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Factors associated with asthma symptoms in Colombian subpopulations aged 1 to 17 and 18 to 59: Secondary analysis of the study "Prevalence of asthma and other allergic diseases in Colombia 2009-2010"

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Abstract

Background: Asthma, a chronic inflammatory lung disease, is one of the leading causes of disability, demands on health resources, and poor quality of life. It is necessary to identify asthma-related risk factors to reduce the presence and development of symptoms.

Objective: This study aimed to explore the association of multiple possible factors with asthma symptoms in two subpopulations, children, adolescents, and adults, in six cities in Colombia.

Materials and methods: This was an observational analytical case-control study based on a cross-sectional study conducted as a secondary analysis of the prevalence of asthma and

other allergic diseases in Colombia during 2009 and 2010. Weighted logistic regressions were conducted for each population.

Results: Out of the 5978 subjects in the cross-sectional survey, 747 were identified as cases, and 3109 were identified as controls. The prevalence of asthma was 30.8% in the child and adolescent population and 14.7% in the adult population. Among the various factors studied, those associated with asthma symptoms in children/adolescents were: a family history of asthma (OR 2.4; 95% CI 1.3–4.7) and rhinitis (OR 2.0; 95% CI 1.1–3.6); acetaminophen consumption at least once a month (OR 3.6; 95% CI 2.1–6.2); and the presence of birds at home (OR 2.0; 95% CI 1.1–3.8). Regarding food consumption: fruit consumption (OR 3.8; 95% CI 1.1–12.7). In adults, the factors that showed significant association were: a family history of allergic diseases (rhinitis OR 3.3; 95% CI 2.3–4.6), atopic eczema (OR 4.4; 95% CI 2.8–7.0), or asthma (OR 1.8;95% CI 1.3–2.6); acetaminophen consumption at least once a month (OR 2.0; 1.5–2.8); the presence of dogs at home (OR 1.4;95% CI 1.03–1.8), exposure to second-hand smoke (OR 1.7; 95% CI 1.2–2.2), and exposure to exhaust fumes during the day (OR 1.7; 95% CI 1.04–2.7).

Conclusions: Our findings suggest that different cultural, environmental, and family factors are associated with asthma symptoms in children and adolescents, and these associations are evident in both males and females.

Introduction

The prevalence of allergic diseases such as asthma is increasing worldwide, especially in low- and middle-income countries.[1] The World Allergy Organization has estimated that 40% of the world's population is affected by allergic diseases.[2] Studies indicate that the prevalence of allergic diseases in tropical countries is comparable to that in temperate countries, and in some regions, it may even be higher.[3] Asthma is a chronic disease characterized by airway hyperresponsiveness and inflammation, and symptoms include wheezing, coughing, and dyspnea.[4] This condition is a significant contributor to disability, high health resource utilization, and reduced quality of life on a global scale.[5] This is considered the most frequent chronic disease in children and young adults, which implies a high health-care cost and a significant loss of work productivity.[5]

Due to its rate of occurrence and negative impacts, it is necessary to identify the risk factors related to asthma to reduce its widespread presence and development of symptoms. These factors are very diverse and variable throughout the world. The development of allergies and asthma is determined by the interplay between environmental and inherited factors, the latter accounting for over one-half of the risk.[6] Changes in the Western diet, individual lifestyles (smoking, education, and physical activity), environmental factors, and exposures to allergens and outdoor and indoor pollutants are some of the factors that could contribute to the increased asthma symptoms in the Latin American population.[7]

Studies conducted in Colombia have shown an increase in the prevalence of asthma symptoms from 10.4%[8] to 12%[9] over the past decade. In 2008, a study evaluated the prevalence of asthma and associated factors in children between 6-7 years (n=3256) and 13-14 years (n=3829) in Bogota, Colombia. The study showed a prevalence of 10.4% in the first group and 8.6% in the second. The factors shared by both groups in that study were the consumption of acetaminophen during the last 12 months, maternal education level, the presence of a cat in the house, and the consumption of cereal, among others.[10] Another study also evaluated the factors associated with severe disease in Bogota's 175 asthmatic children aged 2-16. It was identified that children who were never breastfed, whose mothers were younger than 30 years old at the child's birth, and who routinely used acetaminophen, among others, were significantly associated with severe asthma.[11] In 2021, a study described the risk factors and symptoms of 324 students (6–14 years old) diagnosed with asthma in two schools in Cali. The study was conducted via surveys completed by 324 caregivers. Among the main findings, it can be highlighted that 23.8% of children had asthma, and the risk factors for asthma were sex and inadequate flooring.[12] During the same year, a study was conducted in two rural municipalities of Colombia to determine the prevalence of allergic diseases (allergic rhinitis, asthma, and atopic dermatitis) in 261 school-age children. The prevalence of asthma was identified as 8.81%, and it was concluded that the prevalence of allergic diseases in this rural pediatric population was lower than in previous reports on urban populations.[13] Despite the sub-diagnosis of asthma, a study reported a prevalence of 9% of asthma in adults.[14]

For the previously mentioned factors, some studies on asthma have been carried out in pediatric and adult populations in Colombia in recent years. However, no study evaluates these factors jointly in our country's pediatric and adult populations. Therefore, the purpose of the present study was to identify environmental, personal, demographic, and other factors associated with asthma symptoms in six major cities of Colombia (Barranquilla, Bogotá, Bucaramanga, Cali, Medellín, and San Andrés). Also, our goal was to compare the associated factors in

children and adults to support decision-making in these two populations, which should be addressed with different actions. This study will contribute to the development of preventive policies, assist in the planning of care for this disease, and raise awareness among policymakers and health personnel about the magnitude and distribution of the disease. Additionally, evidence was generated on the potential risk/protective factors to set up hypotheses that can be researched in the future, which will help diminish the incidence, prevalence, and burden of asthma in the country.

Materials and Methods

Study design

A nested case-control study based on an observational cross-sectional study conducted in 2009-2010 was the chosen design for this study, which aimed to determine the prevalence of asthma and other allergic conditions in six Colombian cities (Barranquilla, Bogotá, Bucaramanga, Cali, Medellín, and San Andrés) and identify associated factors contributing to asthma symptoms in a population subgroup. A detailed description of the cross-sectional study has already been published.[9] In brief, individuals between 1-59 years old were surveyed between 2009 and 2010. A "case" was defined as a subject who reported current symptoms of asthma in the past year by responding "yes" to the following question: "In the past 12 months, have you (or your child) had wheezing or whistling in the chest when you (or your child) did not have a cold or the flu?" Conversely, "controls" were subjects who had never been diagnosed with asthma, allergic rhinitis, or atopic eczema (dermatitis) by a physician. Individuals excluded from the study included those confined to hospitals or institutions for chronic care, individuals with disabilities, and those with altered mental status, dementia, or mental health issues at the time of the study. We used a school-based stratified design to identify subjects between 5 and 17 years old and a community-based strategy to identify people aged 1-4 and 18-59. The protocol was approved by the Clinical Research Ethics Committee at Fundación Cardioinfantil-Instituto de Cardiología in Bogotá, Colombia (IORG0006438).

