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ORIGINAL ARTICLE

Impact of Particulate Matter ($PM_{2,5}$) and children's hospitalizations for respiratory diseases. A case cross-over study

Impacto del Material Particulado aéreo ($MP_{2,5}$) sobre las hospitalizaciones por enfermedades respiratorias en niños: estudio caso-control alterno

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Abstract

With seven million inhabitants, Santiago de Chile reaches high levels of air pollution in winter, the particulate matter usually exceeds WHO standards. **Objective:** To assess the influence of air pollution caused by particulate matter on children's hospitalizations due to respiratory diseases between 2001 and 2005 in the Metropolitan Region of Chile, independently from the environmental presence of respiratory syncytial virus (RSV). **Material and Method:** 72,479 public and private hospitalizations due to respiratory diseases of children under 15 years of age residing in the study region were analyzed using a time-stratified alternating case-control design. The main evaluations were: hospitalizations due to respiratory diseases (J00-J99), pneumonia (J12-J18); asthma (J21.0 - J21.9), and bronchiolitis (J45 - J46). Daily compilation of temperature data, PM_{10}, $PM_{2.5}$, ozone, respiratory virus (RSV), and environmental humidity. **Results:** Mean values of PM_{10} and $PM_{2.5}$ were 81.5 and 41.2 μg/m^3 respectively. The average temperature was 12.8 ºC and air humidity 72.6%. An increase of 10 μg/m^3 of $PM_{2.5}$ with one and two days of lag was associated with an hospitalizations increase due to respiratory diseases close to 2%, this percentage increased to 5% when the exposure was with eight days of lag, reflecting synergism between particulate matter and respiratory viruses (RSV). **Conclusion:** Short air pollution exposure can lead to children's hospitalizations due to respiratory diseases.

Keywords:
Air Pollution;
Hospitalization;
Child;
Pneumonia;
Bronchiolitis;
Asthma;
Respiratory Syncytial Virus;
Alternate Case-Control Studies

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Introduction

Santiago of Chile presents a serious problem of atmospheric pollution due to respirable particulate matter in fall and winter, and due to photochemical pollution (ozone) in spring and summer months[1].

This is due to the geographical and meteorological conditions of the Metropolitan Region atmospheric basin that affect its ventilation capacity and the natural emissions as well as those produced by the daily activities of its inhabitants[2].

Evidence of the link between particulate matter and damage to public health is consistent and shows its adverse effects to exposures experienced in urban settlements around the world, in both developed and developing countries[3-8]. The range of adverse health effects is wide, affecting both the respiratory and cardiovascular systems, where young children and older adults are the most susceptible among the general population[9]. The risk increases with the exposure intensity. The threshold existence for such effects is poorly supported. In fact, effects have been described at low levels, not much higher than baseline concentrations estimated at 3 to 5 $\mu g/m^3$ in the U.S. Epidemiological evidence shows adverse particle effects at short- and long-term exposures[10].

The respiratory effects of air pollution have been described mainly for particulate matter and ozone. In the lungs of Fresno inhabitants (Central Valley of California), wall thickening, terminal bronchioles remodeling, collagen increase, interstitial inflammatory cells, and macrophages with particulate matter[11] have been reported. These changes were most pronounced in the first generation of the terminal bronchiole, suggesting that the accumulation of coal and mineral dust in the lung mainly affects the central acinar region.

Residence in an area with high levels of particulate matter produces pulmonary retention of large numbers of particles, some of which seems to be combustion products. This was detected by comparing lungs of Mexico City residents with residents of Vancouver Canada, whose 3-year averages of PM_{10} (particulate matter $\leq$ 10 µm aerodynamic diameter) were 66 and 14 $\mu g/m^3$ respectively[12]. On the other hand, it has been reported that 96% of the particles detected in lung tissue from autopsies have a diameter of < 2.5 µm, evidencing the importance of $PM_{2.5}$ as an atmospheric pollutant[13].

