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Air pollution and hospital admissions and deaths due to respiratory infections in megacity of Tehran: A time series analysis

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ABSTRACT

Introduction: Air pollution is one of the main causes for the significant increase of respiratory infections in Tehran. In the present study, we investigated the associations between short-term exposure to ambient air pollutants with the hospital admissions and deaths.

Materials and methods: Health data from 39915 hospital admissions and 2459 registered deaths associated with these hospital admissions for respiratory infections were obtained from the Ministry of Health and Medical Education during 2014-2017. We used the distributed lag non-linear model (DLNM) for the analyses.

Results: There was a statistically positive association between $PM_{2.5}$ and AURI in the age group of 16 years and younger at lags 6 (RR 1.31; 1.05-1.64) and 7 (RR 1.50; 1.09-2.06). AURI admissions was associated with O_3 in the age group of 16 and 65 years at lag 7 with RR 1.13 (1.00-1.27). ALRI admissions was associated with CO in the age group of 65 years and older at lag 0 with RR 1.12 (1.02-1.23). PM_{10} was associated with ALRI daily hospital admissions at lag 0 for males. ALRI admissions were associated with NO_2 for females at lag 0. There was a positive association between ALRI deaths and SO_2 in the age group of 65 years and older at lags 4 and 5 with RR 1.04 (1.00-1.09) and 1.03 (1.00-1.07), respectively.

Conclusion: Exposure to outdoor air pollutants including PM_{10}, $PM_{2.5}$, SO_2, NO_2, O_3, and CO was associated with hospital admissions for AURI and ALRI at different lags. Moreover, exposure to SO_2 was associated with deaths for ALRI.

Introduction

Given the rapid urbanization and industrialization globally, and consequently, increases in energy consumption and emissions from industries and transportation, air pollution has become a main environmental challenge [1-3]. Exposure

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to outdoor air pollution can cause a variety of adverse health effects, especially on the respiratory outcomes such as reduction of lung function, asthmatic attacks, exacerbation of chronic obstructive pulmonary disease (COPD), and acute respiratory infection (ARI) (including acute upper respiratory infection (AURI) and acute lower respiratory infection (ALRI)), airway inflammation, increased hospital admissions, and deaths due to respiratory diseases [4-9]. The role of outdoor air pollution in enhancing respiratory diseases (including hospital admission and mortality) has been reported in several investigations [10-13]. Respiratory infections are one of the most important reasons for hospital admissions and mortality, especially among children [14-16].

Exposure to air pollutants can lead to oxidative stress due to the formation of free radicals that can harm the respiratory system, resulting in less resistance to infections [17]. Particulate pollutants can also transport viruses and bacteria [18]. Most previous studies on the association between air pollution and respiratory diseases, especially respiratory infections, have focused on children and fewer studies have been done on adults. Acute respiratory infections are common diseases among adults that considerable part of the burden of diseases is attributed to them [19]. Iran and Tehran (as its capital city) globally rank among the most polluted countries and cities with air pollution being a serious environmental issue. Thus, it is expected that air pollution plays an important role in morbidity from various respiratory diseases including ALRI and AURI [3]. The present study was performed to assess the associations between outdoor criteria air pollutants ($PM_{2.5}$, PM_{10}, NO_2, SO_2, CO, O_3) and hospital admission and deaths due to these diseases in Tehran.

Materials and methods

Data

The present study was conducted in Tehran, the capital of Iran. Tehran is facing serious air pollution problems. The study period is from 2014 to 2017. Air pollutant data were obtained from measuring stations for which at least 75% of the hourly concentration values for PM_{10}, $PM_{2.5}$, NO_2, SO_2, CO, and more than 50% of the hourly concentration values for O_3 were available. As exposure metrics, twenty-four hour average values of PM_{10}, $PM_{2.5}$, and SO_2 were calculated and maximum 8-h averages were calculated for CO and O_3 for any one day. The maximum value during any one day were used as the exposure metric for NO_2. Daily averaged meteorological parameters for relative humidity, wind speed, and temperature was obtained from the Mehrabad Airport meteorological station.

Information on the numbers of hospital admissions and deaths due to respiratory infections was collected from the Ministry of Health based on ICD-10 codes. Respiratory infections included acute upper respiratory infections (AURI) (ICD-10: J00-J06) and acute lower respiratory infections (ALRI) (ICD-10: J09-J18, J20-J22).

Statistical analysis

In this time-series study, we examined the associations between ambient gaseous or particulate matter pollutants and hospital admission/deaths for respiratory infections with a distributed lag nonlinear model. This model by defining a cross basis function simultaneously determines non-linear effects and lag effects. In the cross-basis functions we set the degrees of freedom in the lag-day and concentration of outdoor air pollutant using a trial-and-error approach.

Outdoor air pollutants were PM_{10}, $PM_{2.5}$, NO_2, SO_2, O_3, and CO. Meteorological variables (relative humidity, pressure, wind speed and temperature), and respiratory admissions/deaths were used in the model. For the number of degrees of freedom, we considered a range of 1 to 7. To determine the minimum Q-AIC, the model was fited for the probability of each df values [20, 21]. The degrees of freedom for temperature values and lag-day were 7 and 3, for relative humidity values and lag-day were 7 and 3, and $PM_{2.5}$ concentration and lag-day were 6 and 3, and other air pollutants PM_{10}, $PM_{2.5}$, NO_2, SO_2, O_3, CO concentration and lag-day were 3 and 4.

