had to have received ≥ 1 diagnosis and ≥ 1 prescription for asthma 2 years before or during pregnancy. Asthma control and severity during pregnancy was based on validated indexes. ICD-9 codes 691 and 477 allowed us to identify cases of AD and AR.

Results Maternal asthma during pregnancy was associated with an increased AD risk (adjusted hazard ratio: 1.11, 95% confidence interval: 1.02–1.21), but not of AR (adjusted hazard ratio: 1.04, 95% confidence interval: 0.91–1.20) in children. Asthma control and severity were not associated with either outcome. Maternal AR and intranasal corticosteroid use during pregnancy increased the risk of childhood AR by 70% and 45%.

Conclusions Children of mothers with asthma or AR during pregnancy should be closely monitored to diagnose and treat AD and AR as early as possible. (*J Pediatr* 2009; ■: ■–■).

Atopic conditions, such as atopic dermatitis (AD) and allergic rhinitis (AR), are well known to cluster in families.^{1–3} Having a parent who has an atopic condition, especially in the mother, increases the risk of a child to develop an atopic condition up to 4-fold.^{3–10} Although most studies have looked at maternal history of asthma or atopy, there are few instances where AD and AR development was investigated in relation to atopic conditions during pregnancy. In addition, no study has further assessed the risk of AD or AR among children of mothers with asthma.

The uterine environment has been recognized as having an impact on the propensity of a child to develop atopic conditions later in life.¹¹ There is evidence that maternal asthma status during pregnancy may have an influence on the incidence of atopic conditions in children, as demonstrated in a previous study that concluded that the lack of control and increased severity of asthma during pregnancy was associated with an increased risk of childhood asthma.¹² To our knowledge, no study has assessed whether the level of control and severity of asthma during pregnancy was associated with the development of AD and AR in the offspring. Thus the aim of this study was to further characterize the association between asthma during pregnancy, its level of severity and control, and the incidence of AD and AR in children up to 10 years old.

Methods

Two cohort studies were independently conducted with interlinked data from 3 administrative databases of Quebec, Canada. The Régie de l'assurance-maladie du Québec provides information on medical services for all Quebec residents and dispensed medications for Quebec residents covered by governmental insurance (approximately 43% of the population), including recipients of social assistance and elderly citizens (since 1980) and workers and their families without access to a private drug insurance plan (adherents: they obtain coverage under the public drug plan since January 1997). MED-ECHO provides information on acute care hospitalizations for all Quebec residents, and the Birth and Death Registry, information on births and stillbirths.

A cohort of pregnancies was first constituted by use of these databases.^{12,13} All women with asthma and a sample of those without asthma who had at least 1 singleton pregnancy and who delivered a live-born infant between 1990 and 2002 were included in the cohort. To be considered as having asthma during pregnancy, a woman had to have filled at least 1 prescription and have received at least

AD	Atopic dermatitis
AR	Allergic rhinitis
HR	Hazard ratio
INS	Intra-nasal corticosteroids
95%CI	95% confidence interval

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1 diagnosis (ICD-9 code: 493) for asthma either 2 years before or during the pregnancy of interest. To be considered as without asthma, a woman should not have received any diagnostic code for asthma, nor filled a prescription for an asthma medication during the 1990 to 2002 follow-up period.

The cohort of pregnancies was then restricted to only 1 pregnancy per woman, the closest to 2002, to avoid correlation between children of the same mothers. Two subcohorts of children, born to women with and without asthma from the above-mentioned cohort of pregnancies, were subsequently formed. In each of the subcohorts, children were followed up from birth until the end of drug insurance coverage, 10th birthday, December 31, 2002, or a diagnosis of an atopic condition (either AD or AR, depending on the outcome studied), whichever occurred first. Approvals from the Hôpital du Sacré-Coeur's ethics board and the Commission d'accès à l'information du Québec were obtained before proceeding with the study.