Questionnaire and Data collection

A questionnaire with items developed and validated by "The International Study of Asthma and Allergies in Childhood (ISAAC)"[15] was used, and some items from the current Spanish environmental questionnaire of the ISAAC III Study were added.[16] The variables that were evaluated are listed in Supplementary Table 1. These variables are considered potential factors for the development of asthma such as sociodemographic factors like gender, age, socioeconomic stratum, educational attainment, mother's educational attainment; personal history related to the type of birth, personal or family history of atopy, smoking status; habits such as acetaminophen consumption, hours spent watching television, food consumption

(meat, fish/seafood, fruits, vegetables, among others); and environmental factors including frequency of bus transit and presence of animals in the home. A self-administered questionnaire was given to adolescents (13-17 years) and adults. Parents of children (5-12 years) were interviewed at home by study personnel.

Data management/Statistical analysis

Cases and controls were compared to identify possible factors associated with asthma. The variables assessed for their association with asthma were identical in both subpopulations. Variables were individually evaluated to identify a broad range of explanatory variables that might be associated with asthma in each subpopulation. Explanatory variables with a p-value <0.15 in the univariable analysis were kept for the multivariable weighted logistic regression model. For any variable, the category of response with the lowest prevalence of asthma was chosen as the reference category. Gender and age were clinically important and used as both populations' adjustment variables in the multivariable model. Age was included as a continuous variable.

We performed weighted logistic regression models separately for each sub-population in the study. To assess the statistical significance of interaction terms, we compared the full model that included all interaction terms and the model without these interaction terms using a single Chunk test.[17] Variables without statistical significance during the backward elimination procedure, which were neither confounders nor control variables, were eliminated from the multivariable model. All analyses are presented as weighted statistics using the Taylor series linearization method for variance estimation[18] using Stata Statistical Software for Windows, release 12 (Stata Corp., College Station, TX, USA). Two subpopulation analyses are presented: one for children/adolescents (participants aged 1-17) and the second one for adults (participants aged 18-59) as crude and adjusted odds ratios (OR) as well as 95% confidence intervals (CI). The reduced model was based on the Furnival-Wilson leaps-and-bounds algorithm; Linearity link test p < 0.0001. Adjustment for multiple comparisons was not conducted.

Results

Out of the 5978 subjects in the cross-sectional survey, 747 were identified as cases, and 3109 were identified as controls. The prevalence of asthma during the last twelve months before the survey date was 30.8% in the child and adolescent population and 14.7% in the adult population.

Socio-demographic characteristics

The mean age in the subpopulation of children and adolescents was 8.28 [Standard Deviation (SD): 4.48]. The mean age in the adult population was 37.96 (SD: 12.71). In children and adolescents, the distribution of controls (69.16%) was slightly more than double the proportion of cases (30.83%).

Table 1 Socio-demographic characteristics of cases and controls in children and adolescents group.

Variable	Total N=1276 n (%)	Controls N=776 n (%)	Cases N=500 n (%)	p-value*
Sex				0.14
Female	579 (52%)	412 (53%)	167 (48%)	
Male	543 (48%)	364 (47%)	179 (52%)	
Age	8.28 (4.48)/8.00 (4.00-12.00)	7.82 (4.20)/8.00 (4.00-10.00)	9.30 (4.89)/9.00 (4.00-14.00)	**<0.001**
<5 years	322 (28.70%)	229 (29.51%)	93 (26.88%)	
5-12 years	498 (44.39%)	396 (51.03%)	102 (29.48%)	
>12 years	302 (26.92%)	151 (19.46%)	151 (43.64%)	
Socioeconomic status				**0.043**
1 and 2 (low)	665 (59.27%)	479 (61.73%)	186 (53.76%)	
3 and 4 (middle)	443 (39.48%)	288 (37.11%)	155 (44.80%)	
5 and 6 (high)	14 (1.25%)	9 (1.16%)	5 (1.45%)	
Educational attainment				**<0.001**
Elementary school	778 (69.34%)	605 (77.96%)	173 (50.00%)	
High school	270 (24.06%)	125 (16.11%)	145 (41.91%)	
No answer	1 (0.09%)	1 (0.13%)	0 (0.00%)	
Missing	73 (6.51%)	45 (5.80%)	28 (8.09%)	
Mother´s educational attainment				0.092
No education	192 (17.11%)	127 (16.37%)	65 (18.79%)	
Elementary school	550 (49.02%)	399 (51.42%)	151 (43.64%)	
High school	357 (31.82%)	238 (30.67%)	119 (34.39%)	
Missing	23 (2.05%)	12 (1.55%)	11 (3.18%)	
Shared rooms				0.84
No	320 (28.52%)	220 (28.35%)	100 (28.90%)	
Yes	800 (71.30%)	555 (71.52%)	245 (70.81%)	
Missing	2 (0.18%)	1 (0.13%)	1 (0.29%)	
Combustible material used for cooking				0.70
No	51 (4.55%)	34 (4.38%)	17 (4.91%)	
Yes	1067 (95.10%)	739 (95.23%)	328 (94.80%)	
Missing	4 (0.36%)	3 (0.39%)	1 (0.29%)	
Animals living in the same house				**0.002**
No	667 (59.45%)	485 (62.50%)	182 (52.60%)	
Yes	454 (40.46%)	291 (37.50%)	163 (47.11%)	
Missing	1 (0.09%)	0 (0.00%)	1 (0.29%)	
Dogs				**0.010**
No	789 (70.32%)	564 (72.68%)	225 (65.03%)	
Yes	333 (29.68%)	212 (27.32%)	121 (34.97%)	
Cats				**0.020**
No	1025 (91.35%)	719 (92.65%)	306 (88.44%)	
Yes	97 (8.65%)	57 (7.35%)	40 (11.56%)	
Rodents				**0.022**
No	1104 (98.40%)	768 (98.97%)	336 (97.11%)	
Yes	18 (1.60%)	8 (1.03%)	10 (2.89%)	
Birds				**0.003**
No	946 (84.31%)	671 (86.47%)	275 (79.48%)	
Yes	176 (15.69%)	105 (13.53%)	71 (20.52%)	
Other animals				0.90
No	26 (2.32%)	15 (1.93%)	11 (3.18%)	
Yes	10 (0.89%)	6 (0.77%)	4 (1.16%)	
Missing	1086 (96.79%)	755 (97.29%)	331 (95.66%)	
Fish				0.67
No	25 (2.23%)	14 (1.80%)	11 (3.18%)	
Yes	11 (0.98%)	7 (0.90%)	4 (1.16%)	
Missing	1086 (96.79%)	755 (97.29%)	331 (95.66%)	

(*continues*)

Table 1 Continued.

