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Short-term effects of air pollution on respiratory mortality in Ahvaz, Iran

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Abstract

Background: Urban air pollutants may affect respiratory mortality. This study was conducted to investigate this effect in Ahvaz, one of the most polluted cities in the world.

Methods: The impact of 7 major air pollutants including O_3, PM_{10}, NO_2, CO, and SO_2 were evaluated on respiratory mortality in different gender and age groups using a quasi-Poisson, second degree polynomial constrained, distributed lag model, with single and cumulative lag structures adjusted by trend, seasonality, temperature, relative humidity, weekdays, and holiday. Data were analyzed using the dlnm package in R x64 3.2.5 software. Significance level was set at less than 0.05.

Results: In adjusted models, for each IQR increase of O_3 in the total population, the risk ratio (RR) for respiratory deaths in 0 to 14- day lags was, respectively, 1.009 (95% CI:1.001-1.016) and 1.009 (95% CI:1.002-1.017), and it was 1.021 (95% CI: 1.002-1.040) in cumulative 0 to 14- day lags. For PM_{10}, in the total population and in adjusted models after 0 to 14- day lags and in cumulative lags of 0 to 14 for an IQR increase in the mean concentration of PM_{10}, the RR for respiratory deaths increased significantly and was, respectively, 1.027 (95% CI:1.002-1.051), 1.029 (95% CI:1.006-1.052), and 1.065 (95% CI:1.005-1.128). NO_2 showed a significant association with respiratory deaths only in the 18 to 60 year- old age group and in 9- day lags (RR= 1.318, 95% CI:1.002-1.733). Finally, the results showed that for an IQR increase in the mean concentration of CO and SO_2, the adjusted RR for respiratory deaths in 9- day lags in the total population was, respectively, RR= 1.058 (95% CI:1.008-1.111) and 1.126 (95% CI:1.034-1.220).

Conclusion: Air pollution in Ahvaz is probably causing increased respiratory mortality.

Keywords: Short-term effects, Air pollution, Respiratory mortality, Ahvaz

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Introduction

Clean air is considered as a basic requirement of human health and well-being, and air pollution is a major threat to global health (1-3). Air pollution is growing in large cities and is a great concern for the public health (4, 5). In the Global Burden of Disease Study in 2012, air pollution is one of the 5 major causes of premature deaths and is responsible for 3.4 million premature deaths worldwide(4, 6). Also, it has the first rank among environmental risk factors for adverse health effects (7). Epidemiological studies in different parts of the world have confirmed the acute effects of short- term exposure to air pollution, such as bronchoconstriction and increased asthma symptoms, and chronic effects including chronic lung disease and premature mortality (8-11). These studies provide evidence for the negative effects of urban air pollution on health and a better understanding of biological mechanisms; and in addition to creating an important field of research, they have allowed decision- makers to understand the effects of pollutants and the benefits that can be achieved by control measures (1).

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↑What is "already known" in this topic:
Air pollution is growing in large cities and it has become a great concern for the public health. Most studies on the health effects of air pollution have been conducted in North America and Europe. To date, no quantitative study has been conducted on the effect of air quality on respiratory mortality in Ahvaz.

→What this article adds:
The results indicated that O_3, PM_{10}, NO_2, CO, and SO_2 air pollutants in Ahvaz were associated with respiratory mortality on the same day and multi-day lags.

Most studies on the health effects of air pollution have been conducted in North America and Europe (12-18). However, the effect of air pollution on mortality might be the result of differences in population susceptibility and air pollutants' concentration and components. As a result, there is significant uncertainty in pooled risk estimations (19).

Conducting research in different countries and cities is vital for making local policies. Previous studies have mainly focused on the effects of air pollution on total deaths, and only a limited number of studies have addressed the effect of individual factors, such as age and gender that may be important confounders in the relationship between air pollution and mortality (20, 21).

Ahvaz, the capital of Khuzestan province, is Iran's second largest city in area after Tehran, and it is Iran's fifth populated city. The amount of pollution in this city has increased day by day and has become more severe. In 2011, according to the World Health Organization, Ahvaz was the most polluted city in the world, based on the annual average PM_{10}, which was 372 μg/m^3(22, 23). In Ahvaz, the rate of respiratory problems has increased sharply in recent years, and as of 2011, a new respiratory health crisis occurred in this city, which was repeated in the later years. In 2011, following the first rainfall, the city hospitals faced an increased number of patients with respiratory symptoms, particularly shortness of breath and coughing. This unusual and unexpected number of patients increased gradually, so that within a maximum of 10 hours after the start of a rainfall, 20 000 patients in 2013, 10 400 patients in 2014, and 26 400 patients in 2015 visited the hospitals' emergency departments (24, 25).

