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Prevalence, risk factors, and clinical outcomes of atopic and nonatopic asthma among rural children

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ABSTRACT

Background: Because of time and cost constraints, objective classification of atopic and nonatopic asthma has been limited in large epidemiologic studies. However, as we try to better understand exposure-outcome associations and ensure appropriate treatment of asthma, it is important to focus on phenotype-defined asthma classification.

Objective: To compare atopic and nonatopic asthma in rural children with regard to risk factors and clinical outcomes.

Methods: We conducted a cross-sectional study in rural Saskatchewan, Canada, in 2011. Parents of 6- to 14-year-old children completed a health and exposure survey. Skin prick tests were completed in a subsample of 529 children. Asthma was based physician diagnosis. Asthma status was defined as no asthma, nonatopic asthma, and atopic asthma.

Results: Asthma prevalence was 14.7% of which 32.1% of cases were atopic. After adjustment, early respiratory illness and a family history of asthma were predictors of childhood asthma, regardless of atopic status ($P < .05$). Being overweight and having a dog in the home were associated with an increased risk of nonatopic asthma ($P < .05$). A mother with a history of smoking increased the risk of atopic asthma ($P = .01$). Compared with those with nonatopic asthma, in the past 12 months, children with atopic asthma were more likely to report a sneezy, runny, or blocked nose or have shortness of breath (odds ratio > 2), whereas those with nonatopic asthma were more likely to have parents who missed work (odds ratio > 3). Those with nonatopic asthma had significantly lower forced expiratory volume in 1 second compared with those with atopic asthma.

Conclusion: Exposures may contribute differentially to atopic and nonatopic asthma and result in differential clinical presentation or burden. The study of these characteristics is important for etiologic understanding and management decisions.

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Introduction

Asthma is one of the most prevalent chronic respiratory disorders¹ and costs hundreds of millions of dollars annually in Canada.² It is a heterogeneous condition with several phenotypes³ and most common among children. Atopic and nonatopic

asthma are the most common phenotypes considered with this classification often based on skin tests or blood tests.^{4–6} Because of time and cost constraints, objective classification of atopic and nonatopic asthma has been limited in large epidemiologic studies. However, as we try to better understand exposure-outcome associations and ensure appropriate treatment of asthma, it is important to focus on phenotype-defined asthma classification. Distinct patterns of risk factors for atopic and nonatopic asthma in children have been identified through epidemiologic studies^{4,5,7} and may indicate different causal mechanisms.^{6,8} Although both atopic and nonatopic asthma phenotypes are associated with a family history of asthma,^{5,7} other risk factors vary between the two.⁵

In addition, findings from studies point to an inverse association between farm dwelling and asthma.^{9–11} However, these results are still inconsistent.^{12,13} Some of the inconsistency in the association

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between rural exposures and asthma could result from differences in the exposure-outcome associations between atopic and non-atopic asthma phenotypes, yet very little work has been conducted investigating asthma phenotypes and their risk factors in rural populations.⁶ Although a recent study has suggested the effect of exposures rich in microbes on shaping innate immunity,¹⁴ it is still important to consider clinical profiles of those with atopic and nonatopic asthma.

Our objectives were to estimate the prevalence of atopic and nonatopic asthma and identify risk factors for each phenotype among rural dwelling children. We sought to determine whether there is consistency of predictors between the 2 phenotypes and to compare clinical characteristics (symptoms and lung function) and burden of disease among children with atopic and nonatopic asthma.

Methods

Study Design

Data for this study were from the child component of a rural health study.^{15–17} Methods of this study have been described previously.^{15–17} This is a longitudinal study of children and adults being completed in a rural area. The children's baseline data were collected by 2 methods. The first was a survey phase. The second was a clinical testing phase in a subsample of children in winter and spring 2011. The current analysis was completed using the children's component of the baseline data.

