ORIGINAL ARTICLE

Prevalence of Symptoms of Asthma, Rhinitis, and Atopic Eczema in Brazilian Adolescents Related to Exposure to Gaseous Air Pollutants and Socioeconomic Status

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Abstract

Objectives: To evaluate the relationship between exposure to gaseous air pollutants (ozone [O_3], carbon monoxide [CO], nitrogen dioxide [NO_2], and sulfur dioxide [SO_2]) socioeconomic status and the prevalence of symptoms of asthma, rhinitis and atopic eczema in adolescents.

Subjects and Methods: A sample of 16 209 adolescents from São Paulo West (SPW), São Paulo South (SPS), Santo André (SA), Curitiba (CR), and Porto Alegre (PoA) were enrolled. Data on air pollutants and socioeconomic status were compared to prevalence of symptoms with the Spearman correlation coefficient.

Results: Socioeconomic status was quite similar in all cities. The levels of O_3 in SPW, SPS, and SA, and of CO in SA were higher than the acceptable ones. In relation to O_3 and CO exposures, adolescents from SPW and SA had a significant risk of current wheezing, whereas living in SPW was associated with a high risk of rhinoconjunctivitis, eczema, and flexural eczema and living in CR to rhinitis. Exposure to NO_2 was associated with a high risk of current wheezing in SPW and SA, and of severe asthma in SPW and PoA. Exposure to SO_2 was associated with a high risk of current wheezing in SPW and SA, severe asthma in SPW and PoA, and nighttime cough, eczema, flexural eczema and severe eczema in SPW. Living in SPW, CR, or PoA was associated with a high risk of rhinitis, rhinoconjunctivitis, and severe rhinitis.

Conclusions: Although we did not detect a characteristic pattern for all symptoms evaluated or a specific air pollutant, our data suggest a relationship between higher exposure to photochemical pollutants and high prevalence or risk of symptoms of asthma, rhinitis, and atopic eczema.

Key words: Air pollution. Asthma. Atopic eczema. Rhinitis. Gaseous pollutants. Ozone. Carbon monoxide. Nitrogen dioxide. Sulfur dioxide.

Resumen

Objetivos: Valorar la relación entre la exposición a contaminantes ambientales gaseosos (ozono [O_3], monóxido de carbono [CO], dióxido de nitrógeno [NO_2] y dióxido de azufre [SO_2]), el estatus socioeconómico y la prevalencia de los síntomas de asma, rinitis y eccema atópico en adolescentes.

Sujetos y Métodos: Participaron en el estudio una muestra de 16.209 adolescentes de São Paulo Oeste (SPW), São Paulo Sur (SPS), Santo André (SA), Curitiba (CR) y Porto Alegre (PoA). Los datos sobre los contaminantes atmosféricos y el estatus socioeconómico se compararon con la prevalencia de los síntomas mediante el coeficiente de correlación Spearman.

Resultados: El estatus socioeconómico era bastante similar en todas las ciudades. Los niveles de O_3 en SPW, SPS y SA, y de CO en SA superaron los niveles aceptables. En lo relativo a la exposición a O_3 y CO, los adolescentes de SPW y SA presentaron un riesgo significativo de sibilancias, mientras que vivir en SPW se asoció a un riesgo elevado de padecer rinoconjuntivitis, eccema y eccema en superficie flexora y en CR a rinitis. La exposición a NO_2 se asoció a un elevado riesgo de sibilancias en la actualidad en SPW y SA, y de asma grave en SPW y PoA. La exposición a SO_2 se asoció a un elevado riesgo de sibilancias en la actualidad en SPW y SA, y de asma grave en SPW y PoA. En SPW, se asoció además a tos nocturna, eccema, eccema en superficie flexora y eccema grave. Vivir en SPW, CR y PoA se asoció a un riesgo elevado de padecer rinitis, rinoconjuntivitis y rinitis grave.

Conclusiones: Aunque no hemos detectado un patrón característico de todos los síntomas estudiados o un contaminante atmosférico específico, los datos del estudio sugieren que existe una relación entre una mayor exposición a contaminantes fotoquímicos y un mayor riesgo de prevalencia de síntomas del asma, rinitis y eccema atópico.