Exposure

The main exposure was the presence of maternal asthma during pregnancy, as previously defined. Maternal asthma during pregnancy was also further characterized by level of control and severity, measured with validated indexes on the basis of the Canadian Asthma Guidelines.^{14,15} Non-control of maternal asthma was mainly defined through the use of high doses/week of inhaled short-acting β_2 -agonists, filled prescriptions of oral corticosteroids, or emergency department visits or hospitalizations for asthma, whereas maternal asthma severity was characterized with the daily dose of inhaled corticosteroids and the use of other asthma controller medications (theophylline, long-acting β_2 -agonists, leukotriene-receptor antagonists) throughout pregnancy.

Three levels of control and severity of maternal asthma were selected: mild controlled (reference category for analyses made among children of mothers with asthma), mild uncontrolled, and moderate-to-severe asthma. Globally, mild asthma is characterized by lower doses of short-acting β_2 -agonists (SABA; less than 4 doses/wk) and of inhaled corticosteroids (ICS; less than 500 μ g/d). Moderate-to-severe asthma implies higher doses of ICS combined with other asthma controller medications (theophylline, long-acting β_2 -agonists, leukotriene-receptor antagonists). High number of doses of SABA, use of oral corticosteroids, emergency department visits, and hospitalizations for asthma are considered as markers of lack of asthma control.¹⁵

Outcomes

Two outcomes were independently investigated. A child was considered as having incident AD when ICD-9 diagnostic code "691" (Atopic dermatitis and related conditions) was recorded in the Régie de l'assurance-maladie du Québec or MED-ECHO databases. Similarly, for the study of the incidence of AR, ICD-9 code "477" (Allergic rhinitis) was used.

Potential Confounding Variables

A systematic review of the literature allowed us to identify 22 potential confounding variables to be included in the multivariate analyses. Child-related variables were sex (male/female), small-for-gestational-age (≤ 10 th percentile: yes/no), childhood asthma diagnosis (time-dependent variable), childhood AR or AD diagnosis (time-dependent variables, depending on the outcome under study), and having filled at least 1 antibiotic prescription up to 6 months after birth (time-dependent variable). Maternal sociodemographic characteristics included maternal age at conception (18-34 vs ≥ 35 years old), receiving social assistance in the year before or during pregnancy (yes/no), education level at delivery (<12 , 12-15, >15 years completed), and living in a rural area in the year before or during pregnancy (yes/no). Pregnancy-related variables included intranasal corticosteroid use (INS) during pregnancy (yes/no), mean number of antibiotics prescribed per month during pregnancy (continuous), parity (multiparity/nulliparity), number of prenatal visits (0-5, 6-16, >16 visits), at least 1 obstetrician visit during pregnancy (yes/no), mode of delivery (vaginal delivery, unplanned cesarean section, planned cesarean section), and having a pregnancy in the preceding year (yes/no). Finally, maternal medical conditions studied were AD (yes/no) and allergic rhinitis (AR; yes/no) in the 2 years before or during pregnancy, chronic hypertension (yes/no), diabetes mellitus (yes/no), pregnancy-induced hypertension (yes/no), and gestational diabetes (yes/no).

Statistical Analyses

Crude rates of AD and AR were initially estimated for children of mothers with and without asthma respectively, as well as for the different levels of control and severity of maternal asthma. The association between the main exposure, maternal asthma during pregnancy, and the incidence of AD and AR in children was investigated in 2 independent Cox proportional hazard regression models. Secondary analyses were performed for children of mothers with asthma only. The association between the level of control and severity of maternal asthma and each of the 2 outcomes was investigated independently with 2 Cox proportional hazard regression models.

For each analysis, crude and adjusted hazard ratios (HR) of AD and AR were obtained, and, for multivariate regression models, backward selection of potential confounding variables was used.¹⁶ A full model including all variables was first analyzed. Variables were removed manually, one by one, starting with the variable that had the highest *P* value. During this process, we ensured that removing a variable did not affect the main adjusted estimates (estimates of the exposure) in a substantial manner. The final reduced model was obtained when no additional variable could be removed from the model. Confidence intervals at 95% were calculated for all rates and HRs. All analyses were performed with SAS 9.1 (SAS Institute, Cary, North Carolina).

