Differential susceptibility according to gender in the association between air pollution and mortality from respiratory diseases

Susceptibilidade segundo sexo na associação entre poluição do ar e mortalidade por doenças respiratórias

Marcio Sacramento de Oliveira [1,2]
Antônio Ponce de Leon [3]
Inês Echenique Mattos [4]
Sérgio Koifman [4]

[1] *Escola Politécnica de Saúde Joaquim Venâncio, Fundação Oswaldo Cruz, Rio de Janeiro, Brasil.*
[2] *Coordenação de Vigilância Ambiental em Saúde e Saúde do Trabalhador, Secretaria de Estado de Saúde e Defesa Civil do Rio de Janeiro, Rio de Janeiro, Brasil.*
[3] *Instituto de Medicina Social, Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brasil.*
[4] *Escola Nacional de Saúde Pública Sergio Arouca, Fundação Oswaldo Cruz, Rio de Janeiro, Brasil.*

Correspondence
M. S. Oliveira
Laboratório de Educação Profissional em Vigilância em Saúde, Escola Politécnica de Saúde Joaquim Venâncio, Fundação Oswaldo Cruz.
Av. Brasil 4365, Rio de Janeiro, RJ 21045-900, Brasil.
marcio.sacramento@saude.rj.gov.br

Abstract

This study analyzed the association between air pollution and deaths from respiratory diseases, considering differential susceptibility according to gender. The authors used daily deaths from respiratory diseases (ICD-10, J00-J99), PM_{10}, SO_2, and O_3 levels, and meteorological indicators in Volta Redonda, Rio de Janeiro State, Brazil, from January 2002 to December 2006. The association was estimated by Poisson regression using generalized additive models, where the increase in risk of deaths from PM_{10} to lag 1 was 10.01% (95%CI: 1.81-18.88%) in the total female population and 10.04% (95%CI: 0.90-20.02%) in elderly women. The increase in risk of deaths from PM_{10} to lag 9 was 8.25% in the total male population (95%CI: 0.86-16.18%) and 10.80% (95%CI: 2.18-20.15%) in elderly men. For exposure to SO_2 and O_3, the risk was significant in the total male population and the elderly, respectively. The results emphasize the need for further studies, focusing on modification of the effects of air pollution on health.

Air Pollution; Respiratory Tract Diseases; Disease Susceptibility; Mortality

Introduction

Rapid technological progress in the modern world has produced an increase in the amount and variety of air pollutants, thereby jeopardizing the quality of life on the planet [1,2]. Air pollution has been considered a serious public health problem for some time, acting as an additional health risk factor for humans, animals, and plants [3].

As an example of air pollution, particulate matter accounts for approximately 3% of annual mortality from cardiopulmonary diseases in adults, 5% of mortality from cancer of the trachea, bronchi, and lungs, and 1% of child mortality from acute respiratory infections in urban areas of the world [4].

Recent epidemiological studies provide evidence of the association between different health outcomes and increased daily air pollution levels, especially in more susceptible population groups like children, elderly, and individuals with cardiorespiratory diseases. The majority of these studies have been conducted in large urban areas, especially in the United States and Europe [5,6,7,8,9,10,11], but little is known about the magnitude of the relative impacts of these pollutants on Brazilian cities, where the studies are concentrated mostly in Rio de Janeiro, São Paulo, and Curitiba [12,13,14,15,16,17]. Outside the large Brazilian cities, there has been an increase in the number of studies in the North (Acre State) and Central-West (Mato Grosso and Tocantins

States), concerning the impact of burning biomass on the population's health, conducted by the State Health Departments with encouragement from the Brazilian Ministry of Health, through the Program for Environmental Health Surveillance and Air Quality (VIGIAR), as a strategy for orienting the development of its work, allowing integration of health services and fostering comprehensive actions.

The few studies reporting on health effects of exposure to air pollution due to gender-related differences in susceptibility have been inconclusive and have generally not been designed for this purpose [18,19].

Kim & Hu [20] found that in females, depending on the diameter of the inhaled particles, there was a greater deposition in the upper airways and tracheobronchial and alveolar regions, and that for ultrafine particles, this deposition was more localized and higher in female pulmonary alveoli, suggesting that this can lead to a greater risk of development of respiratory problems in women. These findings are consistent with the hypothesis that greater deposition of particles in the lungs can cause an alveolar inflammatory response, promoting the exacerbation of lung diseases and thus increased susceptibility [21]. Meanwhile, Bennett et al. [22] and Daigle et al. [23] found in their studies that men and women display similar deposition of fine and ultrafine particles in the airways.