In the basic model, cross-basis functions were entered for the outdoor air pollutant (PM_{10}, $PM_{2.5}$, NO_2, SO_2, O_3, CO) and meteorological variables including temperature and relative humidity. Also, we used a natural spline function with 3 degrees of freedom for pressure and wind speed. A natural spline with 7 degrees of freedom were used for time. Holidays and day of week were considered as binary variable and nominal variable, respectively. The final model was selected by comparing the AIC of the models [20, 21].

$$\text{Log}(E(Y_t)) = \alpha + \beta_1(PM_{10}) + \beta_2(PM_{2.5}) + \beta_3(NO_2) + \beta_4(SO_2) + \beta_5(O_3) + \beta_6(CO) + \beta_7(Temp) + \beta_8(RH_t,lag) + \delta{*}DOW + \varepsilon{*}Holiday + ns(Time_t, df_1) + ns(wind, df_2) \quad (1)$$

where t represents the number of the observation; (Y_t) is the number of hospital admissions or death on day t; $E(Y_t)$ equals to daily hospital admissions or death on day *t*; the cross-basis functions such as relative humidity, air pollutants, and temperature; α equals to intercept; β represents the regression coefficient of air pollutants; df1 and df_2 denotes the degrees of freedom for time and wind speed in natural spline function, respectively; DOW equals to day of the week; holiday is the public holidays; δ and ε are the regression coefficients for DOW and holidays.

In order to examine the collinearities among the variables for each outcome in the model, the variance inflation factor (VIF) was calculated. The analyses were performed using R (version 3.6.1) and *dlnm* package. We denote the results as the relative risk (RR, 95% confidence interval) for daily hospital admissions and deaths for the respiratory infections per unit increment in air pollutants concentration.

Results and discussion

The associations between outdoor air pollution and hospital admissions and deaths for respiratory infections were evaluated. Table 1 summarizes the numbers of daily hospital admissions and deaths, the outdoor air pollutant concentrations, and meteorological variables. There were 32198 ALRI and 7717 AURI hospital admissions, and 2443 ALRI deaths during 2014-2017.

Table 1. Daily hospital admissions and deaths counts from respiratory infections, air pollutants and meteorological data for the period 2014-2017

	Count	Mean	SD*	Min	Q1	Median	Q_3	Max
Hospital admissions								
ALRI	32198	26.4	17.2	2	15	22	32	114
AURI	7717	6.6	8.6	0	3	5	8	251
Deaths								
ALRI	2443	2	1.9	0	1	2	3	12
AURI	16	0.01	0.1	0	0	0	0	1
Outdoor air pollutants (μg/m^3)	Total Days							
PM_{10}	1220	88.4	37	17.1	64.2	84	104.6	334.1
$PM_{2.5}$	1220	30.2	12.1	6.1	22.4	27.8	35	90.9
NO_2	1219	115.1	34.8	31.1	92.6	110.7	134.3	341.9
SO_2	1198	51.6	47.9	9.1	22.7	35.8	56.9	435.2
O_3	1147	61.9	26.8	7.7	39.7	59.4	79.6	140.4
CO	1215	3909.8	1150.6	1747.9	3074.2	3672.8	4528.2	9868.1
Meteorological variables	Total Days							
Relative humidity (%)	1218	32.3	16.9	8	18.3	28.6	42.6	90.5
Wind speed (m/s)	1219	3.2	1.4	0.37	2.3	3	3.9	10.1
Temperature (°C)	1219	19.7	10.1	-4.1	10.6	21.4	29.2	36.2

*SD: standard deviation

Table 2. Relative risk (95%CIs) of respiratory infections hospital admissions per 10 µg/m³ increases in PM_{10}, $PM_{2.5}$, NO_2, SO_2, O_3 and 1000 µg/m³ CO by age subgroups

