THE ASSOCIATION BETWEEN AIR POLLUTION AND THE MORTALITY OF ELDERLY PEOPLE DUE ACUTE MYOCARDIAL INFARCTION IN SÃO PAULO, SP, BRAZIL

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ABSTRACT: The resident population of large urban centers faces the constant presence of air pollutants and has limited adaptability to their adverse effects, which may cause health problems. The objective of this work was to verify the association between Atmospheric conditions and the mortality of elderly people from acute myocardial infarction (AMI) in the resident population of the city of São Paulo. The data on ozone (O_3), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), carbon monoxide (CO) and particulate matter (PM_{10}) made available by the Sanitation Company of the state of São Paulo. The notifications of acute myocardial infarction deaths by place of residence were made available by the Mortality Information System for the period from 2000 to 2010. Taking into account the specific characteristics of the data under study, Generalized Estimating Equations modeling was used to capture significant associations and the risk of death in the population exposed to changes in air quality. The model which have better adjustment to the data had happened between the combination of the CO, SO_2, O_3 e PM_{10} pollutants, because of their association reached 5% of significance. Thus, was found, by estimate, that the risk of deaths of the exposure population by AMI, increase in 3% when caused by CO, 6% by SO_2, 4% by O_3 and 9% by PM_{10}. Then we expect, with the results here shown, we can contribute to plan health and environment public policies.

KEYWORDS: atmospheric pollutants; acute myocardial infarction; statistical modeling.

A ASSOCIAÇÃO ENTRE A POLUIÇÃO ATMOSFÉRICA E A MORTALIDADE DE PESSOAS IDOSAS DEVIDO AO INFARTO AGUDO DO MIOCÁRDIO EM SÃO PAULO, SP, BRASIL.

RESUMO: A população residente em grandes centros urbanos enfrenta a presença constante de poluentes atmosféricos e tem pouca adaptabilidade aos seus efeitos adversos, o que pode causar problemas de saúde. O objetivo deste trabalho foi verificar a associação entre as condições atmosféricas e a mortalidade de idosos por infarto agudo do miocárdio (IAM) na população residente da cidade de São Paulo. Os dados de ozônio (O_3), dióxido de nitrogênio (NO_2), dióxido de enxofre (SO_2), monóxido de carbono (CO) e material particulado (PM_{10}) foram disponibilizados pela Companhia de Saneamento do Estado de São Paulo. As notificações de óbitos por infarto agudo do miocárdio por local de residência foram disponibilizadas pelo sistema de informações de mortalidade para o período de 2000 a 2010. Levando em consideração as características específicas dos dados em estudo, utilizou-se a modelagem via equações de estimação generalizadas para captar associações significativas e o risco de óbito na população exposta a alterações na qualidade do ar. O modelo que apresentou melhor ajuste aos dados ocorreu entre a combinação dos poluentes CO, SO_2, O_3 e PM_{10}, a 5% de significância. Assim, verificou-se, por estimativa, que o risco de óbito por IAM da população em exposição, aumentou em 3% quando causada por CO, 6% por SO_2, 4% por O_3 e 9% por

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PM_{10}. Espera-se que, com os resultados aqui mostrados, possa contribuir para planejar políticas públicas de saúde e meio ambiente.

PALAVRAS-CHAVE: poluentes atmosféricos; infarto agudo do miocárdio; modelagem estatística.

1.INTRODUCTION

The vulnerability to cardiovascular disease of people in large urban centres increases as a result of adverse conditions caused by the weather and climate, among other factors. These climatic factors are related, according to Bell et al. (2009), to industrial society based on the use of fossil fuels and other non-renewable natural resources.

Pollutants can be generated by industrial activities, internal combustion engines or burning of trash. They can also be produced by chemical reactions in the atmosphere and released from natural sources. Their concentration is strongly related to weather conditions. Some of the conditions that favour high levels of pollution are slight or no wind and thermal inversions (Pénard-Morand end Annesi-Maesano 2004).

The phenomenon of thermal inversion occurs when a layer of warm air overlies a layer of cold air, trapping the cooler air and hampering the dispersion of air pollutants (Whiteman, 2000). These pollutants form mists, especially in the colder periods of the year (OGA et al., 2008).