Palabras clave: Contaminación atmosférica. Asma. Eccema atópico. Rinitis. Contaminantes gaseosos. Ozono. Monóxido de carbono. Dióxido de nitrógeno. Dióxido de azufre.

Introduction

Fossil fuel combustion emissions by automotive vehicles, associated with urbanization and a westernized lifestyle, are named among the reasons for the rising frequency of respiratory allergic diseases observed in most industrialized countries [1-6].

Over the past 2 decades, studies on air pollution and its effects on human health have provided considerable evidence that asthmatic individuals are at increased risk of developing exacerbations with exposure to air pollutants such as ozone (O_3), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), carbon monoxide (CO) and inhalable particulate matter [7,8]. Nevertheless, the relationship between long-term exposures to air pollutants (especially photochemical air pollutants) and asthma prevalence in developed countries is still debated [1,8]. Although a statistical association between exposure to air pollutants and respiratory disease has been identified in several studies, causality can not be proved in all of them. Moreover, it is difficult to compare and interpret these studies in relation to the pollutant that people were exposed to and the duration and intensity of exposure [1,8]. Venn et al [9] investigated the relationship between local road traffic activity and the occurrence, severity, and persistence of wheezing in schoolchildren. They measured the traffic flow intensity in the neighborhood of primary and secondary schools and related this variable to the prevalence of wheezing in the last year. A positive but nonsignificant dose-related effect of traffic activity on wheeze severity in primary and secondary schoolchildren and on persistence of wheezing in the longitudinal cohort were observed. In studying the relationship between air pollution patterns and their effects upon allergies, other authors have found that exposure to high levels of nitrogen oxide gases, O_3, tobacco smoke, fine and ultrafine particulate matter, and diesel exhaust particles seems to enhance allergic disease [5]. Some surveys suggest that air pollutants, especially diesel exhaust particulates, can trigger allergic sensitization and development of atopic diseases [3,10]. In a recent study, Sichletidis et al [11] determined the effects of air pollutant exposure in children living in different regions of Macedonia. They found distinct levels of air pollutants and observed a detrimental effect on the respiratory system, mainly rhinitis and infectious bronchitis. The highest prevalences of rhinitis and bronchitis were observed in the highly polluted region.

In Brazil, many studies on effects of air pollution on the health of people living in large cities, mainly in São Paulo, the most polluted city in Brazil, have been undertaken in the past decade. These studies have shown an association of air pollution with child respiratory-disease–related deaths, even after a short period of exposure [12] and children's respiratory illness (emergency room visits due to lower respiratory tract diseases, hospital admissions due to pneumonia or bronchopneumonia, and hospital admissions due to asthma or bronchiolitis) [13,14]. Apart from these studies, none have properly applied a population-based design to explore the relationship between the prevalence of asthma and related symptoms. Rios et al [15] evaluated the effects of exposure to air pollution (particulate matter ≤10 μm in diameter) in 2 cities in the state of Rio de Janeiro with distinct patterns of air pollution. They observed a significant relationship between atmospheric pollution and the prevalence of asthma in adolescents obtained by applying the written questionnaire of the International Study of Asthma and Allergies in Childhood (ISAAC).

The objectives of this study were to determine the relationship between exposure to photochemical air pollutants (O_3, NO_2, SO_2, and CO) and socioeconomic status and the prevalence of symptoms of asthma, rhinitis and atopic eczema in adolescents living in Brazilian cities with a high population index and high air pollution levels.

Subjects and Methods

From the 21 centers involved in the ISAAC phase 3 study [16] we selected those with a population density higher than 2800 inhabitants/km^2 with regularly and continuously monitored gaseous air pollutant levels. They were São Paulo West (SPW) and São Paulo South (SPS), in the southeast (7175 inhabitants/km^2); Santo André (SA) in the southeast (3826 inhabitants/km^2); Curitiba (CR) in the south 4041 (inhabitants/km^2); and Porto Alegre (PoA) in the south 2875 (inhabitants/km^2) [17,18].

Adolescents (aged 13-14 years old) from these centers were selected as standardized by the ISAAC protocol [19,20] from among those who attended public and private schools. Information regarding the number of schools and students in each area was obtained from the official records of the city education department. After sample definition, the adolescents filled in the ISAAC written questionnaire in their classrooms. The ISAAC questionnaire that had been previously translated and validated for use in the Brazilian culture [21-23] was applied to 16 209 adolescents. The data obtained was transcribed in a database (Epi-Info) supplied by the ISAAC coordinators.