Studies thus far have shown conflicting results, so that this is still an open question. Therefore, the current study aimed to assess the association between daily exposure to air pollutants and mortality from diseases of the respiratory system, considering differential susceptibility by gender for all deaths and for those in the elderly.

Material and methods

Study area

Volta Redonda is a municipality (county) located at 22º31'23" latitude South and 44º06'15" longitude West in the Vale do Paraíba micro-region, within the Sul Fluminense meso-region in the State of Rio de Janeiro, Brazil. The municipality's total area is 182.8km², of which 54km² comprise the city limits of the municipal seat. Accompanying the Paraíba do Sul river, which cuts through the city of Volta Redonda from Southwest to East, the urban area is located along the banks of the river on a plain surrounded by hills whose altitude varies from 350 meters above sea level along the river to 707 meters at the northeastern tip. According to the National Census Bureau, or Brazilian Institute of Geography and Statistics (IBGE), the total population in 2009 was 261,403. Volta Redonda has a mesothermal climate and high relative humidity (77%), even in the cooler months, when it varies from 71% to 72%. The adjusted mean temperature is 21°C, with a mean annual low of 16.5°C and mean annual high of 27.8°C. Mean annual precipitation is 1,377.9mm, and January and February are the months with the heaviest rainfall. Considered the economic hub of the Sul Fluminense meso-region, the economy of Volta Redonda, although still anchored in industry, is quite diversified, focused to a major extent on services and commerce. The municipality is home to the large steel mill Companhia Siderúrgica Nacional (CSN) and other smaller industries, the Votoran (Votorantim Group) and Tupi (Cimento e Participações – CP) cement factories, the White Martins Oxygen and Nitrogen Plant, the flat steel products company Industria Nacional de Aços Laminados (INAL), the tin mill Companhia Estanifera Brasileira (CESBRA), and S/A Tubonal (steel pipes) (Portal VR. http://www.voltaredonda.rj.gov.br/cidade/índex.php, accessed on 12/May/2010).

Study design

This was an ecological time series study conducted in the Municipality of Volta Redonda from January 1, 2002, to December 31, 2006.

Data collection

Daily reports of deaths from diseases of the respiratory system (ICD-10, J00-J99) were obtained from the Mortality Information System, Ministry of Health (SIM).

Daily records of mean concentrations of particulate matter with aerodynamic size up to 10μm (PM_{10}), sulfur dioxide (SO_2), ozone (O_3), low temperature, and mean relative humidity (RH) were provided by the Rio de Janeiro State Environmental Institute (INEA) from automatic air quality monitoring stations located in Volta Redonda in the following neighborhoods: Jardim Belmonte (west side), Vila Santa Cecília (north side), and Retiro (city center).

The daily averages for the environmental variables from the three stations were calculated after imputing missing data using the modified expectation maximization (EM) algorithm, applied under the assumptions of multivariate normal distribution. In addition to the inter-variable dependency structure, this method also considers the time dependency structures for each variable. The time component contribution of each univariate series was estimated *ad hoc*, that is, additional models were needed for estimating μ_t. In this imputation method, the non-parametric cubic spline was implemented to estimate the time series level [24].

According to the report on the implementation of the INEA environmental monitoring network in Volta Redonda, the monitoring network's spatial configuration provides a correlation between the stations' measurements and coverage of the pollutants with at least 70% efficiency.

Data analysis

Initially, we determined the descriptive statistical measurements (arithmetic mean, standard deviation, and minimum and maximum values) for the variables total deaths from diseases of the respiratory system and for the elderly only (defined here as individuals 65 years or older), stratified by gender, and for PM_{10}, SO_2, O_3, low temperature, and RH. In the time series analysis, the daily counts of total deaths and deaths in the elderly, stratified by gender, were considered dependent variables (Y_t) and the mean daily concentrations of PM_{10}, SO_2, and O_3, one-by-one, were the independent variables (X_t). The following control variables were also considered: days of the week (an indicative variable for each day of the week, in order to control the calendar effect), time (variable sequence 1 after the last day of the study period, to adjust seasonality and long-term tendency), national and local holidays (an indicative variable for each type of holiday), and mean daily low temperature (ºC) and RH (%) (used to adjust for climatic factors).