Variable	Total N=1276 n (%)	Controls N=776 n (%)	Cases N=500 n (%)	p-value*
Turtles				0.91
No	22 (1.96%)	13 (1.68%)	9 (2.60%)	
Yes	14 (1.25%)	8 (1.03%)	6 (1.73%)	
Missing	1086 (96.79%)	755 (97.29%)	331 (95.66%)	
Smoke				**0.014**
No	1107 (98.66%)	770 (99.23%)	337 (97.40%)	
Yes	15 (1.34%)	6 (0.77%)	9 (2.60%)	
Passive smoke				0.071
No	796 (70.94%)	563 (72.55%)	233 (67.34%)	
Yes	325 (28.97%)	212 (27.32%)	113 (32.66%)	
Missing	1 (0.09%)	1 (0.13%)	0 (0.00%)	
Asthma in parents or siblings				**<0.001**
No	856 (76.29%)	644 (82.99%)	212 (61.27%)	
Yes	234 (20.86%)	119 (15.34%)	115 (33.24%)	
Missing	32 (2.85%)	13 (1.68%)	19 (5.49%)	
AR in parents or siblings				**<0.001**
No	783 (69.79%)	605 (77.96%)	178 (51.45%)	
Yes	289 (25.76%)	151 (19.46%)	138 (39.88%)	
Missing	50 (4.46%)	20 (2.58%)	30 (8.67%)	
AE in parents or siblings				**<0.001**
No	935 (83.33%)	697 (89.82%)	238 (68.79%)	
Yes	122 (10.87%)	58 (7.47%)	64 (18.50%)	
Missing	65 (5.79%)	21 (2.71%)	44 (12.72%)	
Cesarean delivery				0.12
No	706 (62.92%)	502 (64.69%)	204 (58.96%)	
Yes	396 (35.29%)	264 (34.02%)	132 (38.15%)	
Missing	20 (1.78%)	10 (1.29%)	10 (2.89%)	
Health care insurance				0.28
No	54 (4.81%)	34 (4.38%)	20 (5.78%)	
Yes	1,049 (93.49%)	733 (94.46%)	316 (91.33%)	
Missing	19 (1.69%)	9 (1.16%)	10 (2.89%)	
Type of health care insurance				**0.043**
Subsidized	316 (28.16%)	235 (30.28%)	81 (23.41%)	
Contributive/Special	728 (64.88%)	496 (63.92%)	232 (67.05%)	
Missing	78 (6.95%)	45 (5.80%)	33 (9.54%)	
Average hours of television				0.068
< 1 hour	129 (11.50%)	81 (10.44%)	48 (13.87%)	
1-2 hours	309 (27.54%)	230 (29.64%)	79 (22.83%)	
3-4 hours	284 (25.31%)	195 (25.13%)	89 (25.72%)	
$\geq$ 5 hours	398 (35.47%)	268 (34.54%)	130 (37.57%)	
Missing	2 (0.18%)	2 (0.26%)	0 (0.00%)	
Average acetaminophen consumption last 12 months				**<0.001**
At least once per week	138 (12.30%)	109 (14.05%)	29 (8.38%)	
At least once per month	195 (17.38%)	85 (10.95%)	110 (31.79%)	
At least four times per year	328 (29.23%)	214 (27.58%)	114 (32.95%)	
At least once per year	348 (31.02%)	276 (35.57%)	72 (20.81%)	
Never	113 (10.07%)	92 (11.86%)	21 (6.07%)	

*p-value based on t-test or chi-square/fisher test.

The proportion of controls (85.33%) was nearly quadruple the proportion of cases (14.67%) in adults. The gender distribution of the subpopulations studied was by the percentage of males and females within the Colombian census for 2009 (19). Most children/adolescents, as well as the majority of adults, were enrolled in a health care insurance plan. The most frequent SES for cases and controls in both populations were low and middle status, also by the distribution of the Colombian census and projections for 2009 (see Tables 1 and 2).[20] The eating habits of both the pediatric and adult populations are described in Supplementary Tables 2 and 3.

Factors associated with asthma symptoms among children and adolescents

The bivariate and multivariate logistic regression analysis results are shown in Table 3. The antecedent of AR in the family was found to be a risk factor for asthma (aOR 1.95, 95% CI% 1.07-3.56) in the reduced analysis. The medical history of asthma was significant in the reduced model (aOR 2.43. 95% CI% 1.27-4.67). Children and adolescents taking acetaminophen at least once per month on average for the last 12 months had increased odds of asthma symptoms (aOR 3.63, 95 CI% 2.11-6.24). Regarding food consumption, we found that children/adolescents who reported eating fruits at least once a week had a higher chance of reporting asthma symptoms (aOR 3.78, 95 CI% 1.12-12.70) than children/adolescents who occasionally or never ate fruits. It was also observed that patients who had birds in their homes (aOR 3.78, 95 CI% 1.12-12.70) were more likely to report asthma symptoms than those who did not have birds. Moreover, frequent cereal consumption was associated with asthma symptoms (aOR 0.08, 95 CI% 0.03-0.24). Middle-class (three and four levels) (aOR 1.78, 95 CI% 1.03-3.08) children and adolescents had higher odds of reporting asthma symptoms compared to lower-class (one and two levels) children/adolescents.

Associated factors for Asthma symptoms among adults

A family history of asthma, AR, and AE was found to be associated with asthma symptoms in adults. These predictors kept statistical significance after adjustment of the rest of the covariates (aOR 1.83, 95% CI 1.31-2.57; aOR 3.27, 95% CI 2.33–4.59; and aOR 4.40, 95% CI 2.76–7.01, respectively) (Table 3). Adults who took acetaminophen at least once a month were more likely to have asthma symptoms (aOR 2.04, 95% CI 1.51–2.76) compared to adults who never took acetaminophen in the 12 months before the survey date. It was also found that patients who were exposed to second-hand smoke were more likely to report asthma symptoms than patients who did not have this contact. This finding was statistically significant in the adjusted model (aOR 1.65, 95% CI 1.22-2.22). Bus traffic in front of their homes for most of the day was also a risk factor for asthma symptoms in the reduced model (aOR 1.66; 95% CI 1.04-2.65).

