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Exposure to NO_2 and children hospitalization due to respiratory diseases in Ribeirão Preto, SP, Brazil

Exposição ao NO_2 e internações por doenças respiratórias em crianças em Ribeirão Preto, SP, Brasil

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Abstract *The effects of exposure to air pollutants on human health are mainly reflected in respiratory diseases in children and elderly ones. An ecological time series study was carried out in Ribeirão Preto/SP data to examine the role of exposure to air pollutants and hospital admissions due to respiratory diseases in children under 10 years old. The study period was between January, 2011 and December, 2013. Particulate Matter (PM_{10}), Nitrogen dioxide (NO_2), and ozone (O_3), temperature and air relative humidity, were analyzed to estimate the association with hospital admissions using a generalized linear model of Poisson's regression with lags of zero up to seven days after exposure to pollutants, adjusted by the day of the week, seasonality and effective temperature. The significance level adopted was $p < 0.05$. NO_2, when analyzed in single pollutant model shown to be significant at lag 2 and 3 and when analyzed in the multi-pollutant model it shown to be significant at lags 2 up to 5, and lag 7 with relative risk between 1.05 and 1.09 per 10 μg/m³ increase in NO_2 concentration, with an excess of 150 hospital admission and substantial increase in costs to Public Health System. The data enable the local health managers can take action to minimize these effects.*

Key words *Air pollutants, Nitrogen dioxide, Particulate material, Ozone, Respiratory diseases*

Resumo *Os efeitos da exposição aos poluentes do ar sobre a saúde humana são principalmente refletidos nas doenças respiratórias, em crianças e idosos. Este estudo, do tipo ecológico de séries temporais, foi realizado em Ribeirão Preto/SP para examinar o papel da exposição a poluentes do ar e internações hospitalares por doenças respiratórias em crianças de até 10 anos de idade. O período de estudo foi entre 01.01.2011 e 31.12.2013. Material partículado (PM_{10}), dióxido de nitrogênio (NO_2) e ozônio (O_3), temperatura e umidade relativa do ar foram analisadas para estimar a associação com internações hospitalares usando um modelo linear generalizado da regressão de Poisson com defasagens de zero até sete dias após a exposição, ajustado pelo dia da semana, sazonalidade e temperatura efetiva. Foi adotado alfa = 0,05. NO_2 quando analisado no modelo unipoluente mostrou significância nos lags 2 e 3 e quando avaliado no modelo multi-poluente foi significativo nos lags 2 até 5, e lag 7, com risco relativo entre 1,05 e 1,09 por 10 μg/m³ de aumento em sua concentração, com excesso de 150 internações e aumento substancial dos custos para o sistema de saúde pública. Os dados permitem que o gestor local de saúde possa tomar medidas para minimizar estes efeitos.*

Palavras-chave *Poluentes do ar, Dióxido de nitrogênio, Material particulado, Ozônio, Doenças respiratórias*

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Introduction

Acute respiratory diseases, especially pneumonia, play an important role in morbidity and mortality, in the world and in Brazil, representing an important cause of death in children in developing countries[1].

In 2014, approximately 370,000 hospitalizations due to acute respiratory infections and asthma in children under 10 years old happened in Brazil, while in the state of São Paulo were about 68,000. There was also in Brazil 1,409 deaths in this age group. The financial expenses for the Unified Health System in Brazil were approximately R$ 260 million and in São Paulo were R$ 56 million[2]. (1 US$ ≈ R$ 2.50)

Daily exposure to air pollutants have been associated with the increased morbidity and mortality due to respiratory acute infectious diseases. These effects were demonstrated in studies in large cities[3,4] and in medium sized[5-9]. In addition, international studies have also shown the harmful effects of air pollution on health[10,11].