		ALRI			AURI		
	lag	Age ≤16	Age 16-65	Age ≥65	Age ≤16	Age 16-65	Age ≥65
PM_{10}	0	1.02 (0.99-1.06)	**1.04 (1.00-1.09)**	0.99 (0.95-1.02)	1.01 (0.95-1.07)	1.06 (0.97-1.14)	1.08 (0.93-1.26)
	1	**1.02 (1.00-1.04)**	1.00 (0.98-1.03)	0.98 (0.96-1.01)	0.98 (0.94-1.02)	1.05 (0.99-1.10)	0.95 (0.86-1.05)
	2	**1.02 (1.00-1.04)**	0.99 (0.96-1.01)	0.98 (0.96-1.00)	0.97 (0.94-1.01)	1.04 (0.99-1.08)	0.96 (0.88-1.04)
	3	**1.02 (1.00-1.04)**	0.98 (0.96-1.00)	0.98 (0.96-1.00)	0.97 (0.94-1.01)	1.03 (0.98-1.07)	1.02 (0.93-1.10)
	4	1.01 (0.99-1.03)	0.98 (0.96-1.00)	0.98 (0.96-1.00)	0.97 (0.99-1.00)	1.02 (0.98-1.07)	1.04 (0.96-1.13)
	5	1.00 (0.98-1.01)	0.98 (0.96-1.00)	0.98 (0.97-1.00)	0.96 (0.98-0.99)	1.02 (0.98-1.06)	1.04 (0.97-1.12)
	6	0.99 (0.97-1.00)	0.98 (0.96-1.00)	0.99 (0.97-1.01)	0.95(0.92-0.98)	1.02(0.98-1.06)	1.02(0.95-1.10)
	7	0.97 (0.95-1.00)	0.99 (0.95-1.02)	0.99 (0.96-1.03)	0.94 (0.90-0.99)	1.02 (0.95-1.09)	0.99 (0.88-1.13)
$PM_{2.5}$	0	0.97 (0.80-1.18)	1.06 (0.83-1.36)	0.99 (0.80-1.22)	1.21 (0.82-1.78)	1.02 (0.60-1.75)	0.98 (0.39-2.48)
	1	0.89 (0.79-1.00)	0.97 (0.83-1.13)	0.94(0.83-1.07)	1.08 (0.85-1.36)	0.78 (0.56-1.08)	0.81 (0.46-1.41)
	2	0.84 (0.75-0.93)	0.91 (0.80-1.05)	0.92 (0.82-1.03)	1.01 (0.82-1.25)	0.65 (0.48-0.87)	0.70 (0.42-1.15)
	3	0.83 (0.74-0.93)	0.90 (0.78-1.04)	0.91 (0.80-1.03)	1.01 (0.80-1.26)	0.61 (0.45-0.84)	0.64(0.37-1.10)
	4	0.85 (0.76-0.95)	0.92 (0.80-1.06)	0.91(0.81-1.03)	1.06 (0.86-1.31)	0.65(0.48-0.87)	0.61(0.37-1.02)
	5	0.90 (0.82-1.00)	0.97 (0.86-1.10)	0.93 (0.84-1.04)	1.16 (0.96-1.41)	0.75 (0.58-0.98)	0.61 (0.39-0.96)
	6	0.98 (0.87-1.09)	1.04 (0.90-1.20)	0.96 (0.85-1.08)	**1.31(1.05-1.64)**	0.91 (0.68-1.23)	0.63 (0.38-1.03)
	7	1.06 (0.91-1.25)	1.12 (0.91-1.36)	0.99 (0.83-1.18)	**1.50(1.09-2.06)**	1.14(0.74-1.75)	0.65(0.32-1.33)
NO_2	0	**1.03 (1.00-1.06)**	0.98 (0.95-1.02)	0.99 (0.95-1.02)	1.03 (0.98-1.09)	1.00 (0.93-1.07)	1.00 (0.89-1.16)
	1	0.98 (0.96-1.00)	0.97 (0.95-1.00)	1.00 (0.98-1.03)	0.97 (0.93-1.00)	1.04 (0.99-1.09)	1.06 (0.97-1.16)
	2	0.98 (0.96-1.00)	0.98 (0.96-1.00)	1.01 (0.98-1.03)	0.97 (0.94-1.00)	1.01 (0.97-1.05)	1.04 (0.97-1.12)
	3	1.00 (0.99-1.02)	0.99 (0.97-1.00)	1.00 (0.98-1.02)	0.99 (0.97-1.02)	0.96 (0.93-0.99)	1.01 (0.95-1.07)
	4	**1.01 (1.00-1.03)**	0.99 (0.98-1.00)	1.00 (0.98-1.01)	1.00 (0.98-1.03)	0.94 (0.91-0.98)	0.99 (0.92-1.06)
	5	**1.01 (1.00-1.02)**	0.99 (0.98-1.01)	0.99 (0.98-1.01)	1.00 (0.98-1.03)	0.95 (0.92-0.98)	0.98 (0.93-1.04)
	6	1.00(0.99-1.01)	0.99 (0.98-1.01)	0.99 (0.98-1.01)	1.00 (0.97-1.02)	0.97 (0.94-1.00)	0.99 (0.93-1.05)
	7	0.98 (0.96-1.01)	0.99 (0.96-1.01)	0.99 (0.97-1.02)	0.98 (0.95-1.03)	1.00 (0.94-1.05)	0.99 (0.90-1.10)
SO_2	0	0.98 (0.95-1.02)	0.99 (0.95-1.02)	1.00 (0.96-1.03)	0.99 (0.93-1.05)	0.93 (0.86-1.02)	0.88 (0.75-1.03)
	1	1.00 (0.97-1.02)	1.00 (0.97-1.02)	0.99 (0.97-1.02)	1.00 (0.96-1.04)	0.97 (0.91-1.03)	0.98 (0.89-1.08)
	2	1.00 (0.98-1.02)	1.01 (0.99-1.03)	1.00 (0.98-1.02)	1.02 (0.98-1.05)	0.99 (0.94-1.04)	0.99 (0.91-1.08)
	3	0.99 (0.97-1.01)	**1.01 (1.00-1.03)**	**1.01 (1.00-1.03)**	**1.03(1.00-1.06)**	0.99 (0.95-1.04)	0.96 (0.89-1.03)
	4	0.99 (0.97-1.01)	1.01 (0.99-1.03)	**1.01 (1.00-1.03)**	**1.03 (1.00-1.07)**	1.00 (0.95-1.05)	0.96 (0.89-1.03)
	5	1.00 (0.98-1.01)	1.00 (0.99-1.02)	**1.01 (1.00-1.03)**	1.02 (0.99-1.05)	1.01 (0.97-1.06)	0.98(0.92-1.05)
	6	1.00 (0.99-1.02)	0.99 (0.97-1.01)	1.01 (0.99-1.02)	1.01 (0.98-1.04)	1.02 (0.98-1.07)	1.02 (0.95-1.09)
	7	1.01 (0.98-1.04)	0.97 (0.95-1.00)	1.00 (0.97-1.02)	0.99 (0.94-1.04)	1.03 (0.96-1.11)	1.07 (0.96-1.19)
O_3	0	0.93 (0.88-0.99)	0.99 (0.92-1.06)	0.95 (0.89-1.02)	1.01 (0.90-1.13)	1.07 (0.92-1.24)	1.30 (0.98-1.71)
	1	0.98 (0.94-1.02)	0.99 (0.94-1.05)	1.00 (0.95-1.05)	0.99 (0.91-1.07)	1.00 (0.91-1.11)	1.02 (0.85-1.23)
	2	0.98 (0.96-1.03)	1.00 (0.96-1.05)	1.00 (0.96-1.04)	0.97 (0.90-1.03)	0.96 (0.88-1.05)	0.96 (0.82-1.13)
	3	0.99 (0.96-1.02)	1.01 (0.98-1.05)	0.99 (0.96-1.03)	0.95 (0.90-1.01)	0.95 (0.88-1.02)	1.00 (0.87-1.14)
	4	0.98 (0.95-1.02)	1.02 (0.98-1.06)	0.99 (0.96-1.03)	0.95 (0.89-1.01)	0.96 (0.89-1.05)	1.03 (0.89-1.20)
	5	0.98 (0.95-1.00)	1.02 (0.98-1.05)	1.00 (0.97-1.03)	0.95 (0.91-1.00)	1.00 (0.94-1.07)	1.06 (0.94-1.20)
	6	0.97 (0.94-1.00)	1.01 (0.97-1.05)	1.01 (0.97-1.04)	0.96 (0.91-1.02)	1.06 (0.99-1.14)	1.09 (0.96-1.24)
	7	0.96 (0.92-1.01)	1.00 (0.94-1.06)	1.02 (0.96-1.08)	0.97 (0.89-1.07)	**1.13 (1.00-1.27)**	1.12 (0.90-1.40)
CO	0	0.91 (0.84-1.00)	0.98 (0.88-1.09)	**1.12 (1.02-1.23)**	0.92 (0.79-1.08)	**1.29 (1.04-1.60)**	1.33 (0.90-1.96)
	1	1.02 (0.96-1.09)	1.01 (0.94-1.09)	1.00 (0.93-1.06)	0.97 (0.87-1.09)	0.89 (0.77-1.04)	**1.41 (1.07-1.85)**
	2	1.01 (0.96-1.06)	1.02 (0.96-1.09)	0.97 (0.92-1.03)	0.98 (0.89-1.07)	0.89(0.79-1.02)	1.19 (0.95-1.50)
	3	0.95 (0.91-1.00)	1.02 (0.97-1.08)	0.98 (0.94-1.03)	0.96 (0.89-1.04)	1.02 (0.91-1.13)	0.97 (0.81-1.17)
	4	0.93 (0.89-0.98)	1.02 (0.96-1.08)	1.00 (0.95-1.05)	0.96 (0.88-1.05)	1.04 (0.93-1.18)	0.89 (0.73-1.09)
	5	0.94 (0.90-0.98)	1.01(0.96-1.06)	1.01(0.96-1.05)	0.97 (0.90-1.04)	0.98 (0.89-1.09)	0.90 (0.76-1.07)
	6	0.97 (0.93-1.01)	1.00 (0.95-1.05)	1.01 (0.97-1.05)	0.98 (0.91-1.05)	0.87 (0.79-0.96)	0.97 (0.82-1.15)
	7	1.00 (0.94-1.07)	0.99 (0.91-1.07)	1.01 (0.94-1.09)	0.99 (0.88-1.12)	0.75 (0.64-0.89)	1.08 (0.80-1.44)