Discussion

This second analysis evaluates possible factors associated with asthma symptoms in a large sample of children/adolescents and adults in Colombia. Factors associated with asthma symptoms included a family history of allergic diseases such as asthma, rhinitis, and atopic eczema, along with acetaminophen consumption at least once a month. Among household factors, having birds in the home was associated with a higher prevalence of asthma symptoms for children/adolescents, while having dogs was a stronger indicator for adults. Regarding food, only fruit consumption was identified as increasing the risk of asthma symptoms in children/adolescents. However, the confidence interval of this association is broad, and further studies assessing this association are needed. In adults, however, passive smoke inhalation and being exposed to auto exhaust fumes for most of the day were significantly associated with asthma symptoms.

It is important to note that allergic diseases, specifically asthma, have been shown to cause significant health problems in the population of underdeveloped tropical countries. (5,21) In fact, important information from tropical countries has shown that there are particularities in these countries that impact the natural history of allergies, requiring further studies to influence the management and prevention of these pathologies.[14] Colombia, a tropical country, is characterized by its climatic variety among cities, which may explain the difference in asthma prevalence among those cities. Also, it has some particularities that directly impact the prevalence of asthma symptoms, such as perennial house dust mite exposure, environmental pollution by vehicle emissions, and other contaminants.[14] Although some risk factors for allergic diseases in the tropics are similar to those in temperate zones, some interesting differences may justify detailed analyses.[15]

Previous studies in Colombia have shown multiple factors associated with asthma symptoms in children, like being female,[12,13] the absence of breastfeeding,[11,12] the frequent use of acetaminophen,[11] the age of the mother at the time of the child's birth (< 30 years),[11] the educational level attained by the mother (primary or secondary),[11,13] existence of older siblings at birth,[11] history of diseases such as bronchiolitis in the child, asthma and rhinitis in the parents, inadequate flooring in the home, and kindergarten attendance.[12]

The above suggests that particular risk factors may influence the differences in the presentation of asthma symptoms. Our population has a higher prevalence of asthma than other countries: 30.8% in children and 14.7% in adults. Variation in the prevalence between countries ranges from 2-3% in areas such as Germany and Spain to 23-32% in places such as Denmark and the UK.[22]

One of our main findings was the association between a family history of atopy and asthma and rhinitis in both populations. However, atopic eczema in parents or siblings was a factor associated with asthma only in adults. These findings are also consistent with those found in a previous study evaluating rhinitis risk factors and with other similar studies that have been carried out in our country.[8,9,23] In conclusion, it is agreed that a family history of atopy

Table 2 Socio-demographic characteristics of cases and controls in adults' group.

Variable	Total N=3030 n (%)	Controls N=2333 n (%)	Cases N=697 n (%)	p-value*
Sex				**0.001**
Female	1727 (63%)	1445 (62%)	282 (70%)	
Male	1007 (37%)	888 (38%)	119 (30%)	
Age	37.96 (12.71) / 38.00 (26.00-49.00)	38.17 (12.61) / 38.00 (27.00-49.00)	36.80 (13.23) / 37.00 (24.00-48.00)	**0.047**
Socioeconomic status				0.34
1 and 2 (low)	1349 (49.34%)	1165 (49.94%)	184 (45.89%)	
3 and 4 (middle)	1303 (47.66%)	1100 (47.15%)	203 (50.62%)	
5 and 6 (high)	81 (2.96%)	68 (2.91%)	13 (3.24%)	
Missing	1 (0.04%)	0 (0.00%)	1 (0.25%)	
Educational attainment				0.052
No education	24 (0.88%)	23 (0.99%)	1 (0.25%)	
Elementary	1582 (57.86%)	1365 (58.51%)	217 (54.11%)	
High school	667 (24.40%)	576 (24.69%)	91 (22.69%)	
Technical	179 (6.55%)	146 (6.26%)	33 (8.23%)	
University	242 (8.85%)	195 (8.36%)	47 (11.72%)	
Others	16 (0.59%)	13 (0.56%)	3 (0.75%)	
No answer	2 (0.07%)	1 (0.04%)	1 (0.25%)	
Missing	22 (0.80%)	14 (0.60%)	8 (2.00%)	
Mother´s educational attainment				**0.007**
No education	1617 (59.14%)	1395 (59.79%)	222 (55.36%)	
Elementary school	559 (20.45%)	463 (19.85%)	96 (23.94%)	
High school	182 (6.66%)	143 (6.13%)	39 (9.73%)	
Missing	376 (13.75%)	332 (14.23%)	44 (10.97%)	
Shared rooms				0.84
No	905 (33.10%)	774 (33.18%)	131 (32.67%)	
Yes	1829 (66.90%)	1559 (66.82%)	270 (67.33%)	
Combustible material used for cooking				0.82
No	101 (3.69%)	87 (3.73%)	14 (3.49%)	
Yes	2631 (96.23%)	2245 (96.23%)	386 (96.26%)	
Missing	2 (0.07%)	1 (0.04%)	1 (0.25%)	
Animals living in the same house				**<0.001**
No	1473 (53.88%)	1291 (55.34%)	182 (45.39%)	
Yes	1261 (46.12%)	1042 (44.66%)	219 (54.61%)	
Dogs				**<0.001**
No	1839 (67.26%)	1598 (68.50%)	241 (60.10%)	
Yes	895 (32.74%)	735 (31.50%)	160 (39.90%)	
Cats				**0.014**
No	2500 (91.44%)	2146 (91.98%)	354 (88.28%)	
Yes	234 (8.56%)	187 (8.02%)	47 (11.72%)	
Rodents				0.26
No	2696 (98.61%)	2303 (98.71%)	393 (98.00%)	
Yes	38 (1.39%)	30 (1.29%)	8 (2.00%)	
Birds				**0.049**
No	2306 (84.35%)	1981 (84.91%)	325 (81.05%)	
Yes	428 (15.65%)	352 (15.09%)	76 (18.95%)	
Other animals				**0.036**
No	47 (1.72%)	35 (1.50%)	12 (2.99%)	
Yes	8 (0.29%)	3 (0.13%)	5 (1.25%)	
Missing	2679 (97.99%)	2295 (98.37%)	384 (95.76%)	
Fish				**0.029**
No	30 (1.10%)	17 (0.73%)	13 (3.24%)	
Yes	25 (0.91%)	21 (0.90%)	4 (1.00%)	
Missing	2679 (97.99%)	2295 (98.37%)	384 (95.76%)	

(*continues*)

Table 2 Continued.