According to studies such as Sole (2001) and Alessandrini et al. (2006) an increase in air pollutants tends to cause warmer winters, increasing the synchronization and release of biogenic allergens in urban centres where there are already large numbers of particles resulting from diesel exhaust. This increment is more severe because the particles carry these allergens to the lungs, from where they enter bloodstream, accelerating the process of respiratory and cardiovascular diseases (Lelieveld et al. 2013).

Air pollution induces the body to produce unstable molecules that trigger inflammatory reactions, with damage to the arteries (Shrey et al., 2011). The different composition of air pollutants, the dose and time of exposure and the fact that humans are usually exposed to pollutant mixtures than to single substances, can lead to diverse impacts on human health (Kampa and Castanas, 2008).

São Paulo State, Brazil, is the most industrialized centre of Latin America, with more than 40 million inhabitants. There are about 19 million vehicles in the area (IBGE, 2014), using different types of fuel: gasoline and ethanol. Air pollution in São Paulo originates predominantly from automotive vehicle emissions. Vehicles are responsible for 98% of CO emissions, 97% of HCs (hydrocarbons), 97% of NOx, 52% of PM and 42% of SOx, according to measurements carried out by CETESB. The objective of this work was to verify the association between air pollutants and deaths due to acute myocardial infarction (AMI) in the elderly population of the city of São Paulo, from 2000 to 2010.

2. MATERIALS AND METHODS

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Daily data were used on the air pollutants ozone (O_3), nitrogen dioxide (NO_2), sulphur dioxide (SO_2), carbon monoxide (CO) and particulate matter (PM_{10}), available by the São Paulo State Sanitation Company (CETESB). Their concentrations were classified in the categories Good and Inadequate. This database contains readings the pollutants carried out 24 hours a day and pollutant measurements were in μg/m³ and ppm. The daily means for each pollutant were calculated. Beta monitoring, coulometry, infrared detection and chemiluminescence measurement were used to determine PM_{10}, SO_2, CO, NO_2 and O_3 emissions, respectively. The air quality was classified as inappropriate when the concentrations of all the pollutants exceeded the reference values set by CETESB. These average values are: CO (9 ppm for 8 hours), SO_2 (20 μg / m³ 29 for 24 hours), O_3 (100 μg / m³ daily maximum of 8 hours), NO_2 (200 μg / m³ for each hour) and PM_{10} (50 μg / m³ for 24 hours). Otherwise, the air quality was considered good. The average of the available measurements was calculated for each day and was considered to be representative of citywide conditions.

Data concerning air temperature (°C), relative humidity (%), rainfall (mm), and atmospheric pressure (hPa) were obtained from the weather database for National Institute of Meteorology – INMET, which keeps historical weather data in digital form.

The records of elderly deaths (60 years or older) vulnerable group due to acute myocardial infarction (AMI) and according to place of residence in São Paulo for the period from 2000 to 2010 were obtained from the Morality Information System of the Ministry of Health, Department of Informatics of SUS - DATASUS. They were coded according to the 9th revision (1998 and 2000) or 10th revision (2001 and 2010) of the International Classification of Diseases (ICD). AMI deaths (ICD-9: 410 or ICD-10: I21) were extracted to construct AMI mortality time series.

These are count data, which are generally assumed to follow the Poisson probability distribution. The Poisson distribution is particularly useful for modelling discrete variables that occur in a given time span, such as the death count, provided that one establishes that the distribution is random with a mean approximately equal to the variance (Zeger and Liang, 1986). In the present study, the count data were obtained in a longitudinal scale, which leads to dependence between the serial observations.

Because of the specific characteristics under study, a generalized estimating equations (GEE) model was employed, which enables the analysis of correlated data, to capture associations between the concentration of air pollutants and deaths caused by AMI.

Taking into consideration the specific characteristics under study, we employed Generalized Estimating Equations (GEE), which enable the analysis of correlated data, to capture associations between the concentration of air pollutants and deaths caused by AMI.