Table 3. Relative risk (95%CIs) of respiratory infections hospital admissions per 10 μg/m³ increases in PM_{10}, $PM_{2.5}$, NO_2, SO_2, O_3 and 1000 μg/m³ CO by sex subgroups

		ALRI			AURI		
	lag	Female	Male	Total	Female	Male	Total
PM_{10}	0	1.00 (0.97-1.04)	**1.02 (1.00-1.05)**	1.01 (0.99-1.04)	1.04 (0.96-1.14)	1.02 (0.97-1.07)	1.04 (0.99-1.10)
	1	1.01 (0.99-1.03)	1.00 (0.98-1.02)	1.00 (0.99-1.02)	1.05 (0.99-1.11)	0.98 (0.95-1.01)	1.01 (0.97-1.04)
	2	0.99 (0.98-1.02)	0.99 (0.98-1.01)	1.00 (0.98-1.01)	1.02 (0.97-1.07)	0.98 (0.95-1.01)	1.00 (0.97-1.03)
	3	0.99 (0.97-1.01)	1.00 (0.98-1.01)	0.99 (0.98-1.01)	0.99 (0.95-1.04)	1.00 (0.97-1.03)	1.00 (0.97-1.03)
	4	0.98 (0.97-1.00)	1.00 (0.98-1.01)	0.99 (0.98-1.00)	0.98 (0.94-1.03)	1.00 (0.97-1.03)	1.00 (0.97-1.03)
	5	0.98 (0.97-1.00)	0.99 (0.98-1.01)	0.99 (0.98-1.00)	0.98 (0.95-1.02)	0.99 (0.97-1.02)	0.99 (0.97-1.02)
	6	0.98 (0.97-1.00)	0.99 (0.98-1.00)	0.99 (0.98-1.00)	1.00 (0.96-1.04)	0.98 (0.95-1.01)	0.99 (0.96-1.01)
	7	0.98 (0.96-1.01)	0.98 (0.96-1.01)	0.98 (0.97-1.00)	1.02 (0.95-1.09)	0.96 (0.92-1.01)	0.98 (0.94-1.02)
$PM_{2.5}$	0	1.00 (0.83-1.22)	1.19 (0.86-1.19)	1.01 (0.89-1.15)	0.88 (0.48-1.60)	1.28 (0.92-1.79)	1.14 (0.80-1.63)
	1	0.97 (0.86-1.09)	0.90 (0.82-1.00)	0.93 (0.86-1.01)	0.79 (0.55-1.13)	1.05 (0.86-1.29)	0.93 (0.75-1.15)
	2	0.95 (0.85-1.05)	0.83 (0.76-0.91)	0.88 (0.82-0.95)	0.75 (0.54-1.03)	0.91 (0.76-1.10)	0.80 (0.66-0.97)
	3	0.94 (0.84-1.06)	0.82 (0.74-0.90)	0.87 (0.80-0.94)	0.76 (0.54-1.07)	0.87 (0.71-1.05)	0.77 (0.63-0.95)
	4	0.95 (0.85-1.06)	0.84 (0.77-0.92)	0.89 (0.82-0.95)	0.83 (0.60-1.14)	0.88 (0.73-1.06)	0.81 (0.67-0.98)
	5	0.97 (0.88-1.07)	0.90 (0.83-0.97)	0.93 (0.87-0.99)	0.95 (0.71-1.26)	0.95 (0.80-1.12)	0.90 (0.76-1.07)
	6	1.00 (0.89-1.12)	0.98 (0.89-1.08)	0.99 (0.92-1.07)	1.12 (0.80-1.56)	1.05 (0.87-1.27)	1.05 (0.86-1.28)
	7	1.03 (0.87-1.21)	1.08 (0.95-1.24)	1.06 (0.95-1.11)	1.34 (0.82-2.17)	1.19 (0.91-1.56)	1.25 (0.94-1.65)
NO_2	0	**1.03 (1.00-1.06)**	0.99 (0.96-1.01)	1.01 (0.99-1.03)	1.06 (0.98-1.14)	1.00 (0.95-1.05)	1.02 (0.97-1.07)
	1	0.98 (0.96-1.00)	0.98 (0.97-1.00)	0.98 (0.97-1.00)	1.01 (0.96-1.06)	1.00 (0.97-1.03)	1.01 (0.98-1.04)
	2	0.98 (0.97-1.00)	0.99 (0.98-1.01)	0.99 (0.98-1.00)	0.99 (0.95-1.03)	0.99 (0.96-1.02)	0.99 (0.97-1.02)
	3	1.00 (0.98-1.01)	1.00 (0.99-1.01)	1.00 (0.99-1.01)	0.98 (0.95-1.02)	0.98 (0.96-1.00)	0.98 (0.96-1.00)
	4	1.00 (0.99-1.02)	1.00 (0.99-1.02)	1.00 (0.99-1.01)	0.99 (0.95-1.03)	0.97 (0.95-0.99)	0.97 (0.95-1.00)
	5	1.00 (0.99-1.02)	1.00 (0.99-1.01)	1.00 (0.99-1.01)	1.00 (0.96-1.03)	0.97 (0.95-0.99)	0.97 (0.96-0.99)
	6	0.99 (0.98-1.01)	1.00 (0.99-1.01)	1.00 (0.99-1.00)	1.01 (0.97-1.04)	0.97 (0.95-0.99)	0.98 (0.96-1.00)
