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1. INTRODUCTION

Atmospheric pollution has been considered as a serious public health issue, especially for more and more people living in the urban city. The level of city population in Brazil reached 87% by 2010 and the cities of the developing world will make up 81 percent of urban humanity (State of World Population, 2011).

Atmospheric pollution is a hazard factor for human health, even the level of air pollution is very low. The most susceptible people to air pollution are children (Braga et al, 1999; 2001; Lin et al., 1999) and the elderly (Atkinson et al., 2001; Martins et al., 2002; Schwartz et al., 1990; 1992). Many studies have reported that there are negative impacts on respiratory mortality and morbidity (Braga et al., 1999; 2001; Lin et al., 1999).

Surface ozone is a pollutant of growing concern in the world (World Health Organization, 2009). Children is the largest subgroup susceptible to surface ozone (World Health Organization, 2005), particularly in terms of respiratory diseases (Schwartz, 2004, Koren, 1995). However, there are relatively few studies assessing the effects of ozone on children and adolescents' respiratory morbidity.

Moreover, most studies assessing the health effects of ozone levels used relatively short timescales (lags) (Fusco et al., 2001; Galán et al., 2003). If the effects of ozone on morbidity/mortality were delayed or lasted for a longer period, using short lags would not exactly capture the effects of ozone. The other issue is that most studies use linear function to examine the effects of ozone on morbidity/mortality. The biological manifestations of the effects of pollution on health apparently display behavior that shows a gap between the individual's exposure to pollutants. This means that the

attendances / admissions observed on a particular day can be related to pollution of that day, as well as pollution observed in previous days. For a more precise definition of the model to be used, it is essential to determine a lag structure (lag) suitable. We chose to use the model distributed lags up to six days after exposure. Thus, using linear model can not reflect the true ozone-health relationship.

In this study, we aimed to explore the relationship between ozone and the respiratory hospital admissions in Campo Grande, Brazil. We also examined whether the ozone-morbidity relationship was non-linear; whether children and elderly were more sensitive to ozone air pollution; and whether effects of ozone on morbidity were delayed.

2. METHODS

2.1 Data collection

This study was conducted in Campo Grande, Brazil. Campo Grande city (20°27'16" S; 54°47'16" W, altitude 650 m) is sited on the Maracaju–Campo Grande plateau. The region is tropical with high temperatures predominating throughout the year. It has high rainfall and high relative humidity (Sant'Anna Neto et al., 2003).

We obtained data on health centers' records of out-patient visits from the Secretary for Municipal Health from January 2004 to 31 December 2008. Respiratory diseases were coded using the 9th Revised International Classification of Diseases (ICD-9: 460 to 519). We also stratified the respiratory morbidity by age (0-4, 5-60, and > 60 years).

We obtained the daily mean ozone concentration (O₃ in ppb) from 2004 to 2010. The

ozone pollution was measured at the monitoring station of the Physics Department of the Federal University of Mato Grosso do Sul. Ozone concentrations were recorded every 15 minutes, which were used to calculate daily mean concentrations.

We collected daily data on mean temperature, relative humidity from the EMPRAPA research station for beef production in Campo Grande.

2.2 Data analysis

A quasi-Poisson regression model with distributed lag non-linear model (DLNM) was used to examine the effects of ozone on morbidity. The quasi-Poisson function has the ability to adjust inference for over dispersion (Hardin & Hilbe, 2011).

The DLNM allows nonlinear function for exposure and lag to be modeled simultaneously in quite flexible ways (Gasparrini et al., 2010, Gasparrini & Armstrong, 2010). To examine the non-linear ozone-morbidity relationship, a DLNM was used for ozone with 5 degrees of freedom natural cubic spline, and 4 degrees of freedom natural cubic spline was used for lag up to 6 days.