Variable	Total N=3030 n (%)	Controls N=2333 n (%)	Cases N=697 n (%)	p-value*
Turtles				0.62
No	35 (1.28%)	25 (1.07%)	10 (2.49%)	
Yes	20 (0.73%)	13 (0.56%)	7 (1.75%)	
Missing	2679 (97.99%)	2295 (98.37%)	384 (95.76%)	
Smoke				0.33
No	2269 (82.99%)	1943 (83.28%)	326 (81.30%)	
Yes	465 (17.01%)	390 (16.72%)	75 (18.70%)	
Passive smoke				**<0.001**
No	2123 (77.65%)	1842 (78.95%)	281 (70.07%)	
Yes	610 (22.31%)	491 (21.05%)	119 (29.68%)	
Missing	1 (0.04%)	0 (0.00%)	1 (0.25%)	
Asthma in parents or siblings				**<0.001**
No	2258 (82.59%)	1990 (85.30%)	268 (66.83%)	
Yes	456 (16.68%)	329 (14.10%)	127 (31.67%)	
Missing	20 (0.73%)	14 (0.60%)	6 (1.50%)	
AR in parents or siblings				**<0.001**
No	2347 (85.84%)	2091 (89.63%)	256 (63.84%)	
Yes	359 (13.13%)	224 (9.60%)	135 (33.67%)	
Missing	28 (1.02%)	18 (0.77%)	10 (2.49%)	
AE in parents or siblings				**<0.001**
No	2554 (93.42%)	2232 (95.67%)	322 (80.30%)	
Yes	154 (5.63%)	86 (3.69%)	68 (16.96%)	
Missing	26 (0.95%)	15 (0.64%)	11 (2.74%)	
Cesarean delivery				**0.007**
No	2532 (92.61%)	2177 (93.31%)	355 (88.53%)	
Yes	155 (5.67%)	121 (5.19%)	34 (8.48%)	
Missing	47 (1.72%)	35 (1.50%)	12 (2.99%)	
Health care insurance				0.13
No	220 (8.05%)	180 (7.72%)	40 (9.98%)	
Yes	2513 (91.92%)	2152 (92.24%)	361 (90.02%)	
Missing	1 (0.04%)	1 (0.04%)	0 (0.00%)	
Type of health care insurance				0.95
Subsidized	891 (32.59%)	762 (32.66%)	129 (32.17%)	
Contributive/Special	1620 (59.25%)	1387 (59.45%)	233 (58.10%)	
Missing	223 (8.16%)	184 (7.89%)	39 (9.73%)	
Average hours of television				0.52
< 1 hour	271 (9.91%)	223 (9.56%)	48 (11.97%)	
1-2 hours	826 (30.21%)	708 (30.35%)	118 (29.43%)	
3-4 hours	591 (21.62%)	507 (21.73%)	84 (20.95%)	
> 5 hours	1040 (38.04%)	890 (38.15%)	150 (37.41%)	
Missing	6 (0.22%)	5 (0.21%)	1 (0.25%)	
Average acetaminophen consumption last 12 months				**<0.001**
At least once per week	589 (21.54%)	539 (23.10%)	50 (12.47%)	
At least once per month	615 (22.49%)	461 (19.76%)	154 (38.40%)	
At least four times per year	722 (26.41%)	607 (26.02%)	115 (28.68%)	
At least once per year	574 (20.99%)	508 (21.77%)	66 (16.46%)	
Never	228 (8.34%)	213 (9.13%)	15 (3.74%)	
Missing	6 (0.22%)	5 (0.21%)	1 (0.25%)	

*p-value based on t-test or chi-square/fisher test.

Table 3 Factors associated with asthma symptoms in the study population.

Factors associated with asthma symptoms among children/adolescents				Factors associated with asthma symptoms among adults			
Variable	Reduced model*			Variable	Reduced model*		
	Odds Ratio	[95% Conf. Interval]			Odds Ratio	[95% Conf. Interval]	
Gender				Gender			
Male	1.38	0.84	2.27	Male	0.92	0.68	1.23
Age in years	1.06	1.00	1.13	Age in years	1.00	0.99	1.01
Socioeconomic status				Socioeconomic status			
1 and 2 (low)	1.00	(base)		1 and 2 (low)	-		
3 and 4 (middle)	1.78	1.03	3.08	3 and 4 (middle)	-	-	-
5 and 6 (high)	1.41	0.27	7.47	5 and 6 (high)	-	-	-
Mother´s educational attainment				Mother´s educational attainment			
No education	1.00	(base)		No education	-		
Elementary school	0.73	0.35	1.50	Elementary school	-	-	-
High school	0.51	0.23	1.17	High school	-	-	-
Dogs in house				Dogs in house			
Yes	-	-	-	Yes	1.37	1.03	1.83
Cats in house				Cats in house			
Yes	-	-	-	Yes	1.48	0.96	2.27
Birds in house				Birds in house			
Yes	2.04	1.09	3.80	Yes	1.00	0.71	1.42
Passive smoke				Passive smoke			
Yes	-	-	-	Yes	1.65	1.22	2.22
Asthma in parents or siblings				Asthma in parents or siblings			
Yes	2.43	1.27	4.67	Yes	1.83	1.31	2.57
AR in parents or siblings				AR in parents or siblings			
Yes	1.95	1.07	3.56	Yes	3.27	2.33	4.59
Atopic eczema in parents or siblings				Atopic eczema in parents or siblings			
Yes	1.82	0.90	3.69	Yes	4.40	2.76	7.01
Cesarean delivery				Cesarean delivery			
Yes	1.27	0.70	2.32	Yes	1.57	0.97	2.54
The insurance plan of the enrolled				The insurance plan of the enrolled			
Subsidized	1.00	(base)		Subsidized	1.00	(base)	
Contributive	0.60	0.31	1.16	Contributive	0.84	0.64	1.12
Average acetaminophen consumption				Average acetaminophen consumption			
At least once per week	1.04	0.36	3.04	At least once per week	0.71	0.47	1.08
At least once per month	3.63	2.11	6.24	At least once per month	2.04	1.51	2.76
Public transportation				Public transportation			
Occasionally	-	-	-	Occasionally	0.93	0.60	1.42
Frequently	-	-	-	Frequently	1.25	0.74	2.13
Most of the day	-	-	-	Most of the day	1.66	1.04	2.65

OR = odds ratio. CI = confidence interval.
*The reduced model was based on the Furnival-Wilson leaps-and-bounds algorithm; Linearity link test p < 0.0001.