Exposure to complex mixtures of atmospheric pollutants, mainly particulate matter and ozone, causes structural lung changes induced by chronic inflammation, causing vascular lung airway remodeling, and repair process alteration. In laboratory animals, exposure to ozone may increase the toxicity of inhaled particles or vice versa[14,15]. In type II alveolar cells in culture (line A549), urban particulate matter, and particles released from diesel and black smoke can be mutagenic by damaging DNA[16].

Inflammation is important in the exacerbation of respiratory diseases promoted by exposure to respirable particulate matter. It has been suggested that physical-chemical reactions occur on the surface of the particles, causing intracellular oxidative stress. Due to the large contact surface between the particles and the pneumocytes, there would be a release of inflammation mediators in the lung, which would recruit inflammatory cells with an exacerbated response that would generate functional and structural damage that would interfere with pulmonary ventilation.

In the lung damage mechanisms, it has been proposed that the sequence of events would begin with the activation of the "inflammatory cascade", which would explain the molecular phenomena that lead to the transcription of pro-inflammatory genes. Respirable particles would cause oxidative stress in cells, with the generation of lipid peroxidation products such as 4-hydroxynonenal and oxidized glutathione (GSSG). This change in the intracellular redox balance would produce the histone acetylation and the DNA rupture, stimulating the mechanisms promotion of genetic transcription. Oxidative stress also directly induces the production of the nuclear factor-kappa B (NF-kappa B), which allows the transcription of pro-inflammatory genes: tumor necrosis factor-alpha (TNF-alpha), interleukins (IL-8; IL-2, IL-6); granulocyte-macrophage colony-stimulating factor (GM-CSF), and Intercellular adhesion molecule-1 (ICAM-1). In addition, oxidative stress and/or direct interaction with particles would stimulate an increase in calcium concentrations (Ca^{+2}), which in turn can stimulate the production of NF-kappa B, with the subsequent greater release of pro-inflammatory substances[17].

Immunological mechanisms have also been proposed that would explain the effects of diesel particulate emissions on asthma. The mechanisms of direct damage to the immune system would be an increase in the production of IgE and IgG immunoglobulins, modulation of cytokine expression with increased interleukins and chemokines levels. Phenomena that would induce the migration of other cell types, mainly eosinophils which are mediators of chronic bronchial inflammation, prolonged peribronchiolar smooth muscle layer contraction, increased bronchial hypersensitivity, and bronchial mucosa damage, clinically relevant aspects of bronchial asthma[18].

Children are a particularly vulnerable group to respiratory problems due to their physical and behavioral characteristics. At this stage of life, the lung has not reached its full development, there is less colla-

teral ventilation and the small-airway resistance represents 50% of the total resistance to airflow[19]. Most alveoli (80%) develop in the postnatal period. As a result, they have less lung volume and less alveolar surface area, therefore, with the same exposure as adults, a higher dose enters the organism. Airways continue to develop in childhood which implies that the peripheral airway (< 2 mm in diameter) generates 50% of the airflow resistance, while in the adult it only corresponds to less than 20%. The absence of collateral ventilation, i.e. pores of Kohn and canals of Lambert, in children, worsen the peripheral airways obstruction. Children breathe more frequently and get more physical exercise than adults, which increases the effective dose of air pollutants captured by the lung. In addition, children have less developed respiratory musculature and less coughing effectiveness in cleaning the central airways. The defensive mechanisms of the lung are not fully developed, causing greater difficulty in removing particles that reach the airways. Finally, children spend more time outdoors than adults, thus the exposure to air pollutants is greater. All this makes them more exposed to air pollution than adults[20]. Therefore, the burden of environmental pollution on the respiratory health of children is greater, especially in developing countries where several other noxae coexist such as indoor air pollution, and malnutrition. Hence the importance of establishing control programs and special attention such as the strategies developed in the environmental pediatrics context.

The hypothesis of this study is that the exposure to respirable particulate matter in Santiago, Chile increases the number of hospitalizations due to respiratory disease in children under 15 years of age, regardless of exposure to respiratory viruses.