In relation to the dependent variable and some control variables, such as meteorological variables, which are not necessarily linear, generalized additive models (GAM) [25] using Poisson regression with non-parametric functions of the cubic smoothing spline type were applied to estimate the association between daily deaths from diseases of the respiratory system and daily levels of these meteorological indicators. Importantly, the smoother is a function of x and y with the same x domain, defined for every point x_0 or sometimes only for the x_i of the sample. For each x_i value, the smoother associates a value $f(x_i)$, the $\hat{f}(x_i)$ estimate of which can be obtained. By definition, the values of this function should be "smoother" than the y values, i.e., they should have a lower variability than the y values [26]. The smoothing procedure was used for time and for the meteorological variables, in order to adjust the trend and both the basic and more long-term seasonal patterns.

After adjusting the dependent variable for the control factors, the independent variables were inserted one-by-one into the models. Since the biological manifestations of the effects of air pollution on health outcomes apparently display a lag type behavior in individual exposure to pollutants [27], the dependent variables were inserted with a lag time of zero to 10 days, one by one, considering the day after exposure, in order for a more precise definition of the model to be used.

The final model's goodness of fit was estimated by residuals analysis and the Akaike information criterion (AIC) [28]. The relative risks (RR) for deaths corresponded to a 10μg/m³ increase in the concentration of air pollutants and 5% level of significance. The data were analyzed with the R software, version 2.12.0, with the ARES statistical library, version 0.7.0 (The R Foundation for Statistical Computing, Vienna, Austria; http://www.r-project.org).

Results

During the study period, which covered 1,826 days, there were 8,518 deaths in the municipality of Volta Redonda, of which 1,058 (12.4%) were due to respiratory diseases. Of these, 788 (74.5%) occurred in elderly individuals (Table 1).

The total number of respiratory deaths in the population varied from 0 to 4 per day. Among the elderly, after stratifying by gender, this figure varied from 0 to 3 deaths (Table 1). The data showed a downward trend in mortality from respiratory diseases in most of the study period. This trend remained stable among women, while among men there was an increase beginning in the winter of 2005.

During the study period, 75% of the mean concentrations of daily PM_{10} emissions remained below 35.95μg/m³, and the highest concentration was 122.70μg/m³ (Table 1), with an annual mean of 30.56 ± 12.16μg/m³, thus below the 50μg/m³ emissions standard. Air pollution emission standards were set in Brazil by the National Environmental Board (CONAMA) under Ruling 003/1990.

The smoothing curve for the PM_{10} temporal distribution showed a seasonal pattern, with an increase in daily emissions during the "winter" (or cool season) and a decrease in the summer, showing a downward trend during most of the study period and a constant trend at the end; SO_2 showed a similar pattern, but with less variation. O_3 showed an erratic behavior, with stability in terms of seasonality and trend from the beginning of the period until September 2004, a downward trend until April 2005, and an upward trend since then (Figure 1). PM_{10} and SO_2 did not display any violation of the daily emission

Table 1

Descriptive analysis of the daily count of total deaths from diseases of the respiratory system (ICD-10: J00-99) and in the elderly, stratified by gender, daily air pollution measurements, and meteorological variables. Volta Redonda, Rio de Janeiro State, Brazil, 2002-2006.

Variables	Descriptors							
	n	%	Days	Missing	Mean	SD	Minimum	Maximum
Total deaths	1,058	100.00	1,826	0	0.58	0.75	0.00	4.00
Females	512	48.40	1,826	0	0.28	0.51	0.00	3.00
Males	546	51.60	1,826	0	0.30	0.54	0.00	3.00
≥ 65 years	788	100.00	1,826	0	0.58	0.75	0.00	4.00
Females ≥ 65 years	400	50.76	1,826	0	0.22	0.45	0.00	3.00
Males ≥ 65 years	388	49.24	1,826	0	0.21	0.46	0.00	3.00
PM_{10} (μg/m^3)	-	-	1,807	19	30.56	12.16	7.58	122.70
SO_2 (μg/m^3)	-	-	1,794	32	9.04	5.11	0.00	56.50
O_3 (μg/m^3)	-	-	1,790	36	59.16	25.45	6.55	171.70
Relative humidity (%)	-	-	1,763	63	81.05	8.76	51.04	99.60
Low temperature (°C)	-	-	1,790	36	18.39	3.26	7.37	25.45

standards, set respectively at 150μg/m^3 and 100μg/m^3. O_3 showed three violations of the standard (161.30, 162.10, and 171.70μg/m^3), which was set at 160μg/m^3.