plays an important role in this disease and, more specifically, suggests a strong association with an early onset of persistent asthma.[24] Several genes have been associated with asthma,[6,25] supporting that a family history of asthma and allergic diseases are strong determinants of asthma. However, the magnitude of the effect varies, with some subtypes having a stronger hereditary component and others being more strongly related to environmental exposures.[24]

Another risk factor that was identified was the consumption of acetaminophen. The consumption of this medication at least once a month increases the likelihood of asthma symptoms in both groups, children/adolescents and adults. Acetaminophen is the most commonly used drug in the world.[26] It is routinely prescribed for fever management in pediatric patients and is associated with asthma exacerbations.[27] It is also widely used in adults to manage acute and chronic pain, and there is evidence of adverse

effects in pathologies such as hypertension and asthma.[26] Over time, the consumption of this drug has become more frequent. One mechanism explaining the effects of acetaminophen in asthmatic patients is that the N-acetyl-p-benzoquinone imine, one of its metabolites, decreases the levels of glutathione, an important antioxidant in the airways.[28] Other mechanisms that have been identified are increased oxidative stress and an imbalance in lipoxygenase activity caused by COX inhibition, which results in increased production of these pro-inflammatory substances.[26] Consumption of this medication has also been associated with worsening symptoms of other allergic diseases, such as rhinitis and atopic eczema,[29] a finding observed in our previous study of allergic rhinitis.[23]

The relationship between asthma and socioeconomic status is complex because the findings in studies on this subject vary. Some show that belonging to a low socioeconomic level implies a lower risk,[30] while others claim that it increases the risk[31] of presenting asthma symptoms, and others state that there is no relationship.[32] In our study, we found a statistically significant association between asthma symptoms and socioeconomic level only in children and adolescents, with a higher risk of presenting asthma symptoms in patients belonging to higher social classes. This finding may be explained by better access to medical care and, therefore, a higher probability of being diagnosed as asthmatic than populations belonging to lower socioeconomic levels.[33]

The ISAAC study highlights that a country's economic development can change, which influences allergic diseases such as asthma, rhinoconjunctivitis, and eczema. Specifically, the third phase of this study evaluated findings in 98 countries that showed a positive association between asthma symptoms and Gross National Income (GNI), although the prevalence of severe symptoms was inversely correlated with GNI. However, caution should be exercised in interpreting the results because of significant income distribution inequalities in most developing countries.[34]

Another risk factor identified in this study was passive smoking, but this finding in our study was only statistically significant in the adult population. Tobacco smoke during pregnancy and early childhood has been shown to permanently damage children's lungs and increase the risk of asthma during this stage of life and adulthood. Both passive exposure and active smoking worsen asthma.[35] Smoking history is associated with a lower relation of FEV1/FVC.[36] It has also been explained that tobacco smoke contains a high concentration of nitric oxide (NO), which exerts negative feedback on NO synthesis and a down-regulation of NO synthase activity in respiratory tract cells. Consequently, endothelial NO synthase expression in pulmonary arteries is reduced in smokers. The marked effects of smoking in asthmatic or atopic individuals may be explained by the higher FeNO levels observed in nonsmokers in these subgroups.[37]

Similarly, exposure to traffic-related air pollution impacts asthma development, persistence, and exacerbation.[35] In our study, we found that adults who reported having buses passing close to their homes during a large part of the day were more likely to present asthma symptoms; in children/adolescents, this finding was not statistically significant. This has been explained because exhaust particles can enhance immune responses to allergens and inflammatory reactions in the airways.[38]

Another factor identified in this study was having animals at home, specifically, in the case of children/adolescents, birds, and adults, the presence of dogs. An association has been observed between exposure to domestic animals and the diagnosis of asthma and, more specifically, the severity of atopic manifestations, probably due to the sensitization caused in some patients. This exposure could be the cause of acute asthma attacks since it is associated with prolonged bronchial hyperresponsiveness.[39] Bird ownership was associated with higher rates of respiratory symptoms, regardless of the time of life in which the bird was kept.[40] It is claimed that birds are significantly associated with asthma.[41] However, the literature on the correlation between asthma development or exacerbations and birds' presence is still scarce.

When evaluating findings in other tropical countries, such as Brazil, it was identified that among 878 children, the prevalence of current asthma was 31.2%, like our results (30.84%). Active asthma was 12.4%, and among the factors associated with asthma were current rhinitis, sharing a bedroom during the first year of life, atopy, use of antibiotics in the first six months of life, having a cat inside the house during the first year of life, premature birth, and, as in our study, use of acetaminophen more than 12 times a year.[43]

On the other hand, a study conducted in Ecuador with an adult population of over 2400 patients found that the prevalence of wheezing in the last 12 months, lifetime, and asthma diagnosed by a physician was 6.3%, 1.9%, and 1.6%, respectively. These rates are lower, with a combined total of 9.8%, compared to the prevalence identified in our study, which was 14.67%.

Among the factors associated with asthma were mold in the home, a cat in the house, and rhinitis at some time.[44] From the review of the available literature, it is possible to state that multiple risk factors have been implicated in the development of the different phenotypes of childhood and adult asthma, among which we can highlight the hereditary component of atopic diseases, the consumption of acetaminophen, smoking, environmental pollution, presence of pets, and consumption of some foods, among other factors that were not evaluated in our study, such as vitamin D deficiency, stress, occupational exposures, among others. A better understanding of the predisposing factors could facilitate public health and primary prevention strategies.[22,45]

Strengths and Limitations

This study is based on the country's population with a representative sample of the six selected cities. It studies the association between personal, environmental, cultural, and socioeconomic factors and asthma symptoms among a wide range of inhabitants of Colombian cities, allowing for an adequate representation of the population. It describes models that explain the association patterns between the different variables and asthma symptoms in each population.

Regarding the limitations of the study, given that it was a study based on surveys, there is a risk of incurring classification errors that reduce the possibility of accurately

identifying associations. This is because the questionnaires were self-completed by the adolescents, and those of the younger children were completed with the help of their parents. Finally, in these case and control studies, recall bias is a possibility that could cause people to be more prone to reporting a greater frequency in certain factors, resulting in an overestimation of certain relationships. Future research will need to investigate the use of other tobacco products, including electronic nicotine delivery systems, hookahs, and cigars, among others, on the association of asthma symptoms.

Conclusions

This study identified the factors associated with asthma symptoms in six cities in Colombia. These findings suggest the presence of different exposure factors (cultural, environmental, family, and dietary) among the children/adolescent and adult populations. Furthermore, the study provides the basis for future investigations to confirm our findings and generate awareness regarding the disease in our country and Latin America. Furthermore, it contributes knowledge regarding the unknown factors our population is exposed to (infant, adolescent, and adult).