For the purpose of this study we considered certain questions of the ISAAC questionnaire to refer to symptoms: current wheezing (wheeze in the last 12 months), severe asthma (wheeze severe enough to limit speech in the last 12 months), nighttime cough (dry cough at night in the last 12 months), rhinitis in the last year (sneezing, runny or blocked nose in the last 12 months), rhinoconjunctivitis (nose problem with itchy, watery eyes in the last 12 months), severe rhinitis (interference with daily activities), eczema (itchy rash that was coming and going for at least 6 months in the last 12 months), flexural eczema (this itchy rash ever in characteristic places), and severe eczema (kept awake at night by this itchy rash in the last 12 months).

Data on air pollutants were obtained from the respective state environmental control agencies. They were collected at the following monitoring stations: CETESB (SPW, SPS and SA) [24], SMMA (CR) [25], and FEPAM (PoA) [26] (Tables 3, 4, and 5). CO was measured by nondispersive infrared absorption, SO_2 by ionic chromatography, NO_2 by chemiluminescence, and O_3 by ultraviolet photometry. Annual mean levels of these pollutants were considered in the analyses. The pollutant levels were compared to the national standard (resolution of the Brazilian national environmental council, CONAMA No. of 28/06/1990): O_3 less than 160 µg/m^3 in 1 hour; NO_2 less than 100 µg/m^3 annual mean; CO less than 9 parts per million (ppm)/8 hours; SO_2 less than 80 µg/m^3 annual mean [24].

Socioeconomic status evaluation was based on the infant mortality rate (number of dead children younger than 1 year old per 1000 live births), poverty index (percentage of people who earn less than half the minimum salary of US$50.00 per month) and mean nominal income for individuals older than 10 years [17,18] (Table1).

The relationships between the frequency of affirmative answers to the selected questions, socioeconomic status, and air pollutants were estimated by the Spearman correlation coefficient. The center with the lowest level of a specific air pollutant was defined as the reference, and the risk of an affirmative answer for each question was expressed as an odds ratio (OR) and 95% confidence interval (CI). In all tests the level for rejection of the null hypothesis was 5%

Results

Table 1 shows socioeconomic indices and the prevalence of affirmative answers to the selected questions for each of the different population centers. Socioeconomic status was quite

Table 1. Socioeconomic Parameters, Latitude, and Prevalence of Symptoms of Asthma, Rhinitis, and Atopic Eczema Among Adolescents (13-14 Years Old) Obtained With the International Study of Asthma and Allergies in Childhood (ISAAC) Written Questionnaire in Different Brazilian Centers*

Center	Latitude South	Socioeconomic Status			Prevalence, %							
		Infant Mortality†, n/1000	Poverty Index‡, %	Mean Nominal Income for People Older Than 10 y, US$	Current Wheezing	Severe Asthma	Nighttime Cough	Rhinitis Last Year	Rhinocon-junctivitis	Severe Rhinitis	Eczema	Flexural Eczema	Severe Eczema
SPW, n=3181	23.30	20.89	11.40	470.21	21.9	5.6	36.2	30.1	19.8	20.2	9.7	6.9	5.4
SPS, n=3161	23.32	20.89	11.40	470.21	18.7	2.9	33.3	27.4	12.2	14.5	7.1	3.6	2.2
AS, n=3232	23.39	14.48	11.68	394.42	23.2	3.0	32.9	28.4	13.8	15.4	7.1	3.4	2.0
CR, n=3628	25.25	22.47	13.45	448.90	18.9	3.1	34.7	39.2	17.2	20.4	6.3	3.7	1.5
PoA, n=3007	28.15	21.33	13.71	478.80	18.2	4.8	35.0	32.1	15.9	20.0	7.0	5.0	5.0

* SPW indicates São Paulo-West; SPS, São Paulo-South; SA, Santo André; CR, Curitiba; PoA, Porto Alegre. † deaths in the first year of life per 1000 live births. ‡ Percentage of population with a family income lower than 0.5 the minimum salary (US$ 50.00); BR$2.50 = US$1.00