Table I. Characteristics of mothers and children of the cohorts

	Children of mothers with asthma during pregnancy				Children of mothers without asthma (n = 18 039)
	All children of mothers with asthma (n = 8226)	Mild controlled maternal asthma (n = 5249)	Mild uncontrolled maternal asthma (n = 1556)	Moderate-to-severe maternal asthma (n = 1421)	
Child					
Asthma	2681 (32.6%)	1579 (30.1%)	526 (33.8%)	576 (40.5%)	2545 (14.1%)
Male sex	4139 (50.3%)	2638 (50.3%)	774 (49.7%)	727 (51.2%)	9308 (51.6%)
Small-for-gestational-age	1146 (13.9%)	684 (13.0%)	206 (13.2%)	256 (18.0%)	1770 (9.8%)
≥ 1 antibiotic prescription filled within the first 6 months of life	2793 (34.0%)	1745 (33.2%)	543 (34.9%)	505 (35.5%)	4129 (22.8%)
Maternal sociodemographics					
≥ 35 years old at conception	647 (7.9%)	379 (7.2%)	123 (7.9%)	145 (10.2%)	2072 (11.5%)
Social assistance	6386 (77.6%)	4033 (76.8%)	1221 (78.5%)	1132 (79.7%)	9953 (55.2%)
Education					
Missing	547 (6.7%)	343 (6.5%)	110 (7.0%)	94 (6.6%)	1245 (6.9%)
<12 years	4701 (57.2%)	3034 (57.8%)	877 (56.4%)	790 (55.6%)	7318 (40.6%)
12-15 years	2529 (30.7%)	1571 (29.9%)	489 (31.4%)	469 (33.0%)	7201 (39.9%)
>15 years	449 (5.5%)	301 (5.7%)	80 (5.1%)	68 (4.8%)	2275 (12.6%)
Living in rural area	1588 (19.3%)	993 (18.9%)	313 (20.1%)	282 (19.9%)	4098 (22.7%)
Pregnancy-related characteristics					
Intra-nasal corticosteroids use	667 (8.1%)	315 (6.0%)	161 (10.4%)	191 (13.4%)	294 (1.6%)
Number of antibiotic prescriptions filled (mean [SD])	0.82 (1.06)	0.70 (0.96)	0.96 (1.10)	1.12 (1.27)	0.35 (0.70)
Multiparity	6122 (74.4%)	3946 (75.2%)	1169 (75.1%)	1007 (70.9%)	12 921 (71.6%)
Number of prenatal visits					
0-5 visits	1168 (14.2%)	746 (14.2%)	221 (14.2%)	201 (14.1%)	2883 (16.0%)
6-16 visits	6617 (80.4%)	4244 (80.9%)	1239 (79.6%)	1134 (79.8%)	14 573 (80.8%)
>16 visits	441 (5.4%)	259 (4.9%)	96 (6.2%)	86 (6.1%)	583 (3.2%)
Obstetrician visit during pregnancy	6795 (82.6%)	4323 (82.4%)	1286 (82.7%)	1186 (83.5%)	14 593 (80.9%)
Mode of delivery					
Vaginal delivery	6566 (79.8%)	4221 (80.4%)	1248 (80.2%)	1097 (77.2%)	14 765 (81.8%)
Unplanned C-section	897 (10.9%)	574 (10.9%)	155 (10.0%)	168 (11.8%)	1838 (10.2%)
Planned C-section	763 (9.3%)	454 (8.7%)	153 (9.8%)	156 (11.0%)	1436 (8.0%)
Pregnancy in the preceding year	557 (31.1%)	1718 (32.7%)	452 (29.1%)	387 (27.2%)	4430 (24.6%)
Maternal medical conditions					
Allergic rhinitis	667 (8.1%)	395 (7.5%)	143 (9.2%)	129 (9.1%)	520 (2.9%)
Atopic dermatitis	130 (1.6%)	74 (1.4%)	26 (1.7%)	30 (2.1%)	166 (0.9%)
Chronic hypertension	210 (2.6%)	132 (2.5%)	30 (1.9%)	48 (3.4%)	247 (1.4%)
Pregnancy-induced hypertension	531 (6.5%)	312 (5.9%)	110 (7.1%)	109 (7.7%)	933 (5.2%)
Diabetes mellitus	219 (2.7%)	131 (2.5%)	40 (2.6%)	48 (3.4%)	279 (1.6%)
Gestational diabetes	690 (8.4%)	401 (7.6%)	158 (10.2%)	131 (9.2%)	1349 (7.5%)