Study Population, Selection, and Recruitment

This study was conducted in 4 rural quadrants of a rural region. Rural was defined as living in a small town (<5,000 people) or rural municipality, a definition in alignment with Statistics Canada's definitions.¹⁸ The participant must also have lived more than 60 km away from an urban area.¹⁵ Initially, meetings were held with the school board directors to discuss the project, followed by communication with the principals of schools within a school division agreeing to participate. All 10 school divisions approached agreed to participate. Of the 43 schools approached, 39 agreed to participate.

Study packages, which included an information letter, survey, consent forms, and assent forms, were distributed to schools. All children aged 6 to 18 years who attended selected schools were eligible to participate in the survey phase. Study packages were sent home through the schools to parents for completion and to be returned to the school for retrieval by the study team. Surveys from 2,382 students were returned (response rate, 42%).

A subset of students in grades 1 to 8 (ages 6–14 years) were selected for clinical testing. Schools included in clinical testing were selected based on higher numbers of survey participation at that school to maximize efficiency. Clinical testing included allergen skin prick tests (SPTs), anthropometric measures, and lung function testing with spirometry. One school division refused to allow clinical measurements in the school. Sixteen schools took part in the clinical testing, with 1,768 students being approached. In total, 584 students completed the clinical testing and survey. These students are included in the current analysis.

This study was approved by the University of Saskatchewan Biomedical Research Ethics Board. Before clinical testing, parents were required to sign a consent form, whereas children completed an assent form. All school divisions involved approved of the study.

Data Collection

Parent-completed surveys

Surveys were distributed through schools to parents for self-completion. These surveys were based on standardized questionnaires, such as the International Study of Allergy and Asthma in

Childhood (ISAAC) questionnaire,¹⁹ American Thoracic Society Children's Respiratory Disease questionnaire,²⁰ and questionnaires used previously in other lung studies.^{21,22} Information was collected on lung and general health, indoor environment, health behaviors, and sociodemographics.

Asthma was defined by the survey question, "Has this child ever been diagnosed as having asthma by a doctor?" Following previous definitions,^{16,17} location of residence was based on the question, "Where is your home located?" The child was considered to live on a farm if he/she reported living on a farm or acreage. If the child reported living in town, he/she was considered to live in a small town. Current parental smoking status was defined as a report of parental smoking for the mother or father at the time of questionnaire completion. Early respiratory illness was considered to have occurred if there was a report of any 1 of the following 4 conditions in the first 2 years of life: bronchitis, pneumonia, whooping cough, or croup. Farming activities were based on the question, "In the past 12 months, on average, how often has this child spent 1 hour near or in the following activities?" The farming activities listed were haying or moving or playing with hay bales, feeding livestock, cleaning or playing in barns, emptying or filling grain bins, cleaning or playing in pens or corrals, and riding horses. The responses of every day, at least once a week, and at least once a month were coded as regular activity, whereas those who responded less than once a month or never were classified as irregular activity.¹⁶

For physical activity levels, participants were designated to the high activity group based on the mean response to the following 2 questions: (1) "Over the past 7 days, on how many days were you physically active for a total of at least 60 minutes per day?" and (2) "Over a typical or usual week, on how many days are you physically active for a total of at least 60 minutes per day?"²³ The mean number of physically active days have been found to be reliable for classifying participants as meeting or not meeting physical activity guidelines of 60 minutes of physical activity on 5 days or more per week.²⁴ On the basis of these guidelines, participants were categorized as physically active if they were active for 5 days or more per week.

Clinical characteristics included respiratory symptoms and allergic symptoms and conditions based on the response to the survey. Respiratory symptoms included wheeze, shortness of breath, and wheeze with exercise. Allergic symptoms and conditions included hay fever and eczema and their associated symptoms.

Burden was based on indicators of care, management, and morbidity and was assessed from the survey. These indicators included breathing medication use, parents missing work, the child missing school, and physical activity levels.