We controlled for temperature and relative humidity using a DLNM with 5 degrees of freedom natural cubic spline for exposure (mean temperature and relative humidity) and 4 degrees of freedom natural cubic spline for lag up to 10 days. We controlled for day of the week using category variable. We controlled for seasonality and long-term trend using natural cubic spline with 7 degrees of freedom per year for time.

3. RESULTS

There were 26941 respiratory hospital admissions during the study period. The averages of O_3 were below the quality standards of ozone pollution (80 ppb) (Table 1). The average counts of daily admissions for respiratory diseases were: total admissions for respiratory diseases (11), 0-4 years of (5), 5-60 years (3), and > 60 years (3) (Table 1).

Figure 1 shows the time series of respiratory hospital admission, ozone and mean temperature. O_3 had a seasonal trend, with higher concentration in summer than winter. Respiratory hospital admissions were higher in winter than summer.

Table 1: Descriptive analysis of respiratory hospital admission, ozone, and weather conditions in Campo Grande, Brazil during 2008-2011

	Médium	D.P	Minimum	1 ^o quartil	Median	3 ^o quartil	Maximum
All years	11	3.30	2.00	8.00	10.00	12.00	23.00
0-4years	5	1.75	1.00	4.00	5.00	6.00	13.00
5-60 years	3	1.21	0.00	2.00	2.00	3.00	8.00
>60 years	3	1.07	0.00	2.00	3.00	3.00	7.00
Ozono	17.56	7.59	0.66	12.97	16.44	20.73	52.76
TEMPMED	23.50	3.51	7.00	22.10	24.20	25.73	30.81
relative humidity	66,06	16,12	19,16	55,00	67,81	78,83	98,00

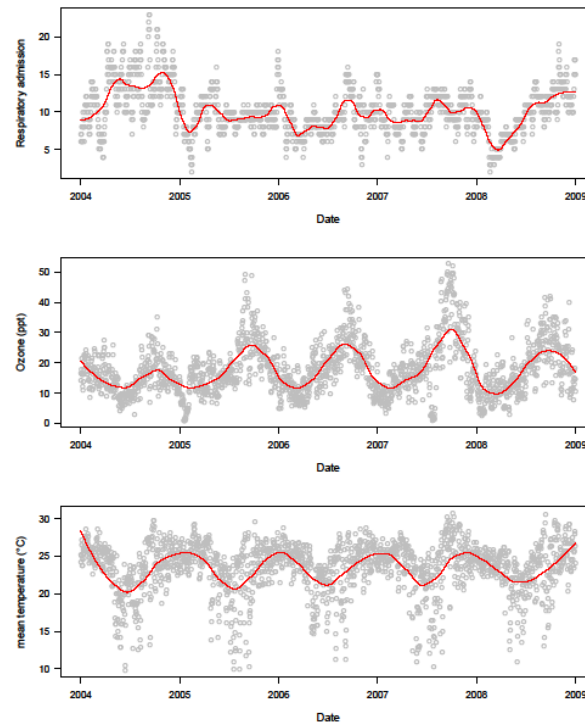


Figure 1: Time series of respiratory hospital admissions, ozone concentration (ppb) and mean temperature ($^{\circ}\text{C}$) during 2008-2011.

Figure 2 shows the relationship between ozone and respiratory hospital admission at lag 0-6 days. We found that the effects of ozone on respiratory hospital admission were non-linear, with a threshold at 13 ppb. The effects of ozone on children and elderly were high than people aged 5-60 years.

Table 2 shows the estimated relative risks corresponds to age group: all year risk with interval $\text{RR}=1.1079$; $\text{CI}:(1.0379 - 1.1826)$; risk of 0-4 years with a range of $\text{RR}=1.1296$; $\text{CI}:(1.0524 - 1.2125)$, 5-

60 years, risk with interval of $\text{RR}=1.014$; $\text{CI}:(0.9410 - 1.0928)$ and > 60 years with risk interval and 1.1546 (1.0406 and 1.2811).