Results

The cohort of 26 265 children comprised 8226 children of mothers with asthma and 18 039 children of mothers without asthma during pregnancy. The level of asthma control and severity during pregnancy among mothers with asthma was mild controlled for 5249 mothers (63.8%), mild uncontrolled for 1556 mothers (18.9%), and moderate-to-severe for 1421 mothers (17.3%). Overall, in the cohorts, AD was diagnosed in 10.0% (95%CI: 9.3%-10.6%) and 8.4% (95%CI: 8.0%-8.8%) of children born to mothers with and without asthma, respectively. Corresponding figures for AR diagnosis were 5.1% (95%CI: 4.6%-5.5%) and 3.6% (95%CI: 3.3%-3.8%), respectively.

Table I displays characteristics of the cohorts of children of mothers with and without asthma. Cohorts were similar according to several characteristics, but a higher proportion of children of mothers with asthma had development of asthma, were born small-for-gestational age, had filled at least 1 antibiotic prescription up to 6 months after birth, and had

a mother receiving social assistance and who had a lower degree of education compared with children of mothers without asthma. Also, a higher proportion of mothers with asthma had filled prescriptions of INS and antibiotics during pregnancy, had given birth in the preceding year, and had received diagnoses of AR, AD, chronic hypertension, diabetes mellitus, pregnancy-induced hypertension and gestational diabetes. **Table I** also displays the characteristics of children of mothers with asthma according to the level of control and severity of maternal asthma. Again, there were many similarities between these children, but comparing with children of mothers who had mild controlled or uncontrolled asthma during pregnancy, a higher proportion of those born to mothers with moderate-to-severe asthma had development of asthma and were born small-for-gestational-age. Additionally, a higher proportion of mothers with moderate-to-severe asthma had used INS and had filled antibiotic prescriptions during pregnancy.

Table II shows crude rates of AD were 2.9 and 2.6 per 100 persons per year in children born to mothers with and

Table II. Crude rates of AD and AR in the cohorts

	AD			AR		
	Number of cases	Person-years	Rate* (95%CI)	Number of cases	Person-years	Rate* (95%CI)
Children of mothers with asthma during pregnancy	822	28 415	2.89 (2.70; 3.09)	416	30 164	1.38 (1.25; 1.51)
Mild controlled	511	17 252	2.96 (2.71; 3.22)	251	18 291	1.37 (1.20; 1.54)
Mild uncontrolled	165	5590	2.95 (2.50; 3.40)	78	5969	1.31 (1.02; 1.60)
Moderate-to-severe	146	5572	2.62 (2.20; 3.05)	87	6903	1.47 (1.00; 1.53)
Children of mothers without asthma	1517	58 498	2.59 (2.46; 2.72)	641	61 545	1.04 (0.96; 1.12)

*Rates are per 100 persons per year.

without asthma, respectively, whereas those of AR were 1.4 and 1.0, respectively. No statistically significant trends in the rates of AD and AR were observed according to the increasing level of severity and of lack of control of asthma during pregnancy, for children of mothers with asthma.