Among the major air pollutants studied are the particulate matter, with less than 10 micra of aerodynamic diameter - PM_{10}, nitrogen dioxide (NO_2), carbon monoxide (CO), ozone (O_3) and sulfur dioxide (SO_2); PM_{10} is emitted from mechanical dispersions of organic materials and the uncontrolled combustion, in addition to the ones that happen in combustion engines of vehicles, incinerators and power plants. NO_2 and NO have as main sources the vehicle fleet and, on a smaller scale, the power plants, gas industries and gas stoves. $O_3$is a secondary pollutant and has as its precursors nitrogen oxides and hydrocarbons, and SO_2 is produced by vehicle and industrial combustion[12,13].

The mechanisms by which they act these pollutants are still poorly understood and, among these mechanisms can be pointed to the formation of free radicals of oxygen and nitrogen resulting from high concentrations of particulate matter, ozone and nitrogen oxides, which initiate inflammatory response the release of mediators such as cytokines that when they reach the systemic circulation lead to effects on the respiratory system, including[14].

Children and elderly people are the most age group affected due to respiratory diseases.

The objective of this study was to estimate the association between the exposure to nitrogen dioxide and admissions due to acute respiratory infections diseases in under 10 years of age children residents in Ribeirão Preto, in the years 2011 to 2013.

Methods

An ecological study of time series was carried out with data of acute tracheitis and laryngitis hospitalizations (J04.0 to J04.9 of ICD-10th revision), pneumonia (J12.0 to J18.9), bronchitis and bronchiolitis (J20.0 the J21.9) and asthma (J45.0 to J45.9) in children of both sexes aged between 0 to 9 years old and residents in Ribeirão Preto. This city is located in Southeastern of Brazil, geographical coordinates 21º 10' S and 47º 48' W, it is a medium-sized city located at 546 m above sea level and had an humid climate with rainy summers and dry winters. It has important agricultural activity favored by soil characteristic of the city (red earth and sandstone) and its main products sugarcane, citrus, among others, and beyond, it has its significant industrial sector. The city presents estimated population of just over 600,000 inhabitants and is located 310 km from São Paulo. It is crossed by Anhanguera and Candido Portinari highway and presents intense flow of heavy vehicles like trucks and buses, with a total fleet vehicle about 500 thousand cars on 2013[15].

The concentration data of pollutants PM_{10}, NO_2, in their daily averages and O_3, in their daily maximum 8 hours, temperature and average relative air humidity were obtained from the São Paulo State Environmental Agency (Cetesb), which has a metering station in Ribeirão Preto. The data of hospitalizations were obtained from the Department of Information and Informatics of the Unified Health System (Datasus) from the city, considering the study period between January 1st, 2011 and December 31st, 2013.

Poisson regression was used to estimate relative risks of exposures in the outcome - hospitalization. A database with daily hospitalization data was constructed for each pollutant and climate variable, considering zero lags up to seven days, because the effects of exposure to pollutants can be evidenced not only on the same day but in subsequent days and seven days lag are the most used window to analyze the effects of air pollutants exposure in human respiratory diseases. Therefore, it was chosen a generalized linear model for Poisson regression (GLM). Models with one pollutant and with two and three pollutants simultaneously were built adjusted for days of the week, by seasonality and the effective temperature (ET), which is calculated using the following mathematical expression.

$$ET = T - 0.4 ° (T - 10) (1 - RH / 100) \quad (1)$$

where RH is relative air humidity and T is the temperature in °C.

In addition, it was considered an increase of 10 μg/m³ on NO_2 levels and calculated the relative risk for hospitalization.

The possible correlations between admissions and pollutants were estimated and it was also calculated the proportional attributable risk (PAR), wher PAR = 1-1 / RR where RR is the relative risk obtained by exponentiation of the coefficients provided by Poisson regression; cost reduction of these hospitalizations were estimated, using average values obtained of Datasus portal. Analyzes were performed using Stata v 9. The results were expressed as relative risk estimate.

Results

One thousand eight hundred and eight hospital admissions occurred during the study period. Mean daily hospital admission was 1.66 (dp = 1.64) and ranging from 0 to 10 hospitalizations per day. Pneumonia (825 hospital admissions – 45.6%) and bronchitis-bronchiolitis (748 - 41.4%) were the most prevalent diseases, asthma (224 – 12.4%) and laryngitis-tracheitis (11 – 0.06%) were the other hospital admissions.