The mean values for relative humidity and low temperature were, respectively, 81.05 ± 8.76% and 18.39 ± 3.26ºC (Table 1).

Figure 2 shows the estimated risk of respiratory deaths due to a 10μg/m^3 increase in PM_{10}, SO_2, and O_3 levels in Volta Redonda. In the first three days after exposure, one can expect, respectively, an increase of 10.01% (95%CI: 1.81-18.88%; p-value = 0.02), 8.56% (95%CI: 0.77-16.95%; p-value = 0.03), and 9.37% (95%CI: 1.72-17.60%; p-value = 0.01) in the risk of deaths due to respiratory diseases in the total female population. In women 65 years or older, the increase in risk on the first, third, and fourth days was 10.04% (95%CI: 0.90-20.02%; p-value = 0.03), 10.57% (95%CI: 1.95-19.92%; p-value = 0.01), and 9.27% (95%CI: 0.66-18.61%; p-value = 0.03), respectively. The risk of death in women was not statistically significant for the other air pollutants (Figure 2).

For the total male population, as well as for men 65 years or older, with a nine-day lag after exposure to PM_{10}, one can expect an increase in risk of deaths of 8.25% (95%CI: 0.86-16.18%; p-value = 0.03) and 10.80% (95%CI: 2.18-20.15%; p-value = 0.01), respectively.

For exposure to SO_2, the effect in the total male population showed a two-day lag and increased risk of 20.25% (95%CI: 0.41-44.01%; p-value = 0.04). In elderly men, no association was observed between SO_2 levels and the outcome. However, on the ninth day after exposure to O_3, the increase in risk of death was 5.88% (95%CI: 0.89-11.12%; p-value = 0.02).

As for PM_{10}, besides differences in effect sizes between women and men, the effect of exposure to the pollutant on respiratory deaths occurred later in men, while in women it occurred beginning on the first day after exposure (Figures 2 and 3).