Multivariate analyses indicate that children born to mothers who had asthma during pregnancy had an 11%

increased risk for development of AD in their first 10 years of life compared with those born to mothers without asthma (**Table III**). Statistically significant increases in the risk for development of AD were also seen if the child had received previous diagnoses of asthma and AR, had filled at least 1 antibiotic prescription up to 6 months after birth, and had a mother who consulted an obstetrician, had more than 16

Table III. Crude and adjusted HR for the association between maternal asthma during pregnancy and the incidence of AD and AR in the offspring

	AD		AR	
	Crude HR	Adjusted HR (95%CI)	Crude HR	Adjusted HR (95%CI)
Maternal asthma during pregnancy	1.16	1.11 (1.02; 1.21)	1.32	1.04 (0.91; 1.20)
Child characteristics				
Atopic dermatitis	N/A	N/A	1.58	1.39 (1.15; 1.67)
Allergic rhinitis	1.82	1.67 (1.25; 2.25)	N/A	N/A
Asthma	1.23	1.16 (1.00; 1.35)	1.93	1.73 (1.49; 2.01)
Male sex	0.92	0.91 (0.84; 0.99)	1.20	1.14 (1.01; 1.29)
Small-for-gestational-age	0.88	0.87 (0.76; 1.00)	0.86	—
≥1 antibiotic prescription filled within the first 6 months of life	1.14	1.12 (1.01; 1.23)	1.28	1.16 (1.02; 1.33)
Maternal sociodemographics				
≥ 35 years old at conception	1.11	—	0.79	—
Social assistance	1.07	—	0.78	0.76 (0.64; 0.90)
Education				
Missing	1.19	—	0.84	—
<12 years	0.95	—	0.86	—
12-15 years	0.88	—	0.93	—
>15 years	Reference	—	Reference	—
Living in rural area	0.64	0.68 (0.61; 0.76)	0.68	0.74 (0.62; 0.87)
Pregnancy-related characteristics				
Intranasal corticosteroids use	1.09	—	2.05	1.45 (1.11; 1.89)
Number of antibiotic prescriptions filled (each additional prescription)	1.01	—	1.14	1.08 (1.01; 1.15)
Multiparity	0.87	0.87 (0.79; 0.95)	0.73	0.74 (0.64; 0.84)
Number of prenatal visits				
0-5 visits	0.74	0.78 (0.69; 0.88)	0.70	0.80 (0.67; 0.95)
6-16 visits	Reference	Reference	Reference	Reference
>16 visits	1.51	1.32 (1.05; 1.66)	2.43	1.80 (1.31; 2.48)
Obstetrician visit during pregnancy	1.44	1.28 (1.13; 1.44)	1.45	1.25 (1.04; 1.50)
Mode of delivery				
Vaginal delivery	Reference	—	Reference	—
Unplanned C-section	1.22	—	0.91	—
Planned C-section	1.03	—	1.04	—
Pregnancy in the preceding year	1.00	—	0.97	—
Maternal chronic conditions				
AR	1.28	—	2.13	1.71 (1.36; 2.14)
AD	1.43	—	1.31	—
Chronic hypertension	1.41	—	1.55	—
Pregnancy-induced hypertension	1.01	—	1.18	—
Diabetes mellitus	1.35	—	1.17	—
Gestational diabetes	1.27	1.20 (1.05; 1.38)	1.29	—

N/A, Not applicable.

prenatal visits, and who had development of gestational diabetes. Variables associated with statistically significant reductions in the risk of development of AD were male sex, being born small-for-gestational-age, having a mother living in a rural area during pregnancy, who was multiparous, and who had a low number of prenatal visits. When studying only children of mothers with asthma only (Table IV), no statistically significant increases were demonstrated according to the level of control and severity of asthma during pregnancy and similar determinants were retained in the final adjusted model.

Neither asthma during pregnancy, nor its level of severity and control, was found to be associated with the incidence of AR in the child's first 10 years of life. However, one of the potential confounding variables was found to be strongly associated with the risk of childhood AR: a 70% increased risk of AR was found among children whose mothers had AR 2 years before or during pregnancy. This association was present in the analyses performed among children of mothers with and without asthma, as well as among children of mothers with asthma. In addition, the incidence of AR was statistically significantly increased if the child had previously been diagnosed with AD or asthma, had filled at least 1 antibiotic prescription up to 6 months after birth, if its mother had filled INS and antibiotics prescriptions during pregnancy, if she had consulted an obstetrician and had more than 16 prenatal visits. Statistically significant reductions in the risk of AR in the child were observed if the mother received social assistance, was living in a rural area, had less than 5 prenatal visits, and if she was multiparous.