The descriptive analysis is in Table 1. In the studied data, there were days that were not accounted for by Cetesb, such as NO_2 with 83 days (7.8%), PM_{10} with 81 days (7.6%) and O_3 with 31 days (2.9%). During the study period, there were 2 days that exceeded of the allowed limit of PM_{10}, 4 overtaking of O_3 and there was none of the NO_2, being the air quality standards set for PM_{10} is up to 120 μg/m³, for the NO_2 is up to 260 μg/m³, for the O_3 is up to 140 μg/m3[16].

The distribution of concentrations of pollutants over time is in Figures 1A - 1D. Figure 1A shows that the concentration of NO_2has a seasonally feature and has an increased concentration in June and July during the coldest months of the year with little rain and less winds allowing less dispersion of pollutants, as well as PM_{10} (1B) that also has this feature.

Table 2 shows the matrix of Pearson correlation coefficients. It can be seen a significant association between hospital admissions and NO_2 and positive associations between pollutants. It is also possible to observe a negative association between the effective temperature with the NO_2, in other words, the lower the temperature, the higher the concentration of this pollutant, except for O_3, that the higher the temperature, the greater its concentration. And it can also be observed that there was no association of PM_{10} with admissions and effective temperature.

Table 3 contains the coefficients of Poisson regression analysis of pollutants concentrations. It can be observed that exposure to NO_2, when analyzed alone, presented itself as a risk factor for hospitalizations in the lag 2 and 3 and, when analyzed together, it is associated with PM_{10} in lag 2 to lag 5 and 7, with ozone in the lag 2, lag 3 and lag 7. In the analysis with other pollutants, NO_2 was strongly associated with the lag 2 (RR = 1.0077), lag 3 (RR = 1.0086), 4 lag (RR = 1.0051), 5 lag (RR = 1.0058) and 7 (RR = 1.0090), as shown in Table 4.

Figure 2 shows that with an increase of 10 μg/m³ in the concentration of NO_2, the relative risk increases up to 9 percentage points. Thereby, it calculates the population attributable fraction (FAP) and, with the reduction of 10 μg/m³, there is a drop of about 150 admissions, generating a decrease in average expenses about R$ 260 thousand, considering the cost of each hospital admission as R$ 1,800.00[17].

Table 1. Descriptive analysis of the study variables. Ribeirão Preto – SP, Brazil, 2011-2013.

	Mean (SD)#	Minimum-Maximum
Hospital admission	1,66 (1,64)	0-10
O_3(μg/m³)	60,3 (23,43)	3-156
PM_{10} (μg/m³)	30,8 (18,56)	6-130
NO_2 (μg/m³)	44,2 (18,30)	10-107
ET ##	26,3 (2,81)	12,0 – 32,9

standard deviation. ## Effective Temperature.

Discussion

This is the first study, as far it is of our knowledge, carried out in Ribeirão Preto, SP, about the effects of NO_2 exposure in pediatric hospitalizations in children of both sexes aged between 0 to 9 years old due to respiratory disease, and it were able to identify the harmful role of exposure to NO_2 and also showed that when considered in association with other pollutants it potentiates the effects of such exposure.

The results of this study can identify a later effect of NO_2 in lags 2 and 3 when analyzed alone and when analyzed together with other pollutants also proved to be a more delayed effect, with significance at lag 2 up to lag 5 and lag 7 after exposure.