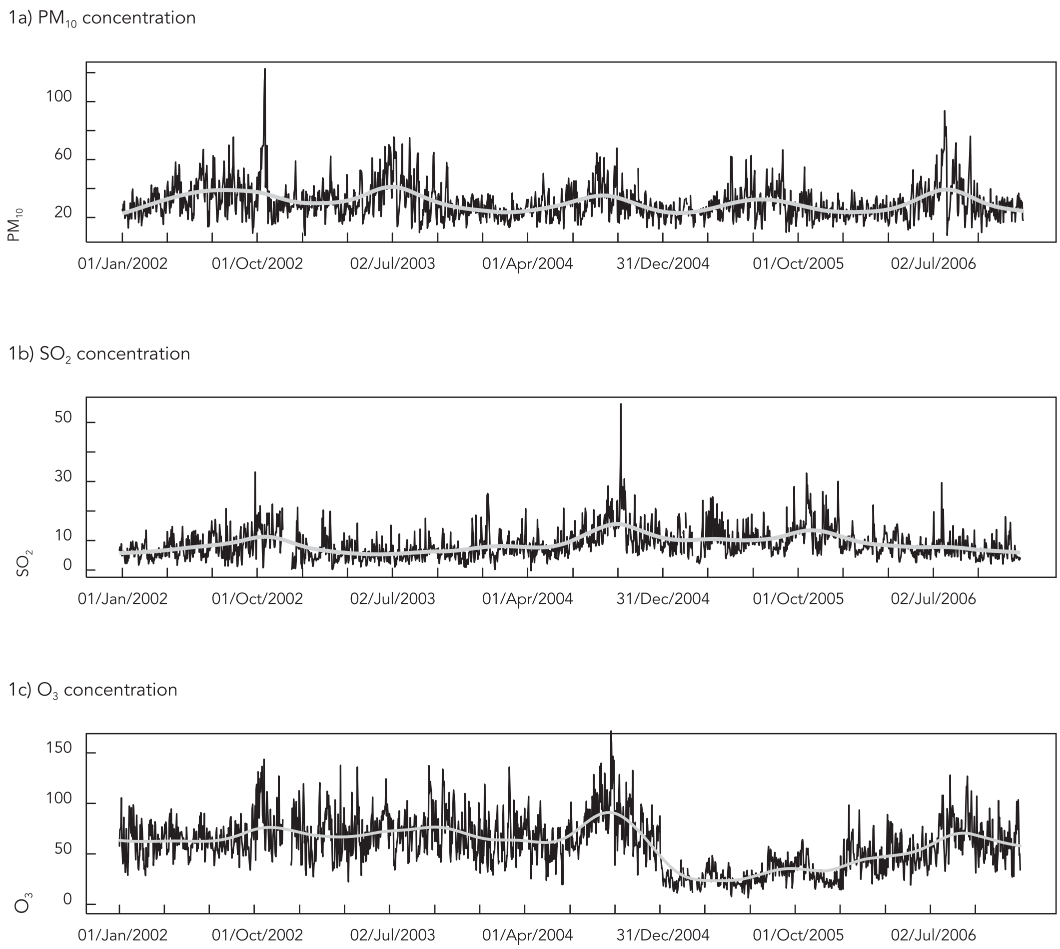
Discussion

There has been an increase in the number of epidemiological studies on the association between air pollution and a wide variety of health outcomes. These include studies on the effects on overall mortality and that due to specific causes such as cardiovascular and respiratory diseases [12,13,14,15,18,19,27,29,30,31,32,33].

According to Castro et al. [3], one of the main advantages of time series analyses is that factors such as socioeconomic status, occupation, or smoking are not capable of confounding the relationship between air pollution and health effects, since these factors do not display significant daily