Table 2. Relationship Between Socioeconomic Status Indexes and Questions on the ISAAC Written Questionnaire, Evaluated With the Spearman Correlation Coefficient*

ISAAC Written Questionnaire	Infant Mortality†	Poverty Index	Mean Nominal Income for People Older Than 10 y
Asthma			
Current wheezing	−0.771	−0.771	−0.143
Severe asthma	0.696	0.725	0.754
Nighttime cough	0.887†	0.841	0.657
Rhinitis			
Rhinitis	−0.029	−0.145	0.464
Rhinoconjunctivitis	0.026	−0.314	0.429
Severe rhinitis	0.657	0.543	0.714
Atopic eczema			
Eczema	0.429	0.429	0.257
Flexural eczema	0.486	0.314	0.600
Severe eczema	0.600	0.714	0.543

* ISAAC indicates International Study of Asthma and Allergies in Childhood.
† Deaths in the first year of life per 1000 live births. ‡ $P<.05$

similar in all cities. A higher prevalence of current wheezing was observed in SA and of severe asthma and nighttime cough in SPW. In CR we observed the highest prevalence of rhinitis in the last year and of severe rhinitis. The highest prevalence of rhinoconjunctivitis was observed in SPW. The highest prevalences of eczema, flexural eczema and severe eczema were observed in SPW. There was a positive and significant correlation between infant mortality and the prevalence of nighttime cough (Table 2).

O_3 levels were higher than the acceptable standard in SPW, SPS, and SA, and the level of CO was higher in SA (Table 3). Levels of NO_2 (Table 4) and SO_2 (Table 5) were below the high acceptable level in all centers studied.

PoA had the lowest levels of O_3 and CO and was considered as the control (Table 3). Adolescents living in SPW and SA had a higher significant risk for current wheezing in comparison with the reference center (PoA). On the other hand, those living in SPS, SA, and CR were protected against severe asthma. There was no effect on nighttime cough (Table 3). Regarding rhinitis, living in CR was associated with a high risk of developing rhinitis in the last year, whereas living in SPS conferred significant protection. A high risk of rhinoconjunctivitis was observed among adolescents living in SPW, while those living in SPS and SA were protected from rhinoconjunctivitis (Table 3). Living in SPS and SA was associated with protection against developing severe rhinitis (Table 3). Living in SPW was associated with a higher risk of eczema and flexural eczema. Protection for flexural eczema and severe eczema was observed among adolescents living in SPS, SA, and CR (Table 3).

The lowest level of NO_2 was documented in CR, considered as the control (Table 4). Living in SPW and SA was associated with a higher risk of current wheezing in comparison with the control center (CR). Living in SPW and PoA was associated with a higher risk of severe asthma. There was no effect on nighttime cough (Table 4). Exposure to NO_2 was associated with protection against developing rhinitis in the last year in all centers. A high risk of rhinoconjunctivitis was documented in SPW and protection in SPS and SA. Living in SPS and SA was associated with protection against developing severe rhinitis (Table 4). A high risk of eczema was observed among adolescents living in SPW. Living in SPW and PoA was associated with a high risk of flexural and severe eczema.

The lowest SO_2 levels were observed in SPS and that center was considered as the control. A higher risk of current wheezing was observed in SPW and SA, severe asthma in SPW and PoA, and nighttime cough in SPW in comparison with the control center (SPS) (Table 5). Living in SPW, CR, and PoA was associated with a high risk of developing rhinitis in the last year, rhinoconjunctivitis, and severe rhinitis (Table 5). Living in SPW was associated with a high risk of developing eczema, flexural eczema, and severe eczema. Living in PoA was also associated with a risk for flexural eczema and severe eczema (Table 5).