	7	0.98 (0.96-1.01)	0.99 (0.97-1.01)	0.99 (0.97-1.00)	1.02 (0.96-1.08)	0.98 (0.94-1.01)	0.99 (0.96-1.03)
SO_2	0	0.97 (0.94-1.00)	1.00 (0.97-1.03)	0.99 (0.97-1.01)	0.95 (0.87-1.03)	0.98 (0.93-1.03)	0.96 (0.91-1.01)
	1	0.99 (0.97-1.01)	1.00 (0.99-1.02)	1.00 (0.98-1.01)	0.99 (0.93-1.05)	0.99 (0.95-1.03)	0.99 (0.96-1.03)
	2	1.00 (0.98-1.01)	1.01 (0.99-1.02)	1.00 (0.99-1.02)	1.01 (0.96-1.06)	1.00 (0.97-1.04)	1.01 (0.98-1.04)
	3	1.00 (0.98-1.01)	**1.01 (1.00-1.02)**	1.00 (0.99-1.02)	1.01 (0.96-1.05)	1.01 (0.98-1.04)	1.01 (0.99-1.04)
	4	1.00 (0.98-1.02)	1.01 (0.99-1.02)	1.00 (0.99-1.02)	1.01 (0.96-1.06)	1.02 (0.99-1.05)	1.02 (0.99-1.05)
	5	1.00 (0.99-1.02)	1.00 (0.99-1.02)	1.00 (0.99-1.01)	1.00 (0.96-1.05)	1.02 (0.99-1.04)	1.01 (0.99-1.04)
	6	1.01 (0.99-1.02)	1.00 (0.98-1.01)	1.00 (0.99-1.01)	1.00 (0.95-1.04)	1.02 (0.99-1.04)	1.01 (0.99-1.04)
	7	1.01 (0.98-1.03)	1.01 (0.97-1.01)	1.00 (0.98-1.01)	0.99 (0.93-1.06)	1.02 (0.97-1.06)	1.01 (0.97-1.05)
O_3	0	0.92 (0.87-0.98)	0.97 (0.93-1.03)	0.95 (0.91-0.99)	0.96 (0.82-1.12)	1.09 (0.99-1.21)	1.05 (0.95-1.16)
	1	0.97 (0.93-1.01)	1.00 (0.97-1.04)	0.99 (0.96-1.02)	0.97 (0.87-1.08)	1.01 (0.95-1.08)	1.01 (0.94-1.08)
	2	0.99 (0.96-1.03)	1.01(0.98-1.04)	1.00 (0.98-1.02)	0.96 (0.87-1.05)	0.98 (0.92-1.03)	0.97 (0.92-1.03)
	3	0.99 (0.96-1.02)	1.00 (0.98-1.03)	1.00 (0.98-1.02)	0.95 (0.88-1.03)	0.97 (0.92-1.02)	0.95 (0.91-1.00)
	4	0.99 (0.96-1.03)	1.00 (0.97-1.03)	1.00 (0.97-1.02)	0.95 (0.87-1.04)	0.98 (0.93-1.03)	0.96 (0.91-1.01)
	5	0.99 (0.96-1.02)	1.00 (0.97-1.02)	0.99 (0.98-1.02)	0.97 (0.90-1.04)	1.00 (0.95-1.04)	0.98 (0.94-1.03)
	6	0.99 (0.96-1.02)	0.99 (0.97-1.02)	0.99 (0.97-1.02)	0.99 (0.91-1.06)	1.02(0.97-1.07)	1.02 (0.97-1.07)
	7	0.99 (0.94-1.04)	0.99 (0.95-1.03)	0.99 (0.95-1.01)	1.01 (0.89-1.15)	1.05 (0.97-1.14)	1.06 (0.98-1.15)
CO	0	0.92 (0.87-0.98)	0.97 (0.93-1.03)	0.95 (0.91-0.99)	0.96 (0.82-1.12)	1.09 (0.99-1.21)	1.05 (0.95-1.16)
	1	0.97 (0.93-1.01)	1.00 (0.97-1.04)	0.99 (0.96-1.02)	0.97 (0.87-1.08)	1.01 (0.95-1.08)	1.01 (0.94-1.08)
	2	0.99 (0.96-1.03)	1.00 (0.98-1.04)	1.00 (0.98-1.02)	0.96 (0.87-1.05)	0.98 (0.92-1.03)	0.97(0.92-1.03)
	3	0.99 (0.96-1.02)	1.01 (0.98-1.03)	1.00 (0.98-1.02)	0.95 (0.88-1.03)	0.97 (0.92-1.02)	0.95 (0.91-1.00)
	4	0.99 (0.96-1.03)	1.00 (0.97-1.03)	1.00 (0.97-1.02)	0.95 (0.87-1.04)	0.98 (0.93-1.03)	0.96 (0.91-1.01)
	5	0.99 (0.96-1.02)	1.00 (0.97-1.02)	0.99 (0.98-1.01)	0.97 (0.90-1.04)	1.00 (0.95-1.04)	0.98 (0.94-1.03)
	6	0.99 (0.96-1.02)	0.99 (0.97-1.02)	0.99 (0.97-1.01)	0.99 (0.91-1.06)	1.02 (0.97-1.07)	1.02 (0.97-1.07)
	7	0.99 (0.94-1.04)	0.99 (0.95-1.03)	0.99 (0.95-1.02)	1.01 (0.89-1.15)	1.05 (0.97-1.14)	1.06 (0.98-1.15)