variations. Meanwhile, factors with such variation and that correlate with pollution are potential confounders and should be adjusted in the analysis. Factors that underwent such adjustment in the current study included meteorological variables (temperature and humidity) and chronological factors such as days of the week

Figure 1

Temporal distribution of daily concentrations and smoothing curve for PM_{10}, SO_2, and O_3. Volta Redonda, Rio de Janeiro State, Brazil, 2002-2006.



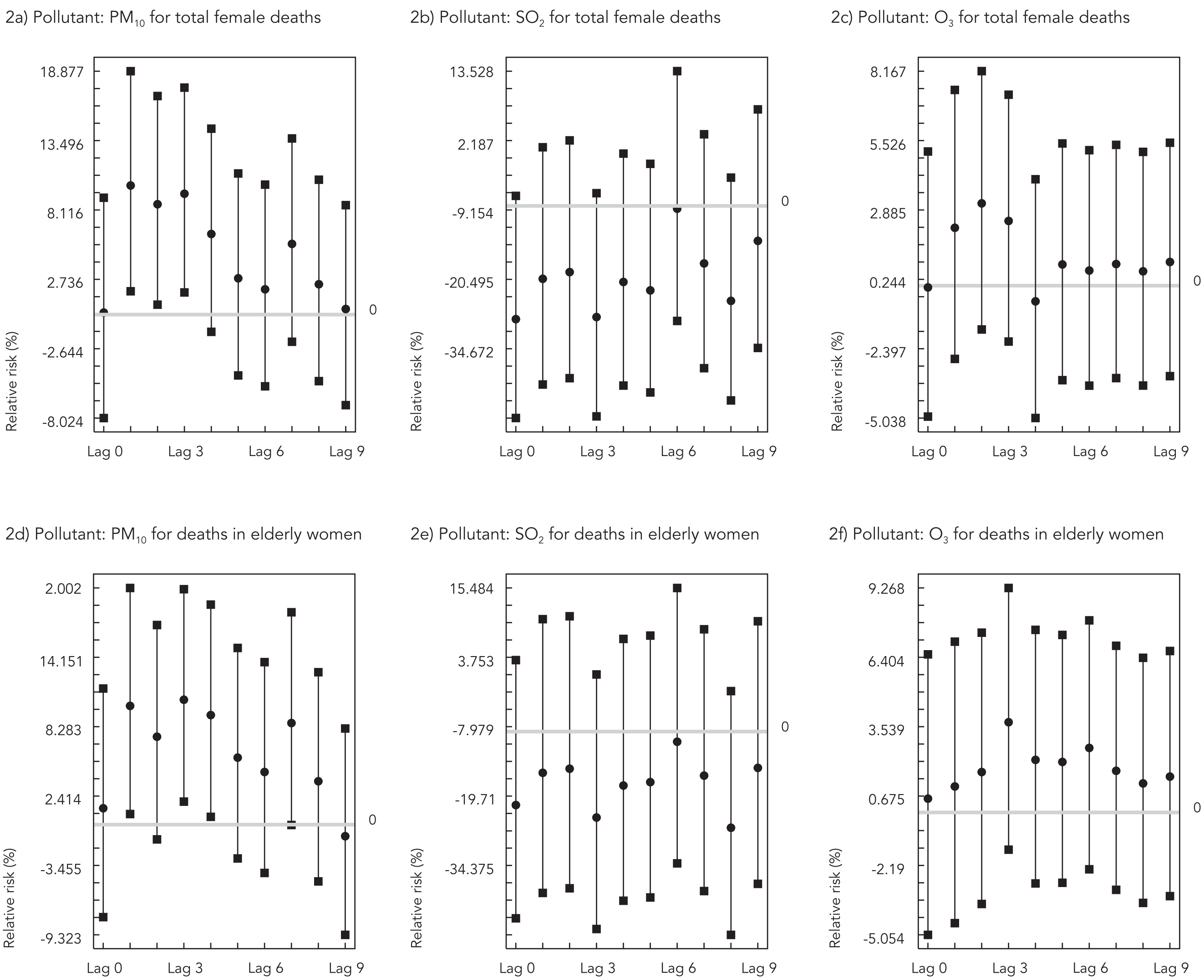
(variable for adjusting the calendar effect), total number of days transpired in the study period (variable for adjusting long-term seasonality), and holidays.