Discussion

In urban areas traffic-related emissions are a major source of air pollution. Fossil fuel combustion and the resuspension of settled road dust particles raised by moving vehicles such as trucks, cars, and buses produce a complex mixture of toxic chemicals, particulate matter, and a variety of irritant gases, including NO_2, SO_2, and O_3 [1,8]. However, although

Table 3. Risk for Symptoms of Asthma, Rhinitis, and Atopic Eczema in Relation to a Center With the Lowest Annual Mean Level of Carbon Monoxide and Ozone in Adolescents (13-14 Years Old) From Different Brazilian Population Centers*

Center	O_3, µg/m³†	CO, ppm	ISAAC Written Questionnaire Items – Odds Ratios (95% Confidence Interval)								
			Current Wheezing	Severe Asthma	Nighttime Cough	Rhinitis Last year	Rhinocon-junctivitis	Severe Rhinitis	Eczema	Flexural Eczema	Severe Eczema
SPW, n=3181	244.0	7.70	1.26‡ (1.11-1.42)	1.20 (0.95-1.50)	1.06 (0.95-1.17)	0.91 (0.82-1.01)	1.31‡ (1.15-1.15)	1.01‡ (0.91-1.49)	1.45‡ (1.20-1.74)	1.42‡ (1.15-1.76)	1.08 (0.86-1.35)
SPS, n=3161	334.0	7.50	1.03 (0.91-1.18)	0.59‡ (0.45-0.78)	0.93 (0.84-1.03)	0.80‡ (0.71-0.89)	0.73‡ (0.64-0.85)	0.68‡ (0.59-0.77)	1.03 (0.85-1.25)	0.71‡ (0.56-0.91)	0.42‡ (0.31-0.56)
SA, n=3232	276.0	9.80	1.36‡ (1.20-1.56)	0.62‡ (0.48-0.81)	0.91 (0.82-1.02)	0.84‡ (0.75-0.94)	0.85‡ (0.74-0.97)	0.73‡ (0.64-0.83)	1.03 (0.85-1.25)	0.68‡ (0.53-0.87)	0.38‡ (0.28-0.51)
CR, n=3628	135.0	7.90	1.05 (0.93-1.19)	0.64‡ (0.50-0.82)	0.99 (0.89-1.10)	1.36‡ (1.23-1.51)	1.10 (0.96-1.25)	1.03 (0.91-1.16)	0.90 (0.75-1.10)	0.73‡ (0.57-0.92)	0.30‡ (0.22-0.41)
PoA, n=3007	65.2	1.51	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00

* O_3 indicates ozone; CO, carbon monoxide; SPW, São Paulo-West; SPS, São Paulo-South; SA, Santo André; CR, Curitiba; PoA, Porto Alegre;ppm, parts per million. † Maximum in 1 hour. ‡ *P*<.05

Table 4. Risk for the Symptoms of Asthma, Rhinitis and Atopic Eczema in Relation to a Center With the Lowest Annual Mean Level of Nitrogen Dioxide in Adolescents (13-14 Years Old) From Different Brazilian Centers*

Center	NO_2, µg/m³	ISAAC Written Questionnaire Items – Odds Ratio (95% Confidence Interval)								
		Current Wheezing	Severe Asthma	Nighttime Cough	Rhinitis Last Year	Rhinocon-junctivitis	Severe Rhinitis	Eczema	Flexural Eczema	Severe Eczema
SPW, n=3181	81.0	1.20† (1.07-1.35)	1.87† (1.47-2.38)	1.07 (0.97-1.18)	0.67† (0.60-0.74)	1.19† (1.06.1.34)	0.99 (0.88-1.11)	1.60† (1.34-1.92)	1.96† (1.57-2.45)	3.62† (2.67-4.92)
SPS, n=3161	39.0	0.98 (0.87-1.12)	0.93 (0.70-1.23)	0.94 (0.85-1.04)	0.59† (0.53-0.65)	0.67† (0.58-0.77)	0.66† (0.58-0.75)	1.14 (0.95-1.38)	0.98 (0.76-1.27)	1.42 (0.98-2.00)
SA, n=3232	33.0	1.29† (1.15-1.45)	0.97 (0.74-1.28)	0.93 (0.84-1.02)	0.62† (0.56-0.68)	0.77† (0.67-0.88)	0.71† (0.63-0.80)	1.14 (0.95-1.38)	0.94 (0.72-1.21)	1.29 (0.90-1.85)
CR, n=3628	15.8	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
PoA, n=3007	34.5	0.95 (0.84-1.08)	1.57† (1.22-2.02)	1.01 (0.91-1.12)	0.73† (0.66-0.82)	0.91 (0.80-1.04)	0.98 (0.87-1.10)	1.11 (0.91-1.35)	1.38† (1.09-1.75)	3.37† (2.47-4.60)