Skin prick tests

All SPTs were completed at the school. SPTs were completed on the forearm and measured after 15 minutes following international standards.²⁵ The panel of allergens selected was chosen because they were considered the most common allergens in the region. These included 6 allergens: *Alternaria* (mold), *Cladosporium* (mold), cat dander, local grasses, wheat dust, and house dust mite (ALK-Abelló Pharmaceuticals Inc, Mississauga, Ontario, Canada). Histamine (10 mg/mL) and saline solution (0.9%) were used as positive and negative controls, respectively. We were interested in the outcome of the presence of atopic and nonatopic asthma. Atopy was defined as a 3-mm or greater wheal formed for any of the allergens compared with the negative control on SPTs. A 3-level categorical asthma status variable was defined based on the previously described definitions of atopy and asthma for which children were defined as having no asthma (no asthma), nonatopic asthma (no atopy but yes to asthma), and atopic asthma (yes to atopy and asthma).

Anthropometric measurements

Height and weight were measured objectively as part of the pulmonary function testing. Height was measured with the patient against a wall using a fixed tape measure with patients standing in socks on a hard floor. Weight was measured using a calibrated spring scale with patients in socks and dressed in normal indoor clothing. From these measures, body mass index (BMI) was calculated as the weight in kilograms divided by square of height in meters.²⁶ Overweight and obesity categories were derived from objectively measured BMI using age and sex cut-off values described by Cole et al.²⁷ These base the cut-off value as the predicted adult equivalent of a BMI of 25 for overweight and of 30 for obese at the age of 18 years. We categorized our BMI status variable as not overweight vs overweight. Overweight also includes obese. As part of the reference group (neither overweight nor obese), we included those who would be classified as underweight.

Lung function testing

Pulmonary function was assessed through spirometry using the forced expiratory maneuver. A dry-rolling seal spirometer (Sensormedics model 922; Sensor Medics Corporation, Anaheim, California) was used to conduct the testing. American Thoracic Society guidelines were followed.^{28,29} Children completed the testing seated while wearing a nose clip. At least 3 and no more than 7 maneuvers were attempted. Before testing each day, calibration of the spirometer was performed using a 3-L syringe. The spirometer was recalibrated at least once if there was an extended length of time of testing or if the temperature changed by 2°C or more. From these tests, we were able to assess forced vital capacity (FVC), forced expiratory volume in 1 second (FEV₁), FEV₁/FVC ratio, and forced expiratory flow between 25% and 75% (FEF_{25%–75%}).

Statistical Analysis

Analyses were completed using SPSS statistical software, version 23 (SPSS Inc, Chicago, Illinois). Statistical significance was based on an α of .05. Initially, descriptive statistics using means (SD) for continuous data and frequencies for categorical data were completed. The variable of primary interest was asthma status (no asthma, nonatopic asthma, atopic asthma). Prevalence of asthma status was calculated. The prevalence of clinical characteristics and risk factors was also calculated for each of the 3 asthma status groups with statistical comparisons completed using the independent-samples χ^2 test and where appropriate, the independent-samples *t* test.

After the descriptive analyses, a risk factor analysis was conducted using multiple polychotomous logistic regression to adjust for potential confounders for which asthma status was the outcome. Variables were selected to the final model based on statistical significance ($P < .05$), biological importance, and the effect that the removal of the variable had on the β coefficients ($>15\%$ change) of the remaining independent variables in the model. The strengths of associations were based on the odds ratios (ORs) and 95% confidence intervals (CIs).

Differences in lung function among the 3 asthma status categories were assessed using analysis of covariance. The outcomes included FVC, FEV₁, FEV₁/FVC ratio, and FEF_{25%–75%}. Each of these analyses was completed after adjustment for age, sex, height, and asthma status.

Results

Overall, the prevalence of asthma was 14.7%. Of the children with asthma, 31.2% were considered to be atopic. Among the no asthma group, 17.7% were atopic. As such, the prevalence of atopic asthma was 4.7%, whereas the prevalence of nonatopic asthma was 10.0%. The prevalence of asthma was not statistically different between farm and nonfarm dwellers (13.2% vs 15.8%) or between

those with atopic vs nonatopic asthma (32.3% in farm dwellers vs 30.4% in nonfarm dwellers).