The study results may not have suffered any influence from differences (since they were small) in the proportion of women in the sample from Volta Redonda or in the percentages of deaths. Thus, the extrinsic factors that might have affected the observed results and that were not possible to determine with the methodology were the prevalence of some respiratory conditions that would explain the greater effect size for PM_{10} and the absence of a significant effect from the other pollutants in women, as well as a more rapid physiological response to exposure in the outcome's manifestation as compared to men, or even a different spatial distribution of women over the course of the day as compared to men, exposing them to the pollutants' impact for most of the day.

The use of GAM allowed to more effectively control the confounding factors (trend, seasonality, cycle, temperature, humidity, holidays, and calendar effect), which could interfere in the data analysis. GAM was chosen as the study's analytical tool because the model allows adjusting non-parametric functions for variables presenting this behavior, thus minimizing possible errors in the effect estimates and their respective standard errors. Poisson regression was used, since it allowed analyzing the counting

Figure 2

For deaths from respiratory diseases, percentage of relative risk for total female deaths and deaths in elderly women related to a 10µg/m³ increase in daily PM_{10}, SO_2, and O_3 levels. Volta Redonda, Rio de Janeiro State, Brazil, 2002-2006.

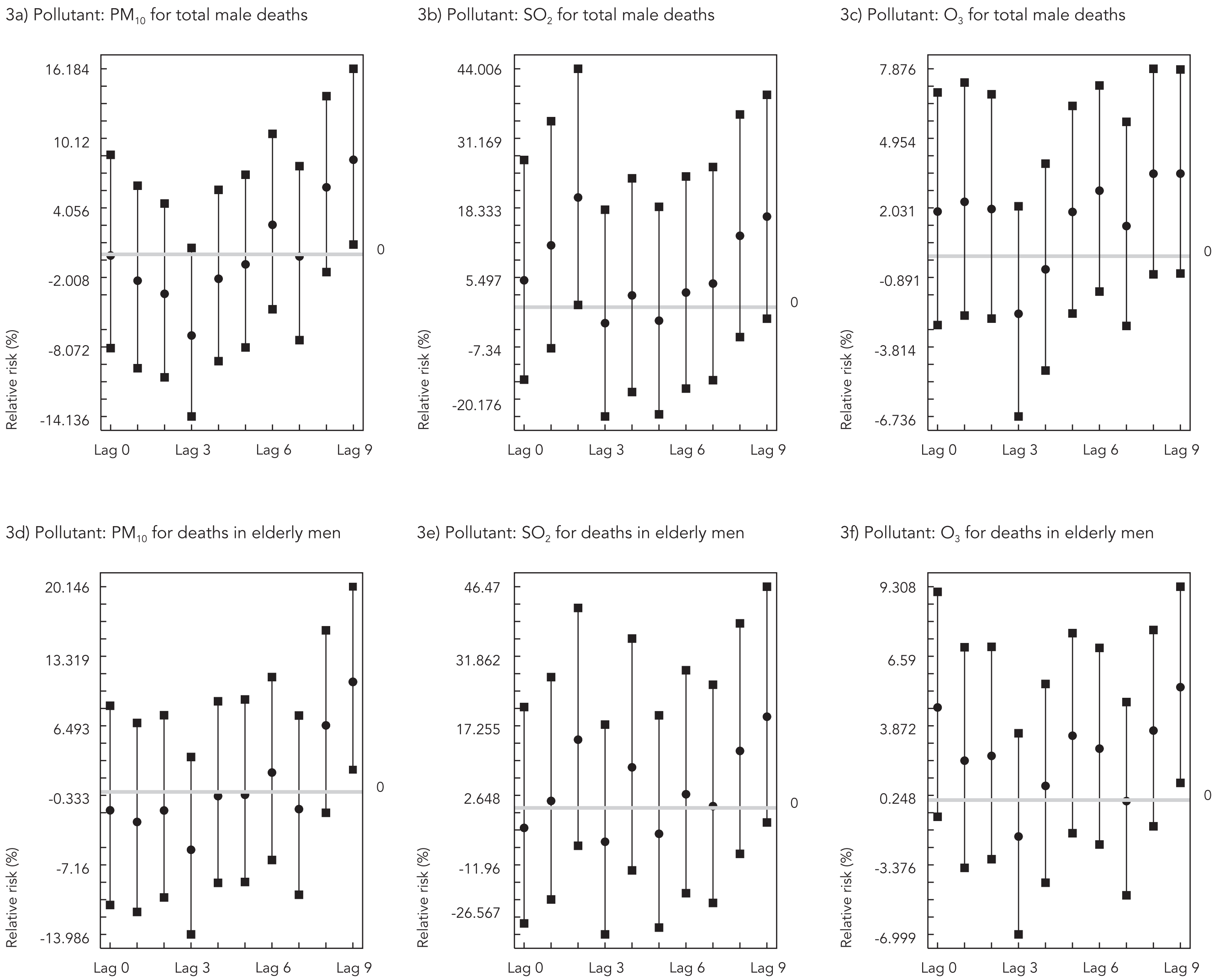


data, the daily number of deaths from respiratory diseases.

Analysis of the data's temporal distribution showed marked seasonality in the PM_{10} and SO_2 levels, increasing in the winter and decreasing in the summer (Figure 1). This can be explained by the characteristics of the mesothermal climate in the municipality of Volta Redonda, with hot, rainy summers and dry winters, where January and February have the heaviest rainfall. Volta Redonda has northwest prevailing winds, but the fact that it is located in the bottom of a valley means that the air is calm most of the time, thus hindering the dispersion of gases and particles. This process is intensified due to the thermal inversion phenomenon, common in the winter, when the pollution layer hangs over the city, forming a barrier to sunlight, decreasing insolation, and preventing the release of heat and new pollution emissions (Portal VR. http://www.voltaredonda.rj.gov.br/cidade/index.php, accessed on 12/May/2010).

Figure 3

For deaths from respiratory diseases, percentage of relative risk for total male deaths and deaths in elderly men related to a 10μg/m[3] increase in daily PM_{10}, SO_2, and O_3 levels. Volta Redonda, Rio de Janeiro State, Brazil, 2002-2006.



This study's findings suggest a direct association between daily variations between PM_{10} and SO_2 levels and deaths from respiratory diseases, with higher risk size among the elderly (Figures 2 and 3). These results corroborate those of other epidemiological studies, suggesting that increases in mortality associated with air pollution are greater among the elderly, and point to an increase in prevalence of chronic obstructive pulmonary disease (COPD) and other diseases of the airways in this population group, which could also be a determinant of susceptibility [7,31,34].

Physiological changes associated with aging explain the greater susceptibility of the elderly to the effects of PM. All components of the respiratory system are normally affected by aging, including spirometry, oxygen diffusion capacity, lung elasticity, chest wall expansion capacity, respiratory muscle strength, maximum oxygen uptake, and peak cardiac output [7]. The elderly are also more susceptible to respiratory infections, in part due to an age-related decline in the specific immune response, ciliary function, and cough reflex [7,32,33].