Therefore, our objective was to determine whether exposure to respirable particulate matter in Santiago of Chile was associated with a higher number of hospitalizations due to respiratory diseases in children under 15 years of age, regardless of the environmental presence of respiratory syncytial virus (RSV), during the winter periods of 2001 to 2006.

Material and Method

Study design and statistical analysis

The case-crossover design was used. The control period considered a temporal stratification with exposures of the same day of the week, month and year respective to the index case, ensuring an unbiased estimation of the conditional logistic regression.

Information on hospitalizations was obtained from the electronic databases of the Department of Statistics and Health Information (DEIS) of the Ministry of Health, Chile. Information from the Hospital Discharge of the Ministry of Health database was extracted from the DEIS website, using a password provided by DEIS to conduct this study.

The DEIS databases are anonymized, i.e. without the names of the persons or their *RUT* (Chilean ID number), in order to comply with Law 19,628 of 08.18.1999 on the protection of the private life of persons.

In order to carry out the study, the national hospital discharges databases for the study period were filtered to build a new database made up of the discharges of the Metropolitan Region residents, from both the private and public health sectors, under the age of 15, with diagnoses of discharges code ICD-10 J00 - J99. For this purpose, the indicated databases were processed with the SPSS software, converted by Stata Transfer to the statistical package STATA version 10 and later combined to the exposure database using the merge command and the date variable.

Study population

Hospitalizations of children in public and private hospitals, residents in the Metropolitan Region of Chile between 2001 and 2005.

Case definition

Any hospitalization due to respiratory disease of patients under 15 years of age residing in the Metropolitan Region during the fall-winter periods from 2001 to 2005 was considered a case.

Inclusion criteria

children under 15 years of age, resident in communes of the Metropolitan Region between March 21, 2001, and September 20, 2005, with a discharge diagnosis of respiratory disease (ICD-10 J00 to J99).

Exclusion criteria

Children hospitalized during the study period in the Metropolitan Region with residence in other communes of the country and with an inpatient stay longer than seven days since the design studies acute events and considers the case to be its own control.

Study variables

Variable 'response'

Hospitalizations due to respiratory disease (ICD-10 codes J00 to J99). The association between contaminants and all respiratory hospitalizations (ICD-10 J00-J99) was explored, in addition to evaluating the association with pneumonia (ICD-10 J12-J18), bronchiolitis (ICD-10 J21.0-J21.9), and asthma (ICD-10 J45-J46).

Exposure to air pollutants assessment

The information came from the Air Quality Monitoring Network (MACAM) which has eight stations for measuring pollutants in the communes of Las Condes, Recoleta, Santiago, La Florida, Pudahuel, El Bosque, Cerrillos, and Cerro Navia. The 24-hour averages of all stations of respirable particulate matter in their PM_{10} and $PM_{2.5}$ fractions were used for the fall to winter (March 21 to September 20) months of 2001 to 2005.

The exposure to ozone for the same period of the year was analyzed by means of the 8-hours ozone concentration, using the arithmetic average of the concentration values of one hour of ozone, corresponding to eight successive hours, between 8 am and 4 pm of the studied days. This exposure indicator was selected because it is the time interval with the highest ozone concentration in Santiago and because it coincides with the hours of the population movement and therefore its exposure.

Virus Exposure Assessment

Information on the viral epidemiological situation for the period under study was obtained from the Virology Laboratory Surveillance System of the Public Health Institute of Chile, which has in the Metropolitan Region five hospitals and five primary healthcare centers. The detection of respiratory viruses in the exudates of respiratory patients was performed using indirect immunofluorescence (IIF) technique. The number of weekly confirmations of RSV was systematically recorded.

Covariates

The gender, age, and health insurance regime were analyzed for each of the identified cases.

Statistical Analysis

Descriptive statistics were used with measures of central tendency and dispersion. The correlation degree between the studied variables was evaluated which allowed showing the sample characteristics and the exposure during the study period.

Inferential statistics were also used to analyze the association between increased particulate matter and hospitalizations due to respiratory diseases in children. In the case-crossover design, conditional logistic regression is used. Results were expressed by estimating the odds ratio (OR) and corresponding 95% confidence intervals (STATA 10).