Generalized Estimating Equations were proposed by Zeger and Liang, (1986) and Liang and Zeger, (1986). The authors based themselves on Generalized Linear Models (GLM). The method is, therefore, an extension of GLM, adding a correlation structure between the observations to obtain consistent and asymptotically unbiased estimates, i.e., in large samples.

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In the Gee Model, $\boldsymbol{y}_i$, is a vector of response variables, obtained by the deaths due to acute myocardial infarction, of dimension t_i x 1, that is, $\boldsymbol{y}_i = (y_{i1}, y_{i2},..., y_{it_i})'$, and $\mathbf{X}_i=(x_{i1}, x_{i2},..., x_{it_i})'$ is the matrix of covariates, of dimension t_i x p, whose rows are the vectors $x_{it}=(x_{it1},..., x_{itp})'$, for the i-th observational unit (i=1,2,..., n) in t-th moments of observation (times), t=1,2,...,t_i. It is assumed, in principle, that the marginal distribution of the random variable Y_{it} is known, that is, $Y_{it} \sim Poisson(\mu_{it})$ and that it belongs to the exponential family.

$$f(y_{it}, \theta_{it}, \varphi) = \exp[y_{it} \ln \mu_{it} - \mu_{it} - \ln(y_{it}!)]$$

In which the index t is included to consider the repeated observations in time. It is assumed that $\theta_{it} = \ln(\mu_{it})$ is the canonical parameter, without practical interest, $b(\theta_{it}) = \exp(\theta_{it}) = \mu_{it}$ is a monotonic and derivable function. In addition, $E(Y_{it}) = \mu_{it} = b'(\theta_{it})$, $Var(Y_{it}) = a_i(\varphi) b''(\theta_{it}) = a_i(\varphi) V(\mu_{it})$, where $V(\mu_{it})$ is the variance function. Also, in a great portion of cases, $a_i(\varphi)=\varphi$. One can therefore define a generalized linear model for each instant of time t, adding a function that makes the link between the random part and the systematic part.

$$\eta_{it} = g(\mu_{it}),$$

where $\boldsymbol{\eta}_{it} = \mathbf{x}'_{it}\beta$ is the linear predictor, $\boldsymbol{\beta}=(\beta_1,\beta_2,\ldots, \beta_p)'$ is the vector of unknown parameters and of interest and g(.) is the link function.

Generalized Estimating Equations are an extension of the quasi-likelihood estimation method proposed by (Wedderburn, 1974), which only requires specification of one variance function for the response variable and the functional relationship between the mean response and the parameters $\boldsymbol{\beta}$. The correlation structure used was of the exchangeable type, in which one considers that the correlation between observations of the variables of the same group is the same. This is the assumed correlation structure in a random effects model with a random intercept for each variable (Laird; ware, 1982).

In this study, we assumed a Poisson probability distribution and a canonical link function (logarithm of the mean), with the linear predictor $\eta_{it} = \ln(\mu_{it}) = \beta_0 + \beta_1 X$, whose exponential of parameter β_1 represents the relative risk (RR), where X represents the dichotomized classifications of air pollutants, considering 0 for good concentrations and 1 for the inappropriate ones, according resolution admitted by CETESB.

According to Agresti, (1996), the definition of the RR is the ratio between the probabilities of success of two levels of the explanatory variable, using the reference category (baseline). In this study, the reference class was the concentration of the pollutant classified as good. To choose the best model, we used the criterion of information based on quasi-likelihood. (Pan, 2001) proposed a method to select models in GEE using information criteria based on the quasi-likelihood ratio, the QIC. This penalizes the value referring to the model (that is, rewards parsimony) so that the smaller the value of QIC, the better the fit of the model. The adjustments and selection of models were developed using the free statistical software R (2.15.0).

3. RESULTS AND DISCUSSION

The exploratory analysis of acute myocardial infarction deaths of São Paulo residents from 2000 to 2010 pointed, on average, to a higher occurrence in the quarter from July to September, the transition period between the winter and spring seasons (Figure 1). The interaction between weather conditions and human health is not linear in time, because it depends on the intensity and duration of the changes (contrast degree), air quality conditions and on each person's metabolism. These factors constantly change with locations and populations (Sette and Ribeiro, 2011). The complex and diverse impact of weather condition variability on human health can be verified directly or lagged in time. These conditions could explain the decrease in the number of deaths from acute myocardial infarction in São Paulo in June and the higher frequency in July, pointing to the lagged effect one month after the start of winter (Gomes et al., 2018).