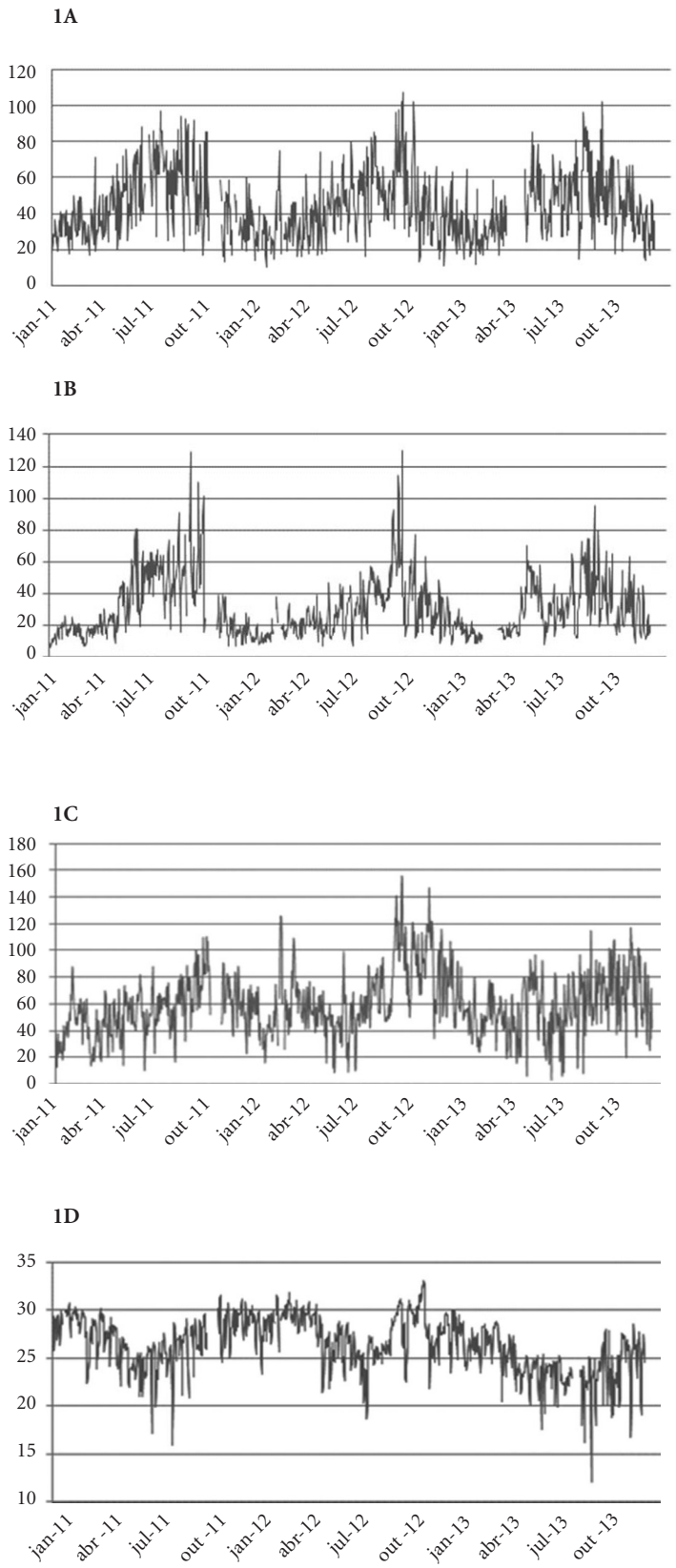

Figure 1. Daily values of concentrations of pollutants in mg/m^3: (1A) NO_2, (1B) $PM_{10,}$ (1C) O_3 and (D). Effective temperature (^{0}C) in Ribeirão Preto – SP, Brazil, 2011–2013.

Table 2. Pearson correlation matrix between pollutants hospital admission – Ribeirão Preto-SP, Brazil, 2011-2013.

	HA[@]	NO_2	O_3	PM_{10}	TE
HA	1	-	-	-	-
NO_2	0,121[##]	1	-	-	-
O_3	- 0,078[#]	0,301[##]	1	-	-
PM_{10}	0,028	0,661[##]	0,547[##]	1	-
ET [§]	-0,104[##]	-0,085[##]	0,293[##]	-0,025	1

[#] p < 0,05 [##] p < 0,01 @ hospital admission [§] Effective Temperature.