The statistical test to determine the association between disease and exposure, in the case-crossover design, is based only on the discordant pairs. The formula for estimating the sample size (m) that depends on the number of discordant pairs, to detect a relative risk ***R*** is given by:

$$m = [Z_\alpha/2 + Z_\beta]\ \sqrt{P(1-P)}^{\,2} / (P - ½)^2$$

where

$$P = \psi/ (1 + \psi) \approx R/(1 + R)$$

ψ corresponds to the odds ratio of the disease exposure ratio and R to the Relative Risk.

The relative risks considered for the calculation were reported by the study of a cohort of children studied by Pino et al., in Santiago[21], which indicated a 1.09 relative risk, requiring at least a total of 6,657 discordant pairs. A p-value < 0.05 was considered statistically significant for the association establishment.

The case-crossover design uses conditional logistic regression as a multivariate analysis method. First, the available information was analyzed from a bi-variable perspective, constructing models with hospitalizations due to respiratory disease (Y), for each of the explanatory selected variables (X).

Subsequently, explanatory models of hospitalizations due to respiratory disease in children were constructed based on the epidemiological history and objectives of this thesis, in order to demonstrate or reject the hypothesis.

The general built conditional logistic model result in:

$$\text{Log } (Y/1\text{-}Y) = \alpha + \beta_1(X_1) + \beta_2(X_2) + \beta_3(X_3) + \beta_4(X_4) + \beta_5(X_5) + \beta_6(X_6)$$

Results

During the study period, 72,479 cases were hospitalized that met the inclusion criteria. It was observed that children younger than one year of age (51.5%), males (56.5%), public healthcare system users (81.91%), and those with pneumonia as discharge diagnosis (29.3%) predominated. About one-third of the cases included in the study stayed only one day hospitalized (Table 1).

The mean concentrations value of PM_{10} and $PM_{2.5}$ was 81.5 and 41.2 $\mu g/m^3$ respectively. The average temperature was 12.8 °C and the relative humidity was 72.6 % (Table 2).

During the study period, 266 days (38 weeks) were observed out of a total of 920 observed days, which met the criteria of having over 100 detected cases per epidemiological week, giving a prevalence of 28.8% days with exposure to RSV.

Particulate matter $PM_{2.5}$ maintains its effect by completing the explanatory model with the variables ozone, temperature, and relative humidity, in the absence of RSV (Table 3). When the coarse fraction ($PM_{2.5\text{-}10}$ particulate matter between 2.5 and 10 μm) is introduced into the model, the effect of $PM_{2.5}$ increases

Table 1. Characteristics of children hospitalized for respiratory diseases, residents in the Metropolitan Region, 2001-2005 (n = 72479)

Variable	n	(%)
Age at hospitalization		
0-1	37334	(51.5)
2-5	21066	(29.1)
6-14	14079	(19.4)
Sex		
Male	40955	(56.5)
Female	31524	(43.5)
Insurance		
Public System	59367	(81.9)
Isapres	10639	(14.7)
Private	927	(1.3)
Other	1546	(2.1)
Diagnosis of discharge		
Respiratory Diseases (J00-J98)*	72479	(100.0)
Pneumonia (J12-J18)*	21220	(29.3)
Bronchiolytis (J21.0-J21.9)*	3276	(4.5)
Asma (J45-J46)*	1037	(1.4)
Other	46946	(64.8)
Days of hospitalization		
≤ 1 day	25652	(35.4)
2 a 6 days	46827	(64.6)

Table 2. Atmospheric pollutants and meteorological variables during the study period

Variables	Media	Ds	p25	p50	p75
MP_{10} (µg/m³)[a]	81.5	35.7	56.7	80.7	105.9
$MP_{2,5}$ (µg/m³)[a]	41.2	18.1	25.3	39.9	53.3
O_3 (ppb)[b]	19.4	12.9	8.9	16.0	27.2
Temperature media (°C)[a]	12.8	3.5	10.2	12.3	14.9
RH (%)[a]	72.6	12.9	63.8	73.8	82.7

[a]24 hours average. [b]8 horas average, between 10:00 y 17:00 ,parts per billion (ppb). MP_{10} annual standard:150 µg/m³ (Chile) 20 µg/m³ (OMS). $MP_{2,5}$ annual standard: 20 µg/m³ Chile);10 µg/m3 (OMS). O_3: 8 hours standard: 61 ppb (Chile); 50 ppb (OMS).

slightly with two, eight, and ten days of delay (Table 4). This fraction shows no association with respiratory diseases.