In São Paulo, winters have lower humidity and rainfall, so the concentration of pollutants in the air increases. These weather conditions increase the mortality risk in elderly people from heart disease mainly in the winter (Fares, 2013).

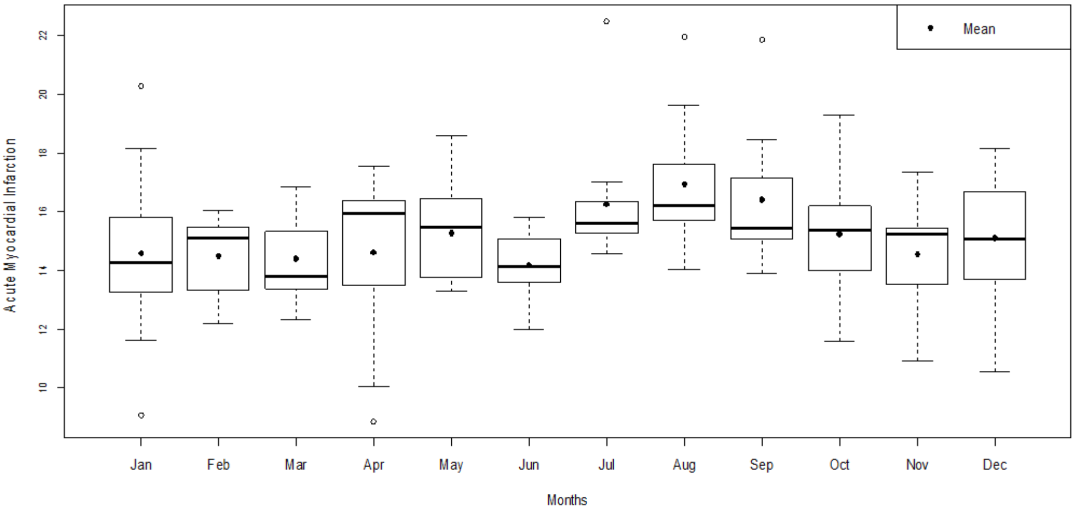

Figure 1 - Variability of the mortality of elderly people due to AMI in the resident population of the city of São Paulo in the period from 2000 to 2010.

The ozone concentration (Figure 2) registered the lowest mean values in the months of May, June and July, revealing an inverse relationship with the other air pollutants (Figure 3), which showed higher averages in winter.

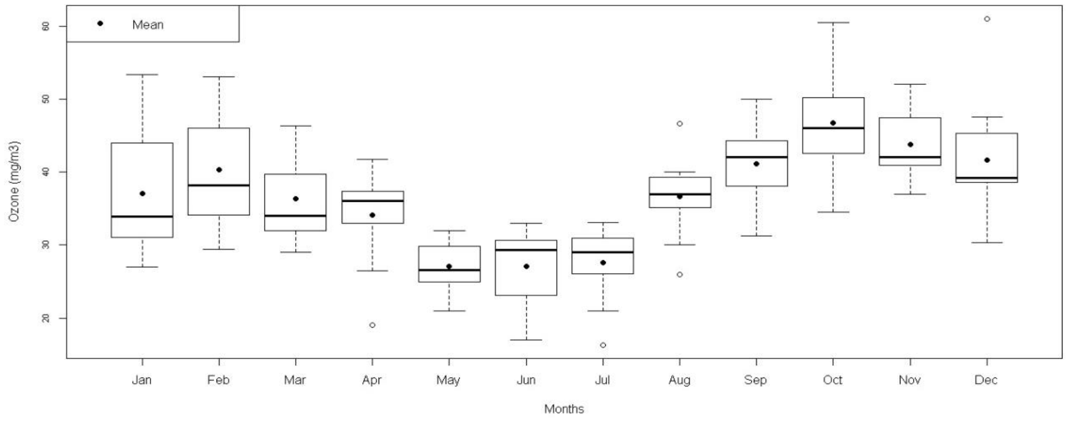

Figure 2 - Variability of Ozone in São Paulo in the period from 2000 to 2010.