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Author Contributions

All authors contributed equally to this manuscript.

Conflicts of Interest

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Supplementary

Table S1 Variables explored in children/adolescents and adults.

Sociodemographic

Gender (female, male)
Age (<5 years, 5-12 years, >12 years)
Educational attainment (elementary school, High school, no answer)
Mother's educational attainment (no education, elementary school, high school, no answer)
Socioeconomic status (1-2 (low), 3-4 (middle), 5-6 (high))

Health care insurance (yes, no)

Type of health care insurance (Subsidized, Contributive/Special)

Personal and family history (yes, no)

Family history of asthma
Family history of allergic rhinitis
Family history of atopic eczema
Cesarean delivery
Smoking
Another person smoking

Habits

Hours watching television per day (< 1 hour, 1-2 hours, 3-4 hours, $\geq$ 5 hours)
Average acetaminophen consumption during the last 12 months (At least once per week, At least once per month, At least four times per year, At least once per year, Never)
Food consumption during the last 12 months (meat, fish/seafood, fruits, vegetables, beans, cereal, pasta, rice, butter, margarine, peanuts, potatoes, milk, egg, hamburgers/hot dogs/other fast food)

Environment

Sharing room (yes, no)
Combustible material used for cooking (yes, no)
Animals living inside the same house: dogs, cats, rodents, birds, other animals (yes, no)
Frequency of bus transit in front of the house (Never, Occasionally, Frequently during the day, During most of the day)

[1]Colombian population is divided into six socioeconomic strata considering urban characteristics such as population density, quality of public areas, and housing characteristics (stratum one corresponds to the lowest and stratum six to the highest).

Table S2 Eating habits of the children/adolescents population in the last 12 months.

Variable	Total N=1276 n (%)	Controls N=776 n (%)	Cases N=500 n (%)	p-value
Meat				0.24
Occasionally or never	43 (3.83%)	29 (3.74%)	14 (4.05%)	
Once or twice a week	273 (24.33%)	178 (22.94%)	95 (27.46%)	
Three or more times a week	806 (71.84%)	569 (73.32%)	237 (68.50%)	
Seafood				0.068
Occasionally or never	757 (67.47%)	541 (69.72%)	216 (62.43%)	
Once or twice a week	294 (26.20%)	189 (24.36%)	105 (30.35%)	
Three or more times a week	69 (6.15%)	46 (5.93%)	23 (6.65%)	
Missing	2 (0.18%)	0 (0.00%)	2 (0.58%)	
Fruits				0.17
Occasionally or never	102 (9.09%)	73 (9.41%)	29 (8.38%)	
Once or twice a week	296 (26.38%)	192 (24.74%)	104 (30.06%)	
Three or more times a week	724 (64.53%)	511 (65.85%)	213 (61.56%)	
Vegetable				0.18
Occasionally or never	192 (17.11%)	142 (18.30%)	50 (14.45%)	
Once or twice a week	328 (29.23%)	230 (29.64%)	98 (28.32%)	
Three or more times a week	602 (53.65%)	404 (52.06%)	198 (57.23%)	
Legumes (beans, lentils and peas)				0.10
Occasionally or never	95 (8.47%)	57 (7.35%)	38 (10.98%)	
Once or twice a week	505 (45.01%)	349 (44.97%)	156 (45.09%)	
Three or more times a week	521 (46.43%)	370 (47.68%)	151 (43.64%)	
Missing	1 (0.09%)	0 (0.00%)	1 (0.29%)	
Cereal				**<0.001**
Occasionally or never	72 (6.42%)	38 (4.90%)	34 (9.83%)	
Once or twice a week	201 (17.91%)	121 (15.59%)	80 (23.12%)	
Three or more times a week	849 (75.67%)	617 (79.51%)	232 (67.05%)	
Pasta				0.21
Occasionally or never	139 (12.39%)	95 (12.24%)	44 (12.72%)	
Once or twice a week	667 (59.45%)	474 (61.08%)	193 (55.78%)	
Three or more times a week	316 (28.16%)	207 (26.68%)	109 (31.50%)	
Rice				**0.002**
Occasionally or never	17 (1.52%)	6 (0.77%)	11 (3.18%)	
Once or twice a week	74 (6.60%)	45 (5.80%)	29 (8.38%)	
Three or more times a week	1,031 (91.89%)	725 (93.43%)	306 (88.44%)	
Butter				0.32
Occasionally or never	528 (47.06%)	374 (48.20%)	154 (44.51%)	
Once or twice a week	311 (27.72%)	205 (26.42%)	106 (30.64%)	
Three or more times a week	283 (25.22%)	197 (25.39%)	86 (24.86%)	
Margarine				**0.029**
Occasionally or never	821 (73.17%)	586 (75.52%)	235 (67.92%)	
Once or twice a week	192 (17.11%)	124 (15.98%)	68 (19.65%)	
Three or more times a week	108 (9.63%)	66 (8.51%)	42 (12.14%)	
Nuts and peanuts				0.081
Occasionally or never	853 (76.02%)	591 (76.16%)	262 (75.72%)	
Once or twice a week	225 (20.05%)	161 (20.75%)	64 (18.50%)	
Three or more times a week	44 (3.92%)	24 (3.09%)	20 (5.78%)	
Potato				0.48
Occasionally or never	61 (5.44%)	39 (5.03%)	22 (6.36%)	
Once or twice a week	396 (35.29%)	269 (34.66%)	127 (36.71%)	
Three or more times a week	664 (59.18%)	467 (60.18%)	197 (56.94%)	
Missing	1 (0.09%)	1 (0.13%)	0 (0.00%)	
Milk				0.77
Occasionally or never	94 (8.38%)	68 (8.76%)	26 (7.51%)	
Once or twice a week	192 (17.11%)	131 (16.88%)	61 (17.63%)	
Three or more times a week	836 (74.51%)	577 (74.36%)	259 (74.86%)	

(*continues*)

Table S2 Continued.