Table 3. Coefficients and standard deviations provided by Poisson regression of admissions to the lags of zero to seven days of exposure to pollutants, Ribeirão Preto – SP, Brazil, 2011 – 2013.

	NO_2	$NO_2 + PM_{10}$	$NO_2 + O_3$	$NO_2 + PM_{10} + O_3$
Lag 0	0.00136 (0.00146)	0.00071 (0.00195)	0.00128 (0.00160)	0.00072 (0.00199)
Lag 1	0.00236(0.00142)	0.00208 (0.00190)	0.00289 (0.00155)	0.00200 (0.00194)
Lag 2	**0.00362 (0.00142)**	**0.00711 (0.00193)**	**0.00496 (0.00156)**	**0.00773 (0.00197)**
Lag 3	**0.00328 (0.00141)**	**0.00809 (0.00192)**	**0.00545 (0.00156)**	**0.00861 (0.00196)**
Lag 4	0.00158 (0.00144)	**0.00484 (0.00192)**	0.00292 (0.00156)	**0.00505 (0.00196)**
Lag 5	0.00119 (0.00145)	**0.00567 (0.00194)**	0.00297 (0.00158)	**0.00583 (0.00198)**
Lag 6	-0,00028 (0.0015)	0.00359 (0.00195)	0.00200 (0.00159)	0.00390 (0.00200)
Lag 7	0.00200 (0.00144)	**0.00824 (0.00198)**	**0.00569 (0.00160)**	**0.00898 (0.00203)**

The values in bold indicated – value < 0,05.

Table 4. Relative risks and respective confidence intervals (95%) of hospitalizations from zero to seven days in the model multipoluente, Ribeirão Preto–SP, Brazil, 2011 – 2013.

NO_2	RR (IC = 95%)
Lag 0	1,001 (0,997 - 1,005)
Lag 1	1,002 (0,998 -1,0068)
Lag 2	**1,008 (1,004 - 1,012)**
Lag 3	**1,009 (1,005 - 1,012)**
Lag 4	**1,005 (1,001 - 1,009)**
Lag 5	**1,006 (1,002 - 1,010)**
Lag 6	1,004(0,999 - 1,008)
Lag 7	**1,009 (1,005 - 1,013)**

The values in bold indicate p – value < 0,05.

Hospitalizations considered in this study, which involved asthma, bronchitis, bronchiolitis, pneumonia, acute tracheitis and laryngitis make up 83% of respiratory diseases hospitalizations in children in this age range[2].

Exposure to nitrogen dioxide was also associated with pediatric hospitalizations in Sorocaba[5], where an acute effect of this pollutant noted the same day of exposure when occurred hospitalization; it should be noted that in Sorocaba the daily average concentration of NO_2 was close to that found in Ribeirão Preto (48.1 μg/m³), which could explain the association of the NO_2 present in both studies but in Sorocaba just one group of disease was studied – Pneumonia (J12 – J18).

On the other hand, in a study conducted in São Paulo, where the concentration of NO_2 was 103.5 μg/m³, it observed that with the increase of 10μg/m³ in NO_2 concentrations had a positive association with admissions due to respiratory diseases most significant on the fifth day after exposure[3], different from our study where the greatest significance in the lag 7, possibly due to the difference in the mean concentration of this pollutant, because in Sao Paulo this concentration was approximately 2.5 times greater with a possible sharper dose-response effect.