Our results showed a positive relationships between outdoor air pollutants and hospital admissions for ALRI and AURI (Table 2). We found a significant association between ALRI admissions with PM_{10} in both ages of 16 years and younger and, between 16 and 65 years at different lags. PM_{10} was associated with ALRI daily hospital admissions at lag 0 with RR 1.02 (1.00-1.05) for males. Also, there were statistically positive association between $PM_{2.5}$ and AURI admissions in the age group of 16 years and younger at lags 6 (RR 1.31; 1.05-1.64) and 7 (RR 1.50; 1.09-2.06). Fig. 1 shows the associations of PM_{10} concentrations with ALRI hospital admissions by sex and age subgroups for each of the 7 lag-days. The highest association was seen in females aged≤16 years at lag 2. In females aged 16 to 65, the highest association was observed at lag 0. For males, the highest association were in the age groups of ≤16 years and 16 to 65 year olds at lag 0. Also, in total the highest association was observed in both age groups of 16 years and younger and, between 16 and 65 years at lag 0. Fig. 2 presents the associations of PM_{10} concentrations with AURI hospital admissions by sex and age subgroups for each of the 7 lag-days. The highest association was observed in females aged ≤16 years at lag 0. Also, in the age group of females from 16 to 65, the highest association was observed at lag 1. For males, the highest association was seen in 16 to 65 year olds and 65 years and older at lag 4 and 0, respectively. Also, the highest total association was observed in both the 16 to 65 year olds and 65 years and older at lag 0. Other studies have reported similar results.

Some researchers observed statistically significant associations between PM_{10} concentrations and respiratory admissions with estimated increase of 0.7% (1.007; 95% CI: 1.002-1.013) [22]. The findings of other researchers showed that increasing the air quality index increased the risk of respiratory infections [23]. In a study, it was found air pollutant impacts on hospital admissions for upper respiratory tract infections from pneumonia that were consistent with our results [13]. In a study conducted in Vietnam to assess the acute effects of outdoor air pollutants on the lower respiratory infections, a positive effect of PM_{10} on the rate of admissions for pneumonia was observed [24].

We found that exposure to increased $PM_{2.5}$ (10 $\mu g/m^3$) concentrations led to higher rates of hospital admissions due to AURI, different from the results of a study by some researchers [25]. One reason might be that the upper respiratory tract is probably more sensitive to air pollution and lower concentrations of pollutants will reach the lower respiratory tract [26]. It seems that a common response to air pollutants and pathogens causing infection is that specific types of signaling proteins direct the cellular pathways that signal inflammation mediated by cytokines and lead to the hypothesis of alteration of innate immune response to infection due to air pollutants [27]. In our study, males were more likely to be affected by particulate pollutants (for each 10 $\mu g/m^3$ increase) in all age subgroups and no effects of $PM_{2.5}$ were observed in females (Table 3). This difference might be because males spend more time outdoors [1].

We obtained evidence of the effects of NO_2 on increased rates of hospital admissions due to ALRI. This result was similar but lower than the observations obtained by researchers in another study [13]. They observed that each interquartile range increase (31 $\mu g/m^3$) in NO_2 concentration resulted in 7.4% (9.5%CI: 3.2, 11.9) increase in upper respiratory tract infection [13]. Some researchers reported that in a study in Ho Chi Minh City (HCMC), there were higher admissions due to lower respiratory infections (ER= 8/50% (95%CI 0.8-16.79)) associated with increased NO_2 concentrations [28]. NO_2 irritates the respiratory system and can cause significant health effects including increased risk of respiratory infections, damage to lung, and death [29]. High concentrations of oxidants and pro-oxidants in nitrogen dioxide lead to the formation of oxygen and nitrogen free radicals. An increase in these radicals initiates an inflammatory response by releasing inflammatory cells and mediators (cytokines, chemokines, etc.) that reach the circulatory system, cause subclinical inflammation that negatively affects the respiratory system [30].

For SO_2, we observed that an increment in SO_2 concentration caused higher rates of ALRI and AURI admissions. Similar findings were reported in previous studies [22, 31]. For example, many researchers earned highest relative risk for respiratory admissions due to SO_2 (1.123; 95% CI: 1.045- 1.207) [31]. In Lanzhou, researchers found a 0.5% increase in total respiratory diseases risk per unit increase of SO_2. Also, they observed that each interquartile range increase in SO_2 (69 μg/m^3) associated in 6.9% (95%CI: 1.5, 26.0) increase in upper respiratory tract infection [13].

For CO, we found that there were significant associations between CO concentrations and increasing risk for admissions for respiratory infections. Similarly, the positive associations were observed between ozone and increasing rates of hospital admissions due to AURI. Our results showed that young females and elderly males were more susceptible to O_3. In a study, it was found that the ≥65 year age group were most vulnerable to air pollutants with no significant differences between males and females [32]. The cumulative effects of air pollutants on respiratory infections hospital admissions are reported in Supplementary Material section
S1-S4.

Our study indicated that there was a statistically significant association between SO_2 and total ALRI admissions at lag 5 (RR 1.02; 1.00-1.05). Significant associations were found between ALRI disease and SO_2 in people 65 years and older at lags 4 and 5 with RR 1.04 (1.00-1.09) and 1.03 (1.00-1.07), respectively. Also, the strongest association between ALRI deaths and the PM_{10} concentrations of was seen at lag 4. The highest associations between ALRI deaths and the concentrations of $PM_{2.5}$ and SO_2 were observed at lag 0 (Fig. 3). Previously, a time series analysis conducted in China reported that exposure to elevated concentrations of SO_2 (10 μg/m^3) increased the mortality risk (1.25%; 95% CI: 0.78- 1.73) [33]. SO_2 is an irritant in the respiratory tract. It is soluble in water resulting in the formation of sulfurous and sulfuric acids and when inhaled, is readily absorbed within airways [34]. In limited exposures to this gas, acute impacts (including decreases in function of lung, cough) are observed. Inhalation of high levels of SO_2 can seriously damage airways [29, 35].