Table 2 and Figure 3 show the relative risks of hospital admissions at 75% percentile of ozone distribution compared with 25% percentile along the lag days. Results show that the effects on hospitalizations were delayed by two days, and lasted for four days.

Table 2: Relative risk of respiratory hospital admissions at at 75% percentile of ozone distribution compared with 25% percentile along the lag days in Campo Grande, Brazil during 2008-2011

	All years	0-4 years	5-60 years	> 60 years
	RR-CI	RR-CI	RR-CI	RR-CI
lag 0	1.0035;(0.9758-1.0321)	1.0153;(0.9850-1.0466)	0.9775;(0.9465-1.0095)	1.0028;(0.9587-1.0488)
lag 1	1.0128;(0.9989-1.0270)	1.0191;(1.0039-1.0345)	0.9921;(0.9764-1.0080)	1.0188;(0.9965-1.0416)
lag 2	1.0119;(1.0046-1.0336)	1.0211;(1.0056-1.0369)	1.0031;(0.9868-1.0196)	1.0292;(1.0061-1.0530)
lag 3	1.0209;(1.0056-1.0365)	1.0209;(1.0043-1.0376)	1.0092;(0.9918-1.0269)	1.0320;(1.0073-1.0573)
lag 4	1.0196;(1.0068-1.0325)	1.0189;(1.0051-1.0328)	1.0115;(0.9970-1.0263)	1.0287;(1.0082-1.0496)
lag 5	1.0160;(1.0021-1.0302)	1.0157;(1.0006-1.0310)	1.0113;(0.9954-1.0274)	1.0215;(0.9992-1.0444)
lag 6	1.0114;(0.9883-1.0352)	1.0120;(0.9870-1.0376)	1.0097;(0.9832-1.0369)	1.0125;(0.9754-1.0509)

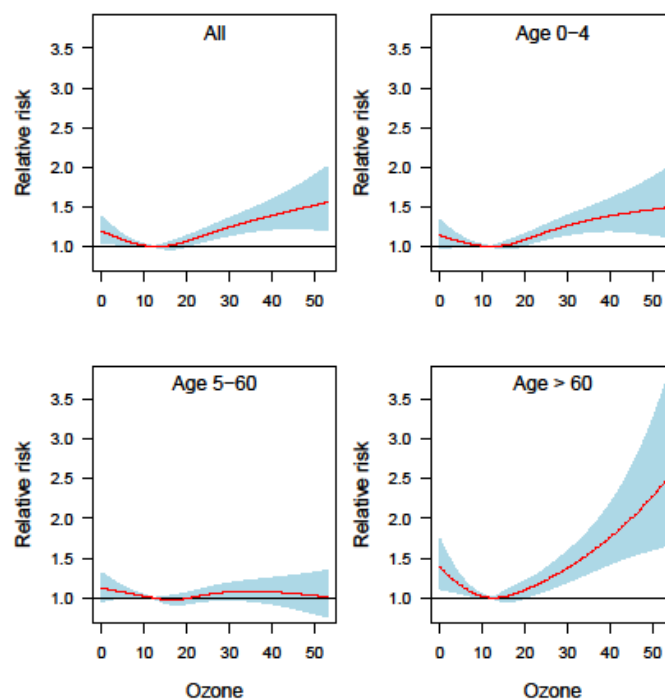


Figure 2: In the relationship between ozone and respiratory hospital admission in Campo Grande, Brazil during 2008-2011.