Variable	Total N=1276 n (%)	Controls N=776 n (%)	Cases N=500 n (%)	p-value
Eggs				**<0.001**
Occasionally or never	82 (7.31%)	41 (5.28%)	41 (11.85%)	
Once or twice a week	395 (35.20%)	272 (35.05%)	123 (35.55%)	
Three or more times a week	643 (57.31%)	461 (59.41%)	182 (52.60%)	
Missing	2 (0.18%)	2 (0.26%)	0 (0.00%)	
Hamburgers/hot dogs or other fast food				**<0.001**
Occasionally or never	813 (72.46%)	592 (76.29%)	221 (63.87%)	
Once or twice a week	264 (23.53%)	170 (21.91%)	94 (27.17%)	
Three or more times a week	45 (4.01%)	14 (1.80%)	31 (8.96%)	
Frequency of public transportation passing through the street where subjects lived				**<0.001**
Never	641 (57.13%)	486 (62.63%)	155 (44.80%)	
Occasionally	187 (16.67%)	112 (14.43%)	75 (21.68%)	
Frequently during the day	135 (12.03%)	89 (11.47%)	46 (13.29%)	
During most of the day	146 (13.01%)	83 (10.70%)	63 (18.21%)	
Missing	13 (1.16%)	6 (0.77%)	7 (2.02%)	

Table S3 Eating habits of the adult population in the last 12 months.

	Total N=3030 n (%)	Controls N=2333 n (%)	Cases N=697 n (%)	p-value
Occasionally or never	90 (3.29%)	71 (3.04%)	19 (4.74%)	
Once or twice a week	584 (21.36%)	508 (21.77%)	76 (18.95%)	
Three or more times a week	2060 (75.35%)	1754 (75.18%)	306 (76.31%)	
Seafood				0.36
Occasionally or never	1504 (55.01%)	1274 (54.61%)	230 (57.36%)	
Once or twice a week	978 (35.77%)	837 (35.88%)	141 (35.16%)	
Three or more times a week	252 (9.22%)	222 (9.52%)	30 (7.48%)	
Fruits				0.50
Occasionally or never	194 (7.10%)	161 (6.90%)	33 (8.23%)	
Once or twice a week	673 (24.62%)	570 (24.43%)	103 (25.69%)	
Three or more times a week	1866 (68.25%)	1601 (68.62%)	265 (66.08%)	
Missing	1 (0.04%)	1 (0.04%)	0 (0.00%)	
Vegetable				0.55
Occasionally or never	218 (7.97%)	187 (8.02%)	31 (7.73%)	
Once or twice a week	736 (26.92%)	619 (26.53%)	117 (29.18%)	
Three or more times a week	1779 (65.07%)	1526 (65.41%)	253 (63.09%)	
Missing	1 (0.04%)	1 (0.04%)	0 (0.00%)	
Legumes (beans, lentils and peas)				0.10
Occasionally or never	231 (8.45%)	187 (8.02%)	44 (10.97%)	
Once or twice a week	1222 (44.70%)	1040 (44.58%)	182 (45.39%)	
Three or more times a week	1280 (46.82%)	1105 (47.36%)	175 (43.64%)	
Missing	1 (0.04%)	1 (0.04%)	0 (0.00%)	
Cereal				0.22
Occasionally or never	202 (7.39%)	173 (7.42%)	29 (7.23%)	
Once or twice a week	444 (16.24%)	367 (15.73%)	77 (19.20%)	
Three or more times a week	2087 (76.34%)	1792 (76.81%)	295 (73.57%)	
Missing	1 (0.04%)	1 (0.04%)	0 (0.00%)	
Pasta				0.35
Occasionally or never	334 (12.22%)	284 (12.17%)	50 (12.47%)	
Once or twice a week	1578 (57.72%)	1359 (58.25%)	219 (54.61%)	
Three or more times a week	822 (30.07%)	690 (29.58%)	132 (32.92%)	
Rice				0.051
Occasionally or never	41 (1.50%)	31 (1.33%)	10 (2.49%)	
Once or twice a week	145 (5.30%)	117 (5.02%)	28 (6.98%)	
Three or more times a week	2548 (93.20%)	2185 (93.66%)	363 (90.52%)	
Butter				0.57
Occasionally or never	1429 (52.27%)	1215 (52.08%)	214 (53.37%)	
Once or twice a week	670 (24.51%)	568 (24.35%)	102 (25.44%)	
Three or more times a week	635 (23.23%)	550 (23.57%)	85 (21.20%)	
Margarine				0.70
Occasionally or never	2007 (73.41%)	1718 (73.64%)	289 (72.07%)	
Once or twice a week	438 (16.02%)	368 (15.77%)	70 (17.46%)	
Three or more times a week	289 (10.57%)	247 (10.59%)	42 (10.47%)	
Nuts and peanuts				0.36
Occasionally or never	2092 (76.52%)	1774 (76.04%)	318 (79.30%)	
Once or twice a week	517 (18.91%)	451 (19.33%)	66 (16.46%)	
Three or more times a week	124 (4.54%)	107 (4.59%)	17 (4.24%)	
Missing	1 (0.04%)	1 (0.04%)	0 (0.00%)	
Potato				0.50
Occasionally or never	123 (4.50%)	102 (4.37%)	21 (5.24%)	
Once or twice a week	740 (27.07%)	625 (26.79%)	115 (28.68%)	
Three or more times a week	1869 (68.36%)	1604 (68.75%)	265 (66.08%)	
Missing	2 (0.07%)	2 (0.09%)	0 (0.00%)	

(continues)

Table S3 Continued.

	Total N=3030 n (%)	Controls N=2333 n (%)	Cases N=697 n (%)	p-value
Milk				0.16
Occasionally or never	188 (6.88%)	154 (6.60%)	34 (8.48%)	
Once or twice a week	404 (14.78%)	337 (14.44%)	67 (16.71%)	
Three or more times a week	2142 (78.35%)	1842 (78.95%)	300 (74.81%)	
Eggs				0.32
Occasionally or never	210 (7.68%)	174 (7.46%)	36 (8.98%)	
Once or twice a week	915 (33.47%)	773 (33.13%)	142 (35.41%)	
Three or more times a week	1604 (58.67%)	1381 (59.19%)	223 (55.61%)	
Missing	5 (0.18%)	5 (0.21%)	0 (0.00%)	
Hamburgers/hot dogs or other fast food				0.97
Occasionally or never	2051 (75.02%)	1752 (75.10%)	299 (74.56%)	
Once or twice a week	595 (21.76%)	506 (21.69%)	89 (22.19%)	
Three or more times a week	86 (3.15%)	73 (3.13%)	13 (3.24%)	
Missing	2 (0.07%)	2 (0.09%)	0 (0.00%)	
Frequency of public transportation passing through the street where subjects lived				0.010
Never	1998 (73.08%)	1724 (73.90%)	274 (68.33%)	
Occasionally	367 (13.42%)	313 (13.42%)	54 (13.47%)	
Frequently during the day	176 (6.44%)	146 (6.26%)	30 (7.48%)	
During most of the day	192 (7.02%)	149 (6.39%)	43 (10.72%)	
Missing	1 (0.04%)	1 (0.04%)	0 (0.00%)	