This study had limitations. First, we used data from one meteorological station for the daily average meteorological variables. We only had access to the average daily temperatures but not to the daily maximum and minimum temperatures. Second, we used the average pollutant concentrations recorded from multiple monitoring stations in Tehran as the individual subject's exposures since we did not have access to the address of residence or workplace.

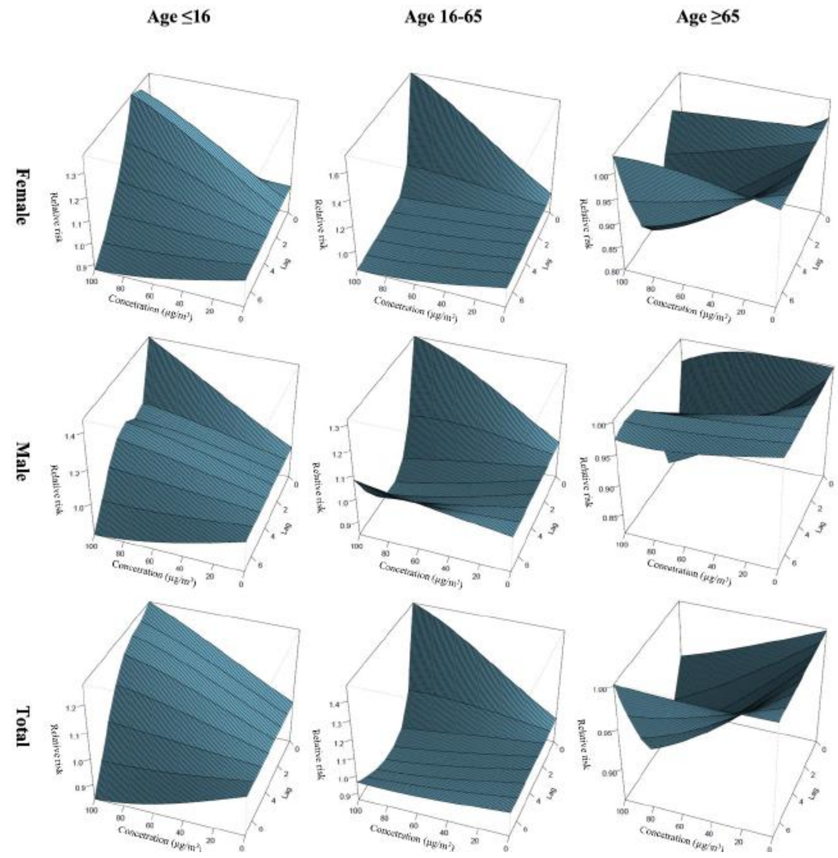

Fig. 1. Association of PM_{10} concentrations with ALRI hospital admissions by sex and age subgroups at 7 lag-days

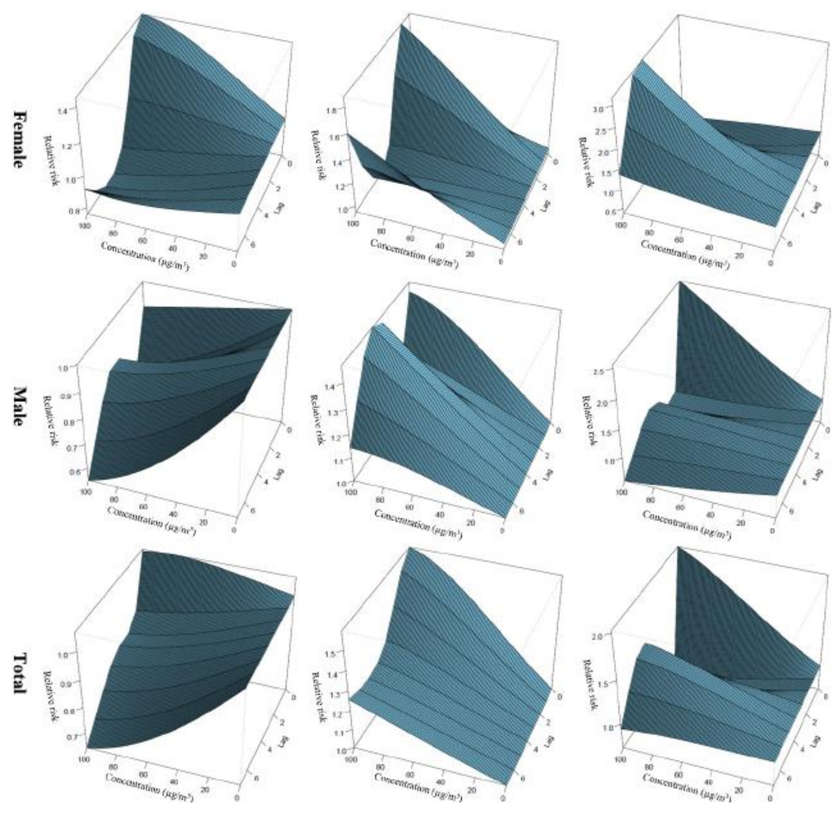

Fig. 2. Association of PM_{10} concentrations with AURI hospital admissions by sex and age subgroups at 7 lag-days