This can be explained by the fact that O_3 production requires the presence of solar radiation, which is lower in this season (Muramoto et al., 2003). Ground-level ozone (the primary constituent of smog) is the most complex, difficult to control and pervasive among the five main pollutants studied. Unlike other pollutants, ozone is not emitted directly into the air by specific sources. Ozone is created by sunlight acting on nitrogen oxides (NOx) and volatile organic compounds (VOC) in the air. Often these "precursor" gases are emitted in one area, but the actual chemical reactions, stimulated by sunlight and temperature, take place in another. Combined emissions from automotive vehicles and stationary sources can be carried hundreds of kilometres from their origins, forming high ozone concentrations over very large regions (WHO, 2008).

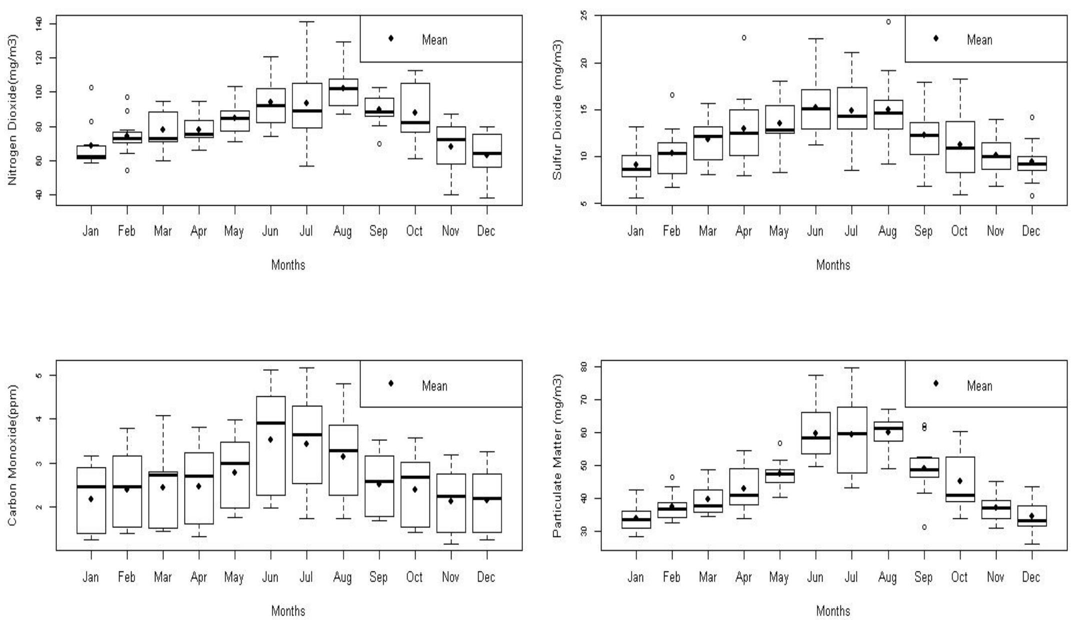

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Figure 3 - Variability of nitrogen dioxide, sulfur dioxide, carbon monoxide and particulate matter in São Paulo in the period from 2000 to 2010.

The main goal of this study was to verify the association between air pollutants and deaths of elderly from acute myocardial infarction in the city of São Paulo. The results show 5% significance between number of deaths with carbon monoxide, sulphur dioxide, ozone and particulate matter. After adjusting the model with all pollutants studied, the effects were not significant when comparing number of deaths and nitrogen dioxide (p-value = 0.718). From the model estimates, the relative risk of elderly people dying from acute myocardial infarction increased by 3%, 6%, 4%, and 9% due to carbon monoxide, sulphur dioxide, ozone and particulate matter, respectively (Table 1). These results show the increasing cardiovascular vulnerability of elderly people when the category of pollutants changes from good to inadequate.

The climate variables air temperature, relative humidity; atmospheric pressure and precipitation were considered but were not significant. Thus, to have parsimonious models, they were removed from the final model.