Ozone and temperature behave in a very similar way with a systematic marginal protective effect in all models which are expected results since only fall-winter periods were evaluated, times in which temperature rises and the presence of very low levels of ozone are not harmful to the population.

The relative humidity on the other hand only behaves marginally protective with lags of one and two days, disappearing its meaning with lags of eight and ten days.

The RSV explains an important part of the model (17 to 27% increase in hospitalizations) and acts synergistically with $PM_{2.5}$ since the hospitalization risk due to $PM_{2.5}$ increases in the presence of RSV with eight and ten days of delay (Table 5).

There was no significant difference in risk by sex in exposure to particulate matter. The risk increases as the age decreases, however, the risk difference between children younger than five years of age and infants younger than one year of age was not statistically significant.

Finally, an increase of 10 µg/m³ of $PM_{2.5}$ particulate matter explained an increase in hospitalizations due to pneumonia (7.7%), bronchiolitis (11.3%), and asthma (8.5%) for eight days of delay.

Discussion

This study hypothesized that some hospitalizations due to respiratory diseases in children would not have occurred had they not been exposed to air pollution. After adjusting for the ozone presence, temperature, and RSV, it was found that an increase of 10 µg/ m³ of $PM_{2.5}$ increased hospitalizations due to respiratory diseases by about 2% with one to two days of delay since exposure, and that this percentage increased to 5% of the total hospitalizations due to respiratory diseases in children when exposure occurred with eight days of delay, reflecting the expected synergy between particulate matter and the virus presence in the environment. The found results are within the range described by authors who have studied the effects of Santiago air pollution on their children. Pino et al. [21] found an association between $PM_{2.5}$ particulate matter levels of 9.0% in symptomatology exacerbation in asthmatic children with a delay of nine days. Ostro determined that consultations in Emergency Services increased from 4 to 12% with increases of 50 µg/m³ of PM_{10}[22]. Ilabaca et al.[23] identified a 3.3 % risk of pneumonia in children, all values compatible with the results of this study since the said publications when evaluating ambulatory morbidity, obviously give values higher than those of hospitalizations, since only a fraction of children who consult due to morbidity require hospitalization.

Air quality, during the studied period, presented averages of particulate matter PM_{10} and $PM_{2.5}$ much higher than those suggested by the World Health Organization's air quality standard and little higher than the primary Chilean air quality standard. However, the strength of the found association, with respect to the prevailing high pollution situation, was a little lower than the values described in international literature. A Canadian study evaluating children aged 2 to 4 years and 5 to 14 years found a risk of emergency

Table 3. Odds Ratio (OR, 95% CI) Respiratory diseases hospitalizations by increments of 10 µg/m³ of $MP_{2.5}$ with 1 and 2 days of lag