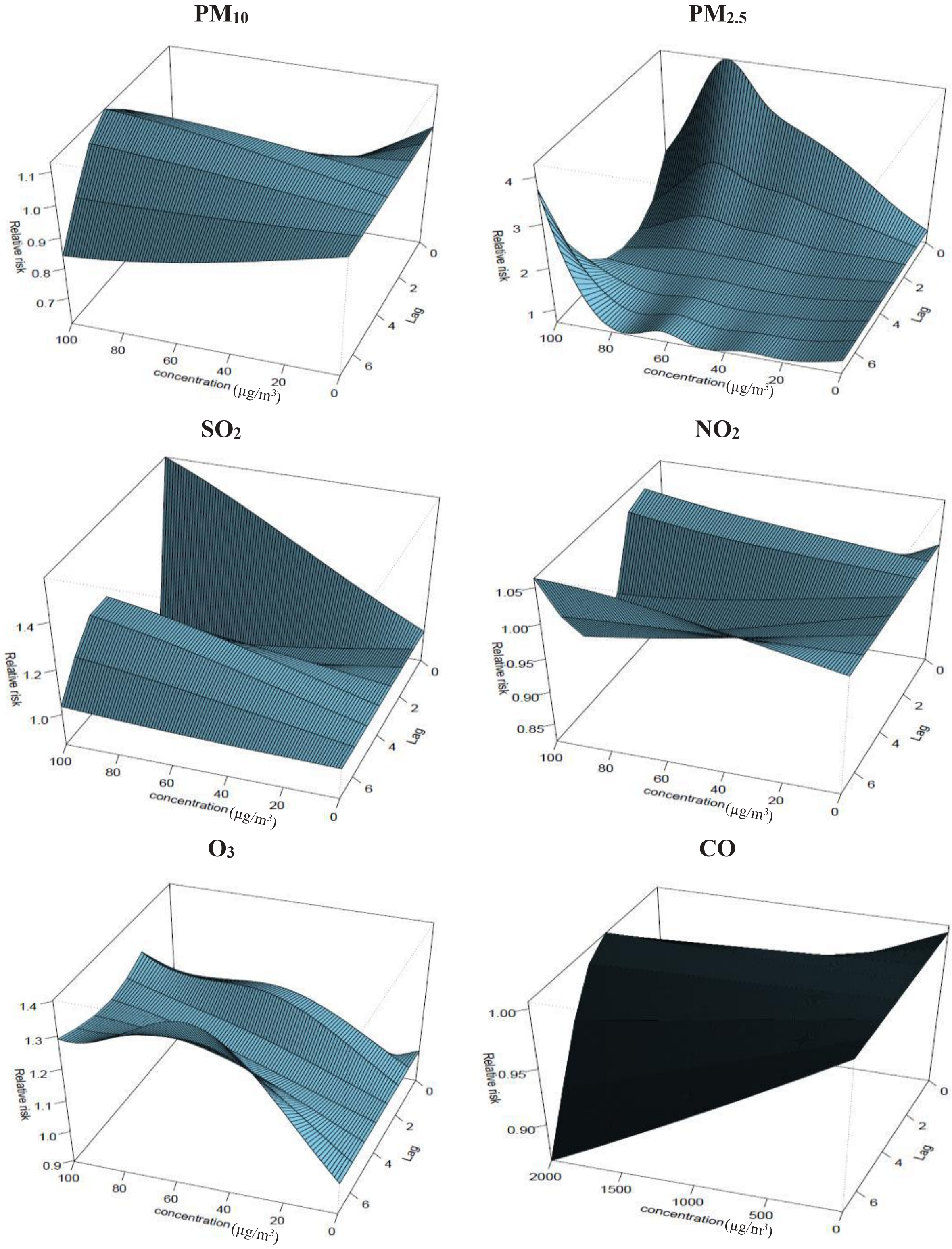

Fig. 3. Association of outdoor air pollutants with ALRI deaths at 7 lag-days

Table 4. Relative risk (95%CIs) of ALRI deaths per 10 µg/m³ increase of SO_2 concentration by age subgroups

	lag	Age ≤16	Age 16-65	Age ≥65	Total
ALRI	0	0.74 (0.13-3.93)	1.06 (0.94-1.19)	1.05 (0.97-1.13)	1.05 (0.99-1.11)
	1	0.92 (0.34-2.50)	0.98 (0.90-1.06)	0.97 (0.92-1.02)	0.97 (0.93-1.02)
	2	0.95 (0.41-2.21)	0.95 (0.89-1.03)	0.99 (0.94-1.03)	0.98 (0.94-1.01)
	3	0.92 (0.41-2.08)	0.96 (0.90-1.02)	1.03 (0.99-1.07)	1.01 (0.98-1.04)
	4	0.94 (0.37-2.42)	0.97 (0.91-1.04)	**1.04 (1.00-1.09)**	1.02 (0.99-1.06)
	5	1.00 (0.43-2.30)	0.99 (0.94-1.06)	**1.03 (1.00-1.07)**	**1.02 (1.00-1.05)**
	6	1.10 (0.46-2.61)	1.02 (0.96-1.08)	1.01 (0.97-1.04)	1.01 (0.98-1.04)
	7	1.21 (0.30-4.82)	1.05 (0.95-1.15)	0.98 (0.92-1.03)	1.00 (0.95-1.05)
	0-1	0.68 (0.09-5.04)	1.04 (0.90-1.20)	1.02 (0.94-1.11)	1.04 (0.96-1.10)
	0-2	0.65 (0.06-6.34)	1.00(0.83-1.19)	1.01(0.91-1.13)	1.01(0.92-1.10)
	0-3	0.60 (0.04-7.51)	0.96 (0.78-1.18)	1.05 (0.93-1.18)	1.02 (0.93-1.13)
	0-4	0.57 (0.03-10.40)	0.94 (0.74-1.20)	1.10 (0.96-1.26)	1.05 (0.94-1.18)
	0-5	0.57 (0.02-16.00)	0.94 (0.71-1.23)	1.14 (0.98-1.33)	1.08 (0.95-1.23)
	0-6	0.63 (0.01-24.24)	0.90 (0.71-1.30)	1.16 (0.98-1.37)	1.10 (0.96-1.27)
	0-7	0.77 (0.01-44.42)	1.01 (0.72-1.42)	1.14 (0.94-1.37)	1.11 (0.95-1.30)

Conclusion

In this study, we observed statistically significant associations between ambient air pollutants in Tehran and daily hospital admissions and deaths from respiratory infections including separate groups by sex and age. The health impacts of particulate pollutants, NO_2, and SO_2 leading to increased hospital admissions from ALRI were similar in females and males. Hospital admissions from respiratory infections were most associated with the highest concentration of PM_{10} on the event day. Furthermore, ALRI deaths were associated with SO_2 in the age group ≥65 years. Thus, the high level of pollution in the metropolis of Tehran and the unfavorable respiratory outcomes make it necessary to pay significant attention to the importance of reducing pollutants and thereby improving public health.

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Competing interests

There is no actual or potential conflict of interest among the authors.

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Ethical consideration

Ethical issues have been completely observed by the authors.

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