The descriptive statistics for personal and environmental variables stratified by asthma status are presented in Table 1. There was a statistically higher prevalence of children with a report of an early respiratory illness, family history of asthma, and a maternal smoking

Table 1

Personal and Environmental Characteristics by Asthma Status^a

Characteristic	No asthma (n = 451)	Nonatopic asthma (n = 53)	Atopic asthma (n = 25)
Patient characteristics			
Age, mean (SD), y	9.6 (2.2)	9.6 (2.1)	10.0 (2.5)
Female	47.7	49.1	32.0
Nonwhite	7.2	11.3	16.0
With early respiratory illness (<2 years of age)	26.2	60.4 ^b	48.0 ^c
Overweight or obese	24.4	43.4 ^b	36.0
Breastfed	82.0	82.7	88.0
Born premature	9.4	15.1	8.3
Low birth weight ($<2,500$ g)	5.5	9.6	16.7 ^c
Firstborn	39.2	35.8	48.0
Day care attendance	57.8	50.9	68.0
Farm-based exposure			
Currently live on a farm	45.5	39.6	41.7
Lived on a farm in first year of life	31.0	34.0	20.0
Mother lived on farm while pregnant	32.1	34.6	20.0
Haying or moving or playing with bales regularly ^d	25.2	25.5	20.0
Feeding livestock regularly ^d	29.1	27.5	20.0
Playing or cleaning in barns regularly ^d	24.5	27.5	12.0
Emptying or filling grain bins regularly ^d	9.2	3.9	0.0
Cleaning or playing in pens or corrals regularly ^d	24.4	17.6	12.0
Riding horses regularly ^d	9.2	9.8	4.0
Family Characteristics			
Mother smoking			
Never smoker	64.0	47.2 ^b	36.0 ^c
Ex-smoker	16.8	26.4	36.0
Current smoker	19.2	26.4	28.0
Father smoking			
Never smoker	55.8	39.6 ^b	48.0
Ex-smoker	17.7	26.4	12.0
Current smoker	26.5	34.0	40.0
Mother smoked during pregnancy	19.2	32.1	29.2
Maternal education with any postsecondary	64.0	57.7	52.2
Paternal education with any postsecondary	47.7	47.2	33.3
Family history of asthma	12.2	32.1 ^b	28.0 ^c
Home exposure			
Dog at home in last 12 months	40.6	56.6 ^b	40.0
Dog in first year of life	28.7	37.3	34.8
Cat in the home in last 12 months	35.9	39.6	56.0 ^c
Cat in first year of life	27.0	35.3	30.4
Home built before 1980	64.1	65.4	81.0
With mold or mildew smell	24.8	24.0	12.0
With home mold	21.1	22.6	28.0
Heating type			
Natural gas	71.8	62.3	76.0
Coal or wood	11.3	17.0	4.0
Other	16.9	20.8	20.0
With major home renovations in last 12 months	27.9	26.4	16.7

^aData are reported as percentage of patients unless otherwise indicated. The percentages reported are column percentages, indicating the proportion of children within the status group (column) who experienced the exposure listed. In the last 12 months refers to exposure at any point in the past 12 months.

^b $P < .05$ comparing no asthma and nonatopic asthma based on independent-samples χ^2 tests.

^c $P < .05$ comparing no asthma with atopic asthma based on independent-samples χ^2 tests.

^dRegularly is defined by a positive response to at least 1 hour at a time taking part in the listed activities every day, at least once a week, or at least once a month.

history among children with atopic or nonatopic asthma compared with those with no asthma. In addition, those with nonatopic asthma were more likely to be overweight, own a dog in the past 12 months, and have a paternal history of smoking than those without asthma. Those with atopic asthma were more likely to be born at a low birth weight and have a cat at home in the past 12 months compared with those with no asthma. There were no statistically significant differences between the nonatopic asthma and atopic asthma groups with regard to the variables considered in Table 1.

After adjusting the analysis for potential confounders, the presence of early respiratory illness and family history of asthma were associated with asthma, regardless of atopic status (Table 2). Although the findings were not statistically significant, a dog at home in the past 12 months ($P = .07$) and being overweight ($P = .06$) were significantly associated with nonatopic asthma. Similarly, mother being an ex-smoker was associated with atopic asthma, although this finding was not statistically significant ($P = .07$).