	Lag 1 (con rezago de 1 día)			*Lag 2* (con rezago de 2 días)		
	Discordant pairs (n)	OR (IC95%)	p	Discordant pairs (n)	OR (IC95%)	p
Respiratory diseases (CIE-10 J00-J99)	273632	1.016 (1.007-1.025)	< 0.0001	307683	1.028 (1.019-1.037)	< 0.0001
Sex						
Male	154476	1.015 (1.004-1.028)	< 0.0001	173601	1.028 (1.017-1.041)	< 0.0001
Female	119156	1.017 (1.004-1.031)	< 0.0001	134082	1.027 (1.014-1.040)	< 0.0001
Age						
Less 1 year old	142005	1.024 (1.012-1.037)	< 0.0001	161725	1.035 (1.023-1.047)	< 0.0001
Less 5 years old	78968	1.021 (1.005-1.038)	< 0.0001	249.735	1.035 (1.025-1.044)	< 0.0001
Disease						
Pneumonie (CIE-10 J12-J18)	85021	1.031 (1.016-1.048)	< 0.0001	92199	1.035 (1.019-1.051)	< 0.0001
Bronchiolytis (CIE-10 J21.0-J21.9)	19849	1.041 (1.007-1.073)	< 0.0001	22913	1.062 (1.028-1.097)	< 0.0001
Asma (CIE-10 J45-J46)	3678	1.001 (0.9244-1.081)	0.861	4106	1.029 (0.953 -1.112)	0.749

Ajusted by $MP_{2.5-10}$, ozone, temperature y RH. OR = *odds ratio;* IC = Confidence interval.

Table 4. Odds Ratio (OR, 95% CI) Respiratory diseases hospitalizations by increments of 10 µg/m³ of $MP_{2.5}$ with 8 and 10 days of lag

	Lag 8 (con rezago de 8 días)			*Lag 10* (con rezago de 10 días)		
	Discordant pairs (n)	OR (IC95%)	p	Discordant pairs (n)	OR (IC95%)	p
Respiratory diseases (CIE-10 J00-J99)	291534	1.051 (1.046-1.061)	< 0.0001	303180	1.021 (1.012-1.030)	< 0.0001
Sex						
Male	164371	1.044 (1.032-1.056)	< 0.0001	170921	1.019 (1.007-1.031)	< 0.0001
Female	127163	1.061 (1.047-1.075)	< 0.0001	132259	1.023 (1.010-1.037)	< 0.0001
Age						
Less 1 year old	154886	1.076 (1.064-1.089)	< 0.0001	160557	1.048 (1.036-1.061)	< 0.0001
Less 5 years old	237.487	1.060 (1.050-1.070)	< 0.0001	246828	1.032 (1.023-1.042)	< 0.0001
Disease						
Pneumonie (CIE-10 J12-J18)	88499	1.077 (1.061-1.095)	< 0.0001	91821	1.047 (1.031-1.064)	< 0.0001
Bronchiolytis (CIE-10 J21.0-J21.9)	22174	1.113 (1.077-1.149)	< 0.0001	22961	1.067 (1.034-1.101)	< 0.0001
Asma (CIE-10 J45-J46)	3764	1.085 (1.004-1.172)	< 0.0001	3960	1.026 (0.951-1.108)	< 0.0001

Ajusted by $MP_{2.5-10}$, ozone, temperature y RH. OR = *odds ratio;* IC = Confidence interval.

services consultation due to asthma of OR 1.08 (1.01-1.16) and OR 1.03 (0.98 -1.07) with a one day delay and an increase in the interquartile range for $PM_{2.5}$[24]. In contrast, another study conducted in a mining industrial region of Turkey showed a higher association of asthma with $PM_{2.5}$ OR 1.25 (1.05-1.50) in children with a delay of four days[25]. This could indicate that the composition of respirable particulate matter in Santiago would have different toxicity characteristics. Several publications have pointed to the specific components importance of the particulate matter in their toxicity induction mechanisms, which would explain part of the variability in results between cities[26-30].

The before mention results may be affected by design limitations. Mainly the exposure assessment carried out on the basis of environmental monitors, which does not allow to identify the true individual exposure and introduces biases in the exposure classification. Also, the qualitative characterization of the presence/absence of a virus can affect the results. However, these biases would not present directionality so they should not be affecting the direction of the association, nor do they allow assuming an overestimate of the effect. On the other hand, among the strengths

Table 5. Explanatory models of hospitalizations, air pollutants and presence of respiratory syncytial virus (RSV)