Discussion

These results demonstrate a small increase in the risk of AD and no increased risk of AR among children of mothers with asthma, compared with those of mothers without asthma. The lack of asthma control and a higher level of severity of asthma during pregnancy were not found to further influence the risk of those atopic conditions.

The current literature provides statistically significant risk estimates for the association between the maternal history of atopic conditions and the risk of childhood AD or AR ranging between 1.2 and 2.4.⁴⁻¹⁰ This study offers more precise estimates of the risk of these atopic conditions in relationship with asthma and AR affecting the mother during pregnancy and takes into consideration a large number of potential confounding variables. In addition, this study also allowed us to further investigate the risk of AD and AR among children of mothers with asthma by considering the level of control and severity of maternal asthma during pregnancy.

The familial clustering of atopic conditions has been previously described and can be explained through a genetic predisposition and/or shared environment.^{1-3,17} In this study, asthma during pregnancy was found to be associated with childhood AD, but not AR. However, maternal AR and INS use during pregnancy were strongly associated with AR in the child, with risk increases ranging between 45% and

Table IV. Adjusted HR for the association between the control and severity of maternal asthma during pregnancy and the incidence of AD and AR in the offspring of mothers with asthma

	Adjusted HRs (95%CI)	
	AD	AR
Control and severity of maternal asthma during pregnancy		
Mild controlled	Reference	Reference
Mild uncontrolled	1.06 (0.89; 1.26)	0.87 (0.67; 1.12)
Moderate-to-severe	0.98 (0.81; 1.18)	0.90 (0.70; 1.15)
Child characteristics		
Atopic dermatitis	N/A	—
Allergic rhinitis	1.92 (1.22; 3.01)	N/A
Asthma	—	1.65 (1.33; 2.04)
≥ 1 antibiotic prescription filled within the first 6 months of life	1.19 (1.02; 1.38)	—
Maternal sociodemographics		
Living in rural area	0.71 (0.58; 0.86)	0.71 (0.53; 0.94)
Pregnancy-related characteristics		
Intranasal corticosteroids use	—	1.52 (1.12; 2.07)
Number of antibiotic prescriptions filled (each additional prescription)	—	1.13 (1.04; 1.22)
Multiparity	0.76 (0.65; 0.88)	0.61 (0.49; 0.75)
Number of prenatal visits		
0-5 visits	—	0.77 (0.57; 1.02)
6-16 visits	—	Reference
>16 visits	—	1.84 (1.16; 2.92)
Maternal chronic conditions		
Allergic rhinitis	—	1.67 (1.25; 2.23)

N/A, Not applicable.

71%. Because AR and asthma are comorbid conditions,^{18,19} it is possible that a stronger association with the incidence of AR is visible for maternal AR rather than for maternal asthma, because a mother with AR might consult a physician more promptly than a mother with asthma if she notices rhinitis-like symptoms in her child. A direct link may also be suggested, because the magnitude of AR risk in children remained constant even when the analysis was conducted among children of mothers with asthma. Specifically, a 71% increased risk was observed among children of mothers with and without asthma, compared with 67% among children of mothers with asthma only. Although it has been previously reported in the literature,^{4,6,8} no association was found between maternal AD and childhood AD. It may be that maternal history of AD was investigated in the previous studies and in the present case, mothers had to have a relatively active condition, because they had to have received at least 1 diagnosis of AD in the 2 years before or during pregnancy.