When comparing the prevalence of respiratory symptoms among the 3 asthma status groups, as expected, those with asthma consistently had a higher prevalence of symptoms considered (Table 3). Table 3 also presents the results of comparisons of burden among the asthma status groups. No difference was found in the proportion of those reporting high activity among the 3 groups. Regardless of nonatopic or atopic asthma status, those with asthma had a higher proportion of reporting using breathing medications and missing school compared with those without asthma. However, only those with nonatopic asthma had a higher proportion of children with parents missing work because of their child's breathing problems. Although some differences between those with nonatopic and atopic asthma were large, these differences were only statistically significant ($P < .05$) for ever reported shortness of breath, sneezing in the past 12 months, and report of hay fever. Differences were also not statistically significant ($P < .10$) for parents having to miss work, report of sleep disturbance in the past 12 months, and everyday or nearly every day medication use. With the exception of parents missing work, in each of these cases, children with atopic asthma had a higher proportion of the outcome being reported.

Figure 1 presents the results comparing lung function across the asthma status groups. Those in the nonatopic asthma group consistently had the lowest lung function. When compared with the no asthma or the atopic asthma group, the nonatopic asthma group had a statistically significant lower FEV₁ compared with the atopic asthma group. In addition, when compared with the no asthma group, the nonatopic asthma group also had significantly ($P < .05$) lower FEV₁/FVC ratio and FEF_{25%–75%}.

Discussion

A major finding of the present study was that asthma was common among these rural dwelling children (14.7%) and that most of those with asthma had nonatopic asthma. Although personal factors of early respiratory illness and family history of asthma were associated with both phenotypes, only trends were seen between other independent risk factors for atopic and non-atopic asthma specifically. In addition, those with atopic asthma generally had a higher proportion reporting symptom and burden indicators, whereas those in the nonatopic asthma group consistently had the lowest lung function.

The prevalence of asthma in our study among these rural dwellers was similar to that seen among other rural dwelling children, which has ranged from 5.3%³⁰ to 14.8%.³¹ In addition, only a small proportion of children with asthma in our study population had evidence of allergen skin test reactivity that was lower compared with results from a study by Moncayo et al⁶ in Ecuador in 2007 among 6- to 16 year-old children (4.7% vs 14.4%). In the study from Ecuador,⁶ atopy was defined by a different SPT panel than ours, and wheeze in the past 12 months was used as a surrogate for asthma classification, also differing from our study.

We found a higher prevalence of nonatopic than atopic asthma, supporting previous evidence^{32–34} and in contrast to the general perception that childhood asthma is generally an atopic disease. The proportion of asthma attributable to atopy in children has been estimated to be 38%, but there is considerable variation among studies (25%–63%).³³ Data from ISAAC phase 2 surveys found that a higher fraction of recent wheezing was attributable to atopy (measured by allergen skin test reactivity) in affluent (41%) compared with nonaffluent countries (20%).³² Among Australian children aged 8 to 10 years, Ponsonby et al³⁴ found that 33% of asthma cases were attributable to atopy (defined as skin test positivity to any of 10 aeroallergens). A study in rural Poland³⁵ among school-aged children found that only 22% of children with asthma were sensitized to indoor allergens (cat or dust) and 17% to outdoor allergens (grass mix or birch pollens). These findings indicate that childhood asthma being an atopic disease may be overemphasized.