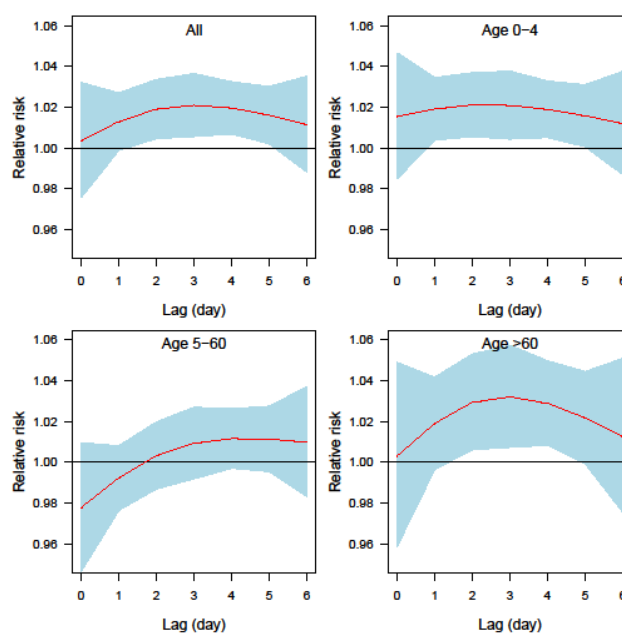


Figure 3: Relative risk of respiratory hospitalizations at 75% percentile of ozone distribution compared with 25% percentile along the lag days in Campo Grande, Brazil during 2008-2011.

4. DISCUSSION

The purpose of this study was to examine the effects of ozone on respiratory hospital admissions in Campo Grande, Brazil during 2008-2011. We found that the ozone-respiratory morbidity

relationship was non-linear. The effects of ozone on respiratory morbidity were delayed by two days and lasted for 4 days for all age groups except people aged 5-60 years. Children and elderly were much more vulnerable to ozone pollution than people aged 5-60 years.

The magnitude of the association ozone pollution and hospital admissions for respiratory disease was similar to studies conducted in San Paulo (Braga et al., 1999; Braga et al., 2001; Lin et al., 1999). This might be caused by that the source of zone pollutant in the two cities is almost the same: the mobile sources, mainly, and stationary sources (industries) and biomass burning in Campo Grande.

Ozone-related epidemiological studies generally assume a linear effect of ozone (Bell et al., 2005). However, Lefohn et al. reported a nonlinear relationship between ozone dose and pulmonary function (Lefohn et al., 2010). The lag effect of air pollutants is also considered a critical factor in health assessments. This study applied DLNM to calculate the nonlinear association and cumulative risks across lag days for air pollutants. The findings enable greater flexibility when presenting the nonlinear ozone exposure-response curve for outpatient visits for total RD.

We found children and elderly were much more sensitive to ozone pollution than adult. Children are highly susceptible to exposure to air pollutants. Minute ventilation is higher in children than in adults because children have higher basal metabolic rates and engage in more physical activity than do adults, as well as because children spend more time outdoors than do adults. On the basis of body weight, the volume of air passing through the airways of a child at rest is twice that of an adult under similar conditions. Pollutant-induced irritation producing a weak response in adults can result in significant obstruction in children. In addition, the fact that their immune system is not fully developed increases the possibility of respiratory infections (Künzli et al., 2010; Künzli, 2005; Salvi, 2007).

Elderly individuals are susceptible to the adverse effects of exposure to air pollutants because they have a less efficient immune system (immunosenescence) and a progressive decline in pulmonary function that can lead to airway obstruction and exercise limitation. There is decreased chest wall compliance and lung hyperinflation requiring additional energy

expenditure to perform respiratory movements, as well as functional decline of organ systems (Sharma & Goodwin, 2006).

Several mechanisms have been suggested to explain the adverse effects of air pollutants. The most consistent and most widely accepted explanation is that, once in contact with the respiratory epithelium, high concentrations of oxidants and pro-oxidants in environmental pollutants such as PM of various sizes and compositions and in gases such as O₃ and nitrogen oxides cause the formation of oxygen and nitrogen free radicals, which in turn induce oxidative stress in the airways. In other words, an increase in free radicals that are not neutralized by antioxidant defenses initiates an inflammatory response with release of inflammatory cells and mediators (cytokines, chemokines, and adhesion molecules) that reach the systemic circulation, leading to subclinical inflammation, which not only has a negative effect on the respiratory system but also causes systemic effects (Künzli et al, 2010; Künzli, 2005).

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