Table 1 - Generalized Estimation Equations Model of the mortality rate from acute myocardial infarction of the resident population of São Paulo in the period from 2000 to 2010.

Model GEE	**Estimated**	**Standard Error**	**P-value**	**RR**	**Confidence Interval (95%)**
Intercept	2.3407	2.3407	<0.001	-	-
CO	0.0316	0.0148	0.0324	1.032	1.001 1.062
SO_2	0.0553	0.0147	<0.001	1.057	1.027 1.088
O_3	0.0426	0.0115	<0.001	1.043	1.020 1.067
PM_{10}	0.0875	0.0171	<0.001	1.091	1.055 1.129

Significance at 5%.

Air pollution can occur from the local to global scale. Sometimes the effects can impact health immediately, but symptoms more often arise with delay of days, months or even years—and often in other cities, countries or continents (WHO, 2008). Nevertheless, according to the WHO (2013), the health effects of short-term pollutant exposure (hours or days) can aggravate lung disease, causing asthma attacks and acute bronchitis, as well as increasing susceptibility to respiratory infections and causing heart attacks and arrhythmias in people with heart disease. Even healthy persons can experience temporary symptoms, such as irritation of the eyes, nose and throat, coughing, chest tightness and shortness of breath.

Elevated levels and/or long-term exposure to air pollution can lead to more serious symptoms and conditions affecting human health (Dapper et al., 2016). This mainly affects the respiratory and inflammatory systems, but can also lead to more serious conditions such as heart disease and cancer (Kampa and Castanas, 2008). People with lung or heart diseases may be more susceptible to air pollution effects. Contact with air pollutants via inhalation and ingestion is much more harmful than skin contact (Gouveia et al., 2006).

The results of this study corroborate those observed by Hanigan et al. (2008), Coelho et al. (2010) and Ignotti et al. (2010), who indicated that the winter months in São Paulo are responsible for an increase in cardiorespiratory diseases related to weather conditions and air pollution.

Studies have shown associations between exposure to classic pollutants (particulate matter, ozone, sulphur dioxide and pollen) and human health in general (Ruidavets et al., 2005; Sicard et al., 2011; Lelieveld et al., 2013). It is important to highlight that this study, in addition to capturing the significant associations, shows that it is possible to obtain consistent estimates of acute myocardial infarction related to air pollution in the resident population of the city of São Paulo.

Liu et al. (2012) found seasonal effects of the air pollutant concentrations in Tianjin, China and mortality due to non-accidental general causes in cardiovascular, cardiopulmonary, respiratory and ischemic heart disease subcategories. Seasonal effects of air pollution were also found in this study for the city of São Paulo. Tianjin and São Paulo are classified as cities with high levels of air pollution (WHO, 2013). The difference of effects was explained by human activity patterns, which change depending on the season. Liu et al. (2012) also suggest that the difference of the pollutants' effects should be taken into account when we modelling mortality data explained by air pollution, which corroborates the results of Hagler et al. (2006) and Galindo et al. (2008). These authors found that the composition of pollutants is noted for variations in the spatial domain, which suggests that seasonal patterns should be examined specifically for each geographic region.

One of the limitations in this study was the lack of information on people's habits that might influence the occurrence of deaths, in order to better adjust the model.

4. CONCLUSIONS

Knowing the influence of air pollution on mortality in large urban centre is relevant because his allows planning better preventive policies. The relation between atmospheric pollutant concentration and deaths from cardiovascular illness is complex, due to the existence of a large numbers of contributing factors.

The presented method proved to be adequate for this kind of study, considering the characteristics of the historical data series and the aim of this research. In fact, the introduction of some variance-covariance structure in the correlated Poisson model adjustment process improved the estimation accuracy, which allowed concluding there are significant effects of the CO, SO_2, O_3 and PM_{10} pollutants to explain death, resulting in increases in the risks of people exposed to air pollution, of 3%, 6%, 4% and 9% respectively.

The model allowed reaching relevant results in the environmental context. Both the interpretation and the magnitude of the parameters must be considered, especially in a public health context, since any distortion can interfere with the planning of actions and the allocation of resources.

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