* NO_2 indicates nitrogen dioxide; SPW, São Paulo-West; SPS, São Paulo-South; SA, Santo André; CR, Curitiba; PoA, Porto Alegre † *P*<.05

Table 5. Risk for Symptoms of Asthma, Rhinitis and Atopic Eczema in Relation to a Center With the Lowest Annual Mean Level of Sulfur Dioxide in Adolescents (13-14 Years Old) From Different Brazilian Centers*

Center	SO_2, µg/m³†	ISAAC Written Questionnaire Items – Odds Ratio (95% Confidence Interval)								
		Current Wheezing	Severe Asthma	Nighttime Cough	Rhinitis Last Year	Rhino-conjunctivitis	Severe Rhinitis	Eczema	Flexural Eczema	Severe Eczema
SPW, n=3181	7.0	1.21† (1.08-1.38)	2.01† (1.56-2.60)	1.14† (1.03-1.26)	1.14† (1.02-1.27)	1.78† (1.55-2.04)	1.50† (1.32-1.71)	1.40† (1.17-1.68)	2.00† (1.58-2.52)	2.58† (1.94-3.44)
SPS, n=3161	7.0	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
SA, n=3232	16.0	1.31† (1.16-1.48)	1.04 (0.78-1.40)	0.94 (0.85-1.04)	1.05 (0.94-1.18)	1.15 (0.99-1.33)	1.08 (0.94-1.24)	1.00 (0.83-1.21)	0.95 (0.73-1.24)	0.92 (0.65-1.30)
CR, n=3628	40.5	1.02 (0.90-1.15)	1.08 (0.81-1.42)	0.93 (0.84-1.02)	1.71† (1.54-1.90)	1.50† (1.31-1.72)	1.52† (1.34-1.73)	0.88 (0.72-1.06)	1.02 (0.79-1.31)	0.71 (0.50-1.02)
PoA, n=3007	0.97 19.3	1.68† (0.85-1.10)	1.01 (1.29-2.20)	1.25† (0.91-1.12)	1.36† (1.12-1.40)	1.48† (1.18-1.57)	0.97 (1.30-1.69)	1.40† (0.80-1.18)	2.41† (1.09-1.80)	(1.80-3.22)

* SO_2 indicates sulfur dioxide; SPW, São Paulo-West; SPS, São Paulo-South; SA, Santo André; CR, Curitiba; PoA, Porto Alegre. † $P<.05$

epidemiologic studies can show statistical associations between levels of individual or combined air pollutants and outcomes, such as rates of asthma, emergency visits for asthma, or hospital admissions, they cannot prove a causative role [1].

Several studies have evaluated the relationship between photochemical air pollutants and respiratory health and allergic diseases. Hirsch et al [27] observed that exposures to NO_2 and CO were associated with increased prevalences of morning cough and bronchitis. In turn, the prevalences of atopic sensitization, symptoms of atopic disease,s and bronchial hyperresponsiveness were not positively associated with exposure to any of these pollutants in that study. Ramadour et al [28] documented no consistent association between annual mean SO_2 or NO_2 levels and prevalences of rhinitis, asthma, or asthmatic symptoms in children living in different regions of France. In contrast, there were statistically significant associations between prevalence of asthmatic symptoms and mean level of O_3 in that study. In another study a moderate increase in long-term exposures to background ambient air pollution (NO_2, SO_2, particulate matter ≤10 µm, and O_3) were associated with increased prevalences of respiratory and atopic indicators in children [29].

Similar results were observed for allergic rhinitis. Hajat et al [30] confirmed that air pollution worsens allergic rhinitis symptoms, leading to substantial increases in consultations for rhinitis. In their study SO_2 and O_3 seemed particularly responsible for the increase, and both seemed to contribute independently.

In the present study, SPW, SPS, and SA had annual mean levels of O_3 that were higher than acceptable. A significant positive association was observed between the prevalence of current wheezing and high levels of O_3 in SPW and SA. Nonetheless, they were protective against severe asthma in SPS, SA, and CR. O_3 is a highly reactive gas that is produced by the action of sunlight on hydrocarbons and nitrogen oxide gas emissions. O_3 oxidizes lung tissues on contact, acting as a powerful respiratory irritant [1,8]. Epidemiologic and clinical studies have shown that O_3 exposure is associated with worsening of athletic performance, reductions in lung function, shortness of breath, chest pain with deep inhalation, wheezing and coughing, and asthma exacerbations among those with asthma [1,8].