The prevalence of asthma and the proportion of atopic asthma were not statistically different between farm and nonfarm dwellers. Our findings support previous work that did not find any effect of farming exposures.^{6,7} In terms of nonatopic asthma, inconsistent results have been reported recently.^{36–38} For example, the PARSIFAL (Prevention of Allergy Risk factors for Sensitization In children related to Farming and Anthroposophic Lifestyle) study team in Europe found that pig farming was notably protective of asthma and atopy.³⁸ In our study, it is possible that agricultural exposures do not

Table 2
Results of Multivariate Analysis for Factors Related to Nonatopic and Atopic Asthma in Children^a

Factor	Nonatopic asthma (Reference: No asthma)		Atopic asthma (Reference: No asthma)	
	OR (95% CI)	P Value	OR (95% CI)	P Value
Age	1.02 (0.88–1.19)	.78	1.17 (0.94–1.44)	.15
Female (reference: male)	1.05 (0.56–2.01)	.88	0.54 (0.21–1.41)	.21
Mother with more than high school (reference: high school or less)	0.87 (0.45–1.70)	.69	0.75 (0.29–1.94)	.56
Early respiratory illness (reference: none)	4.20 (2.19–8.06)	<.001	3.10 (1.23–7.75)	.02
Family history of asthma (reference: none)	3.27 (1.55–6.85)	.002	3.29 (1.10–9.80)	.03
Farm dwelling (reference: not farm)	0.94 (0.45–1.97)	.87	1.43 (0.51–3.97)	.50
Mother ex-smoker (reference: never)	1.46 (0.60–3.54)	.56	3.13 (0.92–10.61)	.07
Mother current smoker (reference: never)	1.06 (0.34–3.36)	.92	2.12 (0.47–9.71)	.33
Smoking during pregnancy (reference: none)	1.84 (0.68–5.00)	.23	1.11 (0.31–4.05)	.87
Dog at home in the past 12 months (reference: no dog)	1.84 (0.96–3.51)	.07	0.77 (0.30–1.99)	.59
Cleaning or playing in pens or corrals regularly ^b (reference: irregular)	0.63 (0.25–1.56)	.32	0.43 (0.11–1.68)	.22
Overweight or obese (reference: not overweight or obese)	1.88 (0.97–3.66)	.06	1.80 (0.70–4.59)	.22

Abbreviations: CI, confidence interval; OR, odds ratio.

^aAdjusted for each variable in the table. Results in bold indicate $P < .05$.

^bRegularly is defined by a positive response to at least 1 hour at a time taking part in the listed activities every day, at least once a week, or at least once a month.

Table 3
Respiratory Symptoms, Allergic Symptoms, Health Care Use, and Morbidity and Indicators Specific to Asthma^a

Outcome	Patients, %			P Value ^b		
	No asthma (n = 451)	Nonatopic asthma (n = 53)	Atopic asthma (n = 25)	No asthma vs nonatopic asthma	No asthma vs Atopic 2asthma	Nonatopic vs atopic asthma
Respiratory symptoms						
Wheeze in the past 12 months	5.5	43.4	56.0	<.001	<.001	.30
Shortness of breath ever	4.5	37.7	62.5	<.001	<.001	.04
Shortness of breath in the past 12 months	2.0	18.9	36.0	<.001	<.001	.10
Wheeze with exercise ever	7.2	52.8	58.3	<.001	<.001	.65
Wheeze with exercise in the past 12 months	4.2	37.7	36.0	<.001	<.001	.88
Allergic symptoms and conditions						
Itchy rash ever	13.8	28.3	24.0	.006	.16	.69
Rash in the last 12 months	13.7	28.3	24.0	.005	.15	.69
Eczema	25.7	35.8	40.0	.12	.12	.72
Sneezing ever	25.2	54.7	68.0	<.001	<.001	.27
Sneezing in the past 12 months	21.8	35.8	64.0	.02	<.001	.02
Hay fever	6.5	11.8	52.4	.17	<.001	<.001
Health care use and morbidity						
Use of breathing medications	1.6	48.1	50.0	<.001	<.001	.88
Parent miss work	5.6	24.5	8.0	<.001	.61	.08
3 Days missed school from chest illness	6.2	20.8	24.0	<.001	.001	.75
High activity in a week	63.4	60.4	64.0	.66	.95	.76
Indicators specific to asthma						
Age of diagnosis, mean (SD), y		3.7 (3.0)	3.1 (2.4)			.40
Visited a physician for asthma in the past 12 months		40.4	50.0			.43
With a written action plan		15.7	30.4			.14
No. of asthma episodes in the past 12 months						
None		37.2	39.1			
1–2		30.2	21.7			
>2		32.6	39.1			.74
Asthma medication use in the past 12 months						
Not every day or nearly every day		71.7	52.0			
Every day or nearly every day		28.3	48.0			.09
Missed school due to asthma		25.0	31.8			.56
Sleep disturbance in the past 12 months		42.3	64.0			.08

^aData are reported as percentage of patients unless otherwise indicated. The percentages reported are column percentages, indicating the proportion of children within the status group (column) who experienced the exposure listed. In the last 12 months refers to exposure at any point in the past 12 months.