Selected Models	Lag	Parameter	Estimate	DS	OR	IC 95%	p
$Log(p/1-p) = \alpha + \beta_1(MP_{2.5}) + \beta_2(O_3) + \beta_3(t) + \beta_4(h) + \beta_5(VRS)$	8	β_1	0.0042	0.0002	1.0042	1.0037 - 1.0048	0.0001
		β_2	-0.0022	0.0006	0.9977	0.9965 - 0.9990	0.0001
		β_3	-0.0187	0.0020	0.9814	0.9775 - 0.9853	0.0001
		β_4	0.0004	0.0005	1.0004	0.9994 - 1.0015	0.6300
		β_5	0.2869	0.0150	1.3323	1.2936 - 1.3721	0.0001
$Log(p/1-p) = \alpha + \beta_1(MP_{2.5}) + \beta_2(O_3) + \beta_3(t) + \beta_4(h) + \beta_5(VRS)$	10	β_1	0.0022	0.0002	1.0022	1.0016 - 1.0028	0.0001
		β_2	-0.0042	0.0006	0.9957	0.9945 - 0.9970	0.0001
		β_3	-0.0045	0.0020	0.9954	0.9915 - 0.9994	0.0001
		β_4	-0.0002	0.0005	1.0002	0.9992 - 1.0013	0.6300
		β_5	0.1885	0.0146	1.2075	1.1732 - 1.2428	0.0001
$Log(p/1-p) = \alpha + \beta_1(MP_{2.5}) + \beta_2(MP_{2.5\text{-}10}) + \beta_3(O_3) + \beta_4(t) + \beta_5(h) + \beta_6(VRS)$	8	β_1	0.0051	0.0004	1.0051	1.0041 - 1.0059	0.0001
		β_2	-0.0011	0.0005	0.9988	0.9978 - 0.9998	0.0020
		β_3	-0.0024	0.0006	0.9975	0.9961 - 0.9988	0.0001
		β_4	-0.0180	0.0020	0.9821	0.9781 - 0.9860	0.0001
		β_5	-0.0003	0.0006	0.9996	0.9983 - 1.0009	0.0280
		β_6	0.2893	0.0150	1.3356	1.2967 - 1.3756	0.0001
$Log(p/1-p) = \alpha + \beta_1(MP_{2.5}) + \beta_2(MP_{2.5\text{-}10}) + \beta_3(O_3) + \beta_4(t) + \beta_5(h) + \beta_6(VRS)$	10	β_1	0.0021	0.0004	1.0021	1.0012 - 1.0029	0.0001
		β_2	0.0001	0.0004	1.0001	0.9992 - 1.0011	0.0021
		β_3	-0.0041	0.0006	0.9958	0.9945 - 0.9971	0.0001
		β_4	-0.0046	0.0020	0.9953	0.9913 - 0.9993	0.0001
		β_5	0.0004	0.0006	1.0004	0.9991 - 1.0017	0.0281
		β_6	0.1881	0.0147	1.2070	1.1726 - 1.2424	0.0001

O_3 = ozone concentration; t= temperature; h= RH; RSV= respiratory syncytial virus presence; $MP_{2.5}$= fine particule (≤ 2,5 µm);$MP_{2,5\text{-}10}$ = coarse fraction (2,5 a 10 µm).

of this study are a) its large number of observations, which makes it possible to show weak associations, b) its capacity to control confusion factor, such as indoor air pollution, smoking, and the socioeconomic condition of children exposed to air pollution, and c) the control of variables dependent on variation over time.

Conclusions

The results of this study confirm the harmful effect of atmospheric pollutants, respirable particulate matter and ozone, on the respiratory health of children, particularly its effect causing hospitalizations due to pneumonia, bronchiolitis, and asthma.

Regarding the combined effect of the respirable particulate matter presence and environmental virus (RSV), this study supports the thesis of the synergistic effect between the two factors on hospitalizations due to pneumonia, as it reflects that the damage caused by particulate matter increases in the presence of viruses in the environment. The possibility of quantifying the association is very relevant because, although it provides relatively low values, as the entire population is exposed, the absolute number of affected people that can be attributed to the phenomenon of pollution, makes it a public health problem.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Financial Disclosure

Authors state that no economic support has been associated with the present study.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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