The risk of rhinitis in the last year was higher in CR despite the lower level of O_3 exposure. A higher risk of rhinoconjunctivitis was observed in SPW. A higher risk of eczema, flexural eczema, and severe eczema were associated with high levels of O_3 only in SPW. In SPS and SA high exposure to O_3 conferred protection against eczema.

The main sources of ambient nitrogen oxide gas emissions are diesel- and gasoline-powered vehicles and coal- and oil-fired power plants. They are produced by the fixation of nitrogen in the air during high-temperature combustion, and there is a high degree of covariation between NO_2 and other outdoor air pollutants that makes comparison difficult. It is suggested that NO_2 may act synergistically with other air pollutants in mediating lower respiratory tract illness among children. Exposure to high levels of NO_2 has been associated with increased risks of respiratory tract symptoms, childhood asthma exacerbations, and reduced lung function growth [8]. In our study, only SPW

had a level of NO_2 that was close to the high permitted level; all other centers were in the middle range of NO_2 patterns. A high risk of current wheezing was observed in SPW and SA. A high risk of severe asthma was observed in SPW and PoA.

Only in SPW was there a higher risk of rhinoconjunctivitis. However, the risk of atopic eczema symptoms was higher in SPW and in PoA.

Controlled human exposure (5 minutes) to inhaled SO_2 induces rapid-onset bronchoconstriction in asthmatic and healthy individuals [1]. In the former, even a low concentration of SO_2 exposure induces increased symptoms, greater decrease in pulmonary function and delayed recovery to normal values from bronchoconstriction [1]. Studies on SO_2 exposure have shown in children an increase in hospital admissions for asthma [4,14]. In our study, levels of SO_2 exposure in all population centers were within the acceptable range, yet high risk was observed in SPW for all symptoms and in CR and PoA for rhinitis symptoms, flexural, and severe eczema.

The physiological effects of CO on asthma are poorly understood. Higher levels of CO were observed in SA and were associated with a high risk of current wheezing.

The city of São Paulo has the third largest population concentration in the world. It has around 9.8 million inhabitants living within the city limits (1501 km^2). If we consider the whole metropolitan area, however, the population is twice as large. The altitude of the city ranges between 720 and 850 m and it has a topography varying from lowlands, hills and ridges to mountains. It is estimated that 90% of air pollutants delivered in the city are released from the intense traffic of motor vehicles. The western region of São Paulo has a varying climate and topography that leads to poor dispersion of pollutants and it is crossed by main roads with heavy motor vehicle traffic. This explains why this sector is one of the most polluted in the city. Moreover, all students evaluated with the ISAAC protocol in that area were of low socioeconomic status and many of them lived in slums. In the SPS, there is the second busiest airport of the country adding to the pollution from heavy vehicular traffic. The city of SA, located near the region southeast of São Paulo, is at the same altitude as São Paulo and has intense motor vehicle traffic and a transitional climate. It is also a large industrial city.

Living or studying in areas under such conditions has been demonstrated to be associated with high risk of respiratory symptoms [3,31,32] and indeed in SPW, one of the most polluted areas in São Paulo, there was a higher prevalence of the symptoms evaluated. A study performed in Cartagena, Spain, confirmed the association between air pollution (NO_2, SO_2 and particulate matter) and a higher prevalence of atopic eczema and a trend for more severe eczema [33]; other authors have reported similar findings [34]. The differences in socioeconomic status of the participants from the cities evaluated were slight, probably explaining why we found no relationship between that variable and the prevalence of symptoms of asthma, rhinitis, or atopic eczema.

The limitations of ecological analyses are well known [35]. In particular, an association at the region level may be due to complex biases and may not apply at the individual level. So, as with all ecological studies, this study is limited by the lack of precise exposure estimates, and caution should be exercised in inferring cause-effect relations [35]. Despite the limitations, and although we have not found a characteristic pattern of behavior for all symptoms evaluated or for a particular air pollutant, our data suggest a relationship between higher exposure to photochemical pollutants and a higher risk of symptoms of asthma, rhinitis, and atopic eczema.

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