The increased susceptibility of elderly to particulate matter may also be to due lifelong exposure to environmental substances that are harmful to health, as well as to previous respiratory infections, as observed by Meyer et al. [35] in a study of healthy non-smokers from 65 to 78 years of age. The authors observed an increase in neutrophils, immunoglobulins (IgG, IgA, and IgM), and interleukin-6 (IL-6) in fluid from bronchoalveolar lavage, as compared to samples from individuals 20 to 36 years of age. For the age group 65 years and older, one can assume a high prevalence of chronic respiratory diseases. This could explain the "harvesting" pattern observed in the increase in deaths from this cause, since in this case, exposure to air pollutants would mainly affect a more susceptible and/or vulnerable population subgroup on days following exposure to higher levels of the pollutant. Importantly, given the harvesting phenomenon, the negative (or protective) effects of pollutants can already occur just a few days after exposure. However, if for the existing pollution levels, the size of the susceptible group does not undergo major changes over time, the harvesting phenomenon will not have a great impact in decreasing the number of susceptible individuals, and thus it will still be possible to observe the effects of pollutants after several days of exposure.

The current study showed differences in the size effect between the elderly and the overall population, as well as between genders. As mentioned in this study, although most epidemiological studies on this theme were not conducted specifically for this purpose, some studies report not having observed differences in effect size between genders, while others suggest that exposure to air pollution can affect men and women differently.

Pope et al. [18] found that more polluted cities in the United States showed slightly higher (but not statistically significant) risk of mortality from cardiopulmonary disease in non-smoking women as compared to non-smoking men, when compared to less polluted cities (RR = 1.57 in females and RR = 1.24 in males). Frampton et al. [19] examined the respiratory effects of exposure to ultrafine carbon particles in healthy and asthmatic men and women. Although some outcomes showed small differences between genders, such as a reduction in peripheral blood monocytes and T-lymphocyte activation in healthy women, the overall results did not allow concluding that there are differences in susceptibility between men and women.

Measurable gender differences in immune and inflammatory responses could also explain the greater female susceptibility; for example, women have a higher $CD4^+$:$CD8^+$ lymphocyte ratio than men, and their peripheral blood monocytes produce more prostaglandin E_2 (PGE_2) and less tumor necrosis factor α (TNF-α) when stimulated [36,37].

Thus far, there is not sufficient evidence to rule out the possibility that gender may be related to health risk size from exposure to air pollution. Physiological differences between men and women suggest a possible difference in the response to given levels and especially to different chemical compositions of air pollutants. The current study showed different gender patterns in the trend, size effect, and lag time after exposure. These results emphasize the need for further studies focusing on modification of the effect of air pollution on human health, considering gender as a probable factor in susceptibility to the occurrence of death following exposure to air pollutants, especially in individuals older than 65 years.

Conclusions

In Volta Redonda, the highest concentrations of pollutants (except O_3) and deaths from respiratory diseases occurred in the coolest months. Daily PM_{10} and SO_2 emissions were associated with mortality from respiratory diseases, even when emissions were within or close to the standards set by the CONAMA. The association was stronger in women, especially among the elderly, and showed a later effect on the outcome in men as compared to women. The risk of deaths tended to increase in men as time after exposure increased, while the opposite was observed in women from the same age bracket.

Resumo

O estudo avaliou a associação entre poluição do ar e óbitos por doenças respiratórias, considerando susceptibilidade diferencial segundo sexo. Foram utilizados óbitos diários por doenças respiratórias (CID-10, J00-J99), níveis de PM_{10}, SO_2, O_3 e indicadores meteorológicos de Volta Redonda, Rio de Janeiro, Brasil, de janeiro de 2002 a dezembro de 2006. A associação foi estimada por MAG de regressão de Poisson, onde para lag 1, o aumento do risco dos óbitos por PM_{10} foi de 10,01% (IC95%: 1,81-18,88%) no total da população feminina e 10,04% (IC95%: 0,90-20,02%) em idosas. No total da população masculina, para lag 9, o aumento do risco de óbitos por PM_{10} foi de 8,25% (IC95%: 0,86-16,18%) e de 10,80% (IC95%: 2,18-20,15%) para os idosos. Para exposição ao SO_2 e O_3, o risco foi significativo no total da população masculina e em idosos respectivamente. Os resultados reforçam a necessidade de estudos adicionais, centrando-se na modificação dos efeitos da poluição do ar sobre a saúde.

Poluição do Ar; Doenças Respiratórias; Suscetibilidade a Doenças; Mortalidade

Contributors

M. S. Oliveira was responsible for the study design, literature search, data collection and analysis, interpretation of the findings, and writing of the article. A. Ponce de Leon contributed to the data analysis and writing of the article. I. E. Mattos participated in the study design, interpretation of the findings, and writing of the article. S. Koifman participated in the study design, interpretation of the findings, and writing of the article.

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