In addition to our study, Nicolussi et al. also found an association between respiratory diseases and air pollutants in Ribeirao Preto, showing an association to air pollutants with allergic diseases in school children, the symptoms of allergic rhinitis were more frequent in the dry season and coincided with the increase in PM_{10} and NO_2[18]. This study confirms the association found by

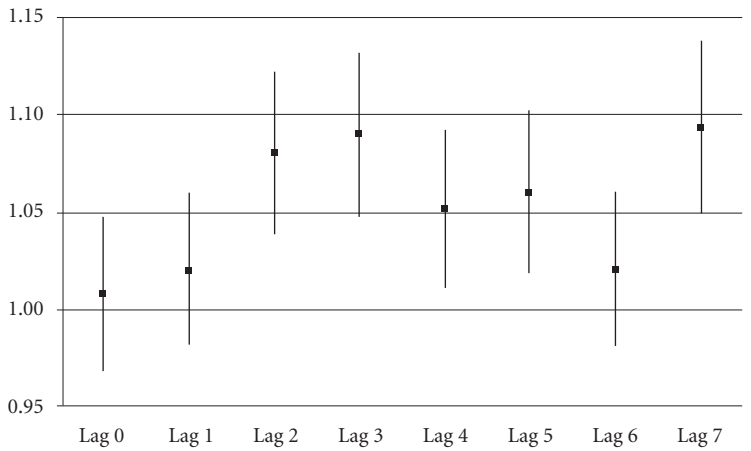

Figure 2. Relative risks and respective intervals of confidence in the hospitalizations according to the increase of 10 μg/m^3 in the concentration of NO2,in the lags of zero to seven days in exposure to pollutants, Ribeirão Preto – SP, Brazil, 2011 – 2013.

Castro et al.[19], in which there was a positive association between exposure to NO_2 and lung function, with an increase of 10 μg/m^3 for the pollutant study, there was a decrease in peak expiratory in lags 2 and 3, even if these articles do not make reference to other respiratory diseases mentioned in our work, the harmful effect of NO_2 is the same presented by our article in Ribeirao Preto.

In Rome, admissions for respiratory diseases in children were associated with NO_2 and O_3, where ozone had a strong effect on acute respiratory diseases and NO_2 with hospitalizations by asthma[10].

As can be observed the NO_2 has a great role in admissions for respiratory diseases, because with the increase of 10 μg/m^3 in their concentrations, would increase 150 hospitalizations, that is, there would be an excess in hospital costs an average of R$ 260 thousand, for it is important to the development of public policies that reduce risks to Public Health, especially in the children's health.

Nitrogen dioxide, in the presence of sunlight, reacts with hydrocarbons and oxygen forming ozone, being one of the main precursors of this pollutant in the troposphere. Nitrogen dioxide, when inhaled, reaches the outermost portions of the lung due to its low solubility in water[11]. Its toxic effect is related to the fact that he is an oxidizing agent. The acute exposure to NO_2 increases bronchial responsiveness, and wheezing and exacerbation of bronchial asthma, chronic obstructive pulmonary disease and cardiovascular diseases can occur and may also increase susceptibility to infections[20].

This study may have limitations, one of them is that in this article were studied only the pollutants O_3, PM_{10} and NO_2, but not the impact of exposition to other pollutants such as CO and SO_2, which are not quantified by measuring station of Cetesb. The data of air pollution were detected in a fixed monitoring site, not representing with accurately the level of individual exposure to pollutants; this could underestimate the impact of pollution on health. It is also assumed that children moved freely, and it has a restricted movement around town exposing themselves to pollutants on an ongoing basis.

Another limitation lies in the fact that they are secondary data that even obtained from official source (Datasus) may contain diagnostic erros; on the other hand, this source is commonly used in epidemiological studies about the effects of pollution on health, but it has a more important aspect which is the accounting effect of the procedure. In addition, the Datasus does not tell the nutritional status, housing, medical history of the child, breastfeeding and passive smokers that may be associated with respiratory diseases.

Despite all these limitations it was still possible to find association between pollution and hospital admissions due to respiratory diseases and it was the nitrogen dioxide that had statisti-

cal significance, and can be considered a risk factor for respiratory diseases. The results presented here allow municipal manager to deploy policies aiming the reduced concentrations of air pollutants with the possible decrease of the incidence of hospitalizations due to respiratory diseases, reduce financial costs for the Public Health System (SUS) and also reduce the social costs of the child and his family.

Collaborations

PC Camargo, LF Nakazato e LFC Nascimento participated in all stages of the article.

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