Consistent with the current knowledge, having previous development of other atopic conditions (asthma and AR, or asthma and AD) was a strong predictor, respectively, of the incidence of AD and AR.^{3,5,7,10} Male sex was associated with an increased risk of AR and a reduced risk of AD.^{5,20-22}

Multiparity and living in a rural area during pregnancy were found to have protective effects on the incidence of both AD and AR. This is in accordance with the "hygiene

hypothesis,” which proposes that some viral and bacterial infections and certain environmental components during pregnancy and early infancy could limit the development of atopic responses in children.^{20,23} In the analyses performed within the entire cohort (26 265 children), antibiotic use during pregnancy was found to be associated with an increased risk of AR, and antibiotic use by the child within the first 6 months of life (which may also be seen as a proxy for infections occurring early in life) was found to increase the risk of both AD and AR. Those results contrast with the “hygiene hypothesis” described above, but those variables could be seen as sources of microbial disturbance in the child, which could favor the skewing toward a Th2-biased immune profile, therefore increasing the propensity for a child to have development of atopic responses.^{24,25}

The protective association between being born small-for-gestational age and AD has been described in the past, but the cause etiology of this relationship is unknown.⁶ As the nutritional route has long been investigated as a potential mechanism to primary prevention of AD,^{1,17} it could be suggested that the present protective effect might be the reflection of increased care in the introduction of formulas and solid-food diet and allergen avoidance among small-for-gestational-age infants.

An increased risk of AD and AR is present among children whose mothers have consulted an obstetrician during pregnancy and who have had a high number of prenatal visits, which may also be seen as proxies for the presence of other maternal comorbidities not considered in this study. This may indicate a greater potential for diagnosis, resulting from closer follow-up and an increased maternal awareness and/or need for medical care. Conversely, children whose mothers received social assistance have a reduced risk for development of AR, consistent with the idea that this condition is less likely to be investigated in those children, compared with children born in families of higher socioeconomic status.²¹

A 20% increased risk of AD was found in association with gestational diabetes. To the best of our knowledge, this is the first time such an association is reported. Even though the etiologic explanation remains unknown, gestational diabetes could be seen as an indicator of pregnancy complications, because previous studies have reported borderline-significant associations between pregnancy complications (including antepartum hemorrhage, preterm contractions and placental problems) and AD.²⁴

Use of administrative health databases confers many advantages to this study. The large sample size allows for isolating small effect sizes and the inclusion of multiple potential confounding variables within a single statistical analysis. The outcomes, AD and AR, were identified by use of physician diagnoses of these conditions. Also, because the information is collected prospectively and independently of the outcomes, the potential for recall bias is not an issue. This constitutes a net advantage for measures of medication intake and previous medical diagnoses because patients are not being asked to recall very precise information over long periods of time.

Although rates of AD and AR are consistent with rates reported in a survey of the Quebec population,²⁶ it is possible that there is an overrepresentation of more severe cases in the cohort, as very mild AD or AR might not result in a medical visit, and rhinitis might be difficult to diagnose in younger children.^{19,21} Also, only the diagnostic codes of AD and AR were used to identify cases in this study; medications to treat AD and AR, such as topical corticosteroids (cream and ointments) and oral antihistamines, were not used because they are nonspecific to those conditions, and some of them are available as over-the-counter drugs. Furthermore, although 22 potential confounding variables were included in the multivariate analyses, residual confounding is still possible because lifestyle and many environmental characteristics were not available in the databases. Administrative databases are also subjected to a certain degree of coding errors, and finally, to be included in this study, women and children had to be insured by the government for their medications. As a result, women and children from higher income families are underrepresented in this study population, because they are mostly covered by private insurance for their medications. Therefore it may be more difficult to generalize the results to children born in families of higher socioeconomic status.

Results from this study, conducted with one of the largest cohorts of children of mothers with and without asthma, indicate that children born to women with asthma during pregnancy are 11% more likely to have development of AD compared with children of mothers without asthma. Moreover, we found that children whose mothers had AR during pregnancy were 70% more likely to have AR diagnosed within the first 10 years of life. Children born to mothers who have asthma or AR during pregnancy should be closely monitored to diagnose and treat AD and AR as soon as possible in these children. ■

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Appendix

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