^bOn the basis of independent-samples χ^2 tests for categorical comparisons and independent-samples *t* test for age of diagnosis.

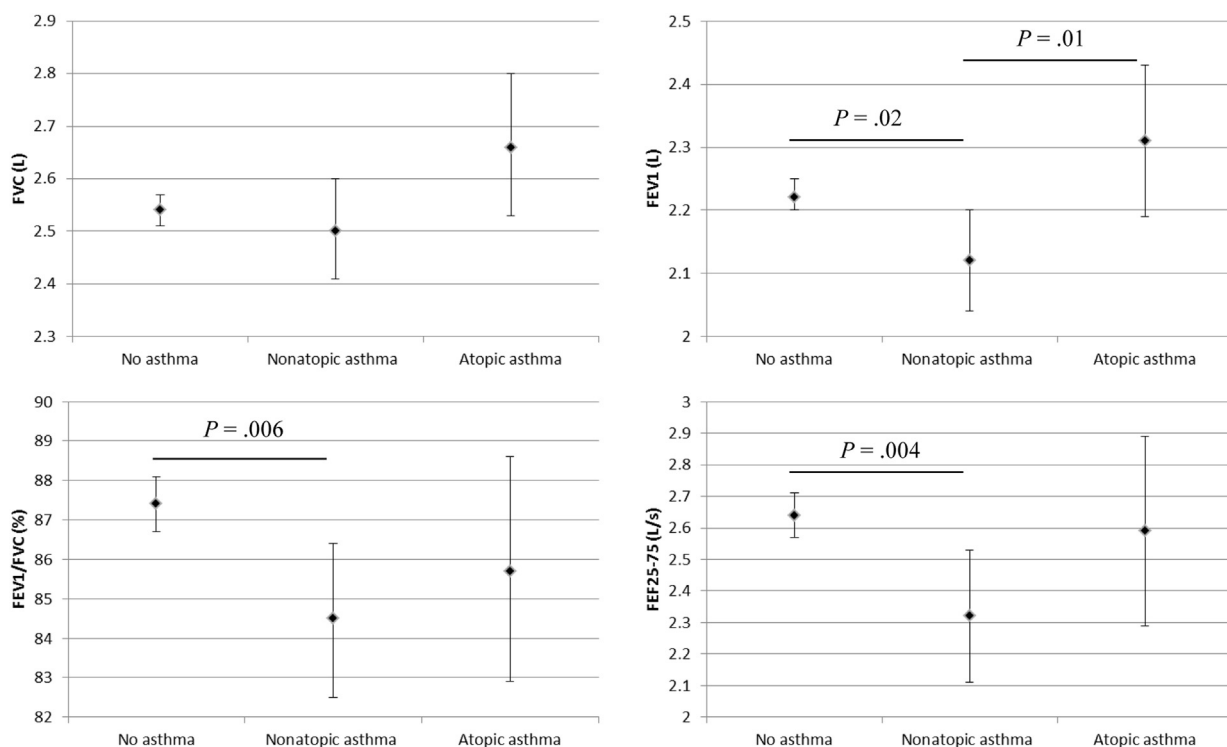


Figure 1. Mean lung function test results by asthma status. Statistical comparisons are based on analysis of covariance after adjustment for age, height, sex, and asthma status. Error bars indicate SDs. FEF_{25%-75%}, forced expiratory flow between 25% and 75%; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity.

vary appreciably between rural Saskatchewan town and farm dwellers where the towns were small and adjacent to farming areas. Despite this, a recent study of different farm lifestyles found differences between areas where there is lower asthma and varied innate immunity response with increased microbial exposure.¹⁴ Type of farming may be important to consider. In our study, among those who lived on a farm, the most common commodities reported were grain (76.8%) and beef (70.8%). Type of farming was not associated with asthma prevalence and did not influence associations with other variables in the model (data not shown).

Our findings indicate that although FEV₁ was lower among children with nonatopic asthma compared with atopic asthma, other lung function measures did not differ significantly between the 2 groups. In addition, those with nonatopic asthma had lower FEV₁, FEV₁/FVC ratio, and FEF_{25%–75%} than controls, whereas those with atopic asthma were not statistically different from controls. In our study population, it is possible that children with atopic asthma are more recognizable or expected within the age group and therefore are more treated, as observed as a trend in our current study, whereas children with nonatopic asthma may be overlooked and undertreated.

Our results add to the literature regarding differences in lung function between atopic asthma groups, although the overall association between lung function and atopic asthma status still remains unclear. In a previous case-control study conducted between 1995 and 1997 with 61 patients with asthma aged 5 to 15 years in Turkey, children with atopic asthma had lower lung function (FEV₁, FVC, and peak expiratory flow rate) than children with nonatopic asthma.³⁹ However in a separate study conducted between 2002 and 2009 in Santiago, Chile,⁴⁰ among 136 school-children (mean [SD] age, 9.07 [2.5] years) with a diagnosis of asthma or recurrent wheezing, there was no difference in FEV₁ between the atopic and nonatopic groups based on SPTs.

We found that most measures of current morbidity among those with asthma did not vary significantly by atopic status. When measures of morbidity varied by atopic status, they were worse in the atopic asthma group. The exception to this was lung function, as described above. Given the atopic asthma status, a higher prevalence of sneezing and hay fever among children with atopic asthma is plausible. In addition, increasing asthma severity has been associated with increasing atopy.⁴¹

Aside from personal factors, we found trends of differing associations for nonatopic and atopic asthma. We must, however, be cautious of these findings given the lack of statistical significance. A dog at home in the past 12 months and being overweight were both associated with nonatopic asthma, whereas mother being an ex-smoker was associated with atopic asthma. Meta-analyses of pet ownership studies have indicated inverse associations with sensitization to aeroallergens and suggested positive associations with nonatopic asthma.⁴² Being overweight or obese increases the risk of asthma in nonatopic children.^{43,44} It has been suggested that these effects may be mediated through systemic inflammation, which may be a key factor in mediating the effects of overweight and/or obesity.⁴⁵ In our study, the association between ex-smoking mothers and asthma but not current smoking mothers may reflect changes in smoking behavior of the mother after the diagnosis of asthma.

There are some limitations that are worth noting. First, participation rates in this study should be considered. However, when compared with children who did not take part in the clinical testing, those who took part were similar with regard to most characteristics, including history of asthma or report of allergic disease. Exceptions were those who took part were significantly more likely to be male (54% vs 48%) and younger (mean age, 9.6 years vs. 10.3 years), although the importance of each of these differences is questionable. This participation rate cannot rule out the possibility of a selection bias.

Second, asthma status can be misclassified given that the history of diagnosis is based on parent report. Nevertheless, questionnaires have been widely used to define respiratory outcomes in epidemiologic studies in children and have generally been accurate.⁴⁶ The issue of disease misclassification was reduced when categorizing asthma phenotypes because atopy was measured objectively. We also consider lung function as an objective measure, further increasing the strength of our study. The principal methodologic limitations of our study were its cross-sectional design and the lack of temporal assessment to establish a causal association.

In summary, we found no associations between farm residential status and asthma phenotypes (atopic and nonatopic asthma) among school-aged children in this rural region. Although personal characteristics were associated with atopic and nonatopic asthma consistently, other observed differences in associations between risk factors and asthma status should be interpreted with caution. Lung function measured by spirometry was generally lower in the nonatopic asthma group compared with other groups.

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