The most important causes of particulate matter air pollution in Ahvaz are its geographic location and topography, proximity to the Saudi desert, and emerging sources of dust in the neighboring countries. Other sources are transportation and existence of industries including oil, natural gas, and steel that have exposed this city to natural and man-made air pollution (26, 27).

To date, no quantitative study has been conducted on the effect of air quality on respiratory mortality in Ahvaz, and the only available knowledge is through studies performed using the Air Q model to estimate the effects of air pollution on respiratory and cardiovascular diseases (28-30).

In the present study, the relationship between major air pollutants (O_3, PM_{10}, NO_2, CO and SO_2) and respiratory mortalities on a daily basis was evaluated in different age and gender groups and up to 14-day lags after exposure to air pollutants.

Methods

Health Outcome Data

This study was based on data recorded from March 2008 until March 2015 from Ahvaz, Iran. Daily data about mortality due to respiratory diseases in different age and gender subgroups were obtained from Ahvaz City Health Authority.

Exposure Assessment

Ambient air pollution data were inquired from Khuzestan Province Environmental Protection Agency for 7 major pollutants, which included particulate matter less than 10 μm (PM_{10}), nitrogen dioxide (NO_2), carbon monoxide (CO), sulfur dioxide (SO_2), and ozone (O_3). PM_{10} was the only type of particulate matter recorded at the air quality monitoring stations.

There are 4 air quality monitoring stations in Ahvaz including the Environmental Protection Agency station, Naderi Square station, University Square station, and Meteorological organization station. According to Environmental Protection Agency experts, the air quality monitoring station locations were representative of ambient air quality of the whole city (22).

Data from Ahvaz EPA showed that there is variation across the city with regards to the concentration of air pollutants based on hour, day, week, and month, but not based on location (23).

Studies (31, 32) have shown that meteorological parameters affect respiratory mortality; thus, to control their confounding effect, data on meteorological parameters, such as average temperature and relative humidity, were inquired on a daily basis from the Bureau of Meteorology of Khuzestan Province. The daily data of respiratory mortality was matched with pollutants and meteorological parameters.

City Presentation

Ahvaz, with an area of 8152 square kilometers, is the capital city of Khuzestan province and is located between 31º20′ N and 48°40′ E (28). According to 2011 census, 286 032 households and 1 056 589 people live in Ahvaz (33) (Fig. 1).

Statistical Analysis

The association between respiratory mortalities with mean daily air pollution was analyzed using a quasi-Poisson, second degree polynomial constrained, distributed lag model using single and cumulative lag structures, adjusted by trend, seasonality, temperature, relative humidity, weekdays, and holidays. Single day lag effects of air pollutant exposure were estimated for 1 to 14- day lags. Distributed lag models (DLM) with 0 to 14- day lags

*Fig. 1.*Location of Ahvaz in Iran

were also used to estimate respiratory mortalities with potential cumulative exposure effects. Analysis was done for total deaths, age, and gender subgroups. Previous research (8, 9, 34) has shown that the effects of air pollutants are not the same in different age and sex groups.

Analyses were performed using the dlnm package in R x64 3.2.5 software. We calculated lags only up to 14 days, as we were looking for the more acute effects of air pollution on respiratory mortalities. Significance level was set at less than 0.05.

Results

The total number of respiratory mortalities between March 2008 and March 2015 in Ahvaz (2557 days) was 1824 cases, with an average of almost 22 deaths per month. The number of respiratory mortality was higher in males and in the group older than 60 years compared to females, 18 to 60 years' age group, and younger than 18 group (Table 1). Respiratory disease mortality in all people, males, and over 60 year-old group showed a significant increase from 2009 (Fig. 2).

The most major air pollutants in Ahvaz were particulate matter smaller than 10 micrometers; moreover, the daily average of PM_{10} during 2008 and 2015 was 237.2 $\mu g/m^3$, ranging from 25.0 to 4498.0. The average rate of this pollutant has been higher than the acceptable level of 100 $\mu g/m^3$. Other descriptive statistics about respiratory mortality, air pollution, and climate parameters are presented in Table 1.

The results of single lag and cumulative lag models on the relationship between respiratory death and air pollutants in the total population and in gender and age subgroups for each IQR increase in average pollutant concentration are presented in Tables 2 and 3 and Fig. 3.

In the adjusted models in the total population for each IQR increase of O_3, which was about 72.7$\mu g/m^3$, the risk ratio for respiratory deaths in 0 to 14- day lags was 1.009 (95% CI:1.001-1.016) and 1.009 (95% CI:1.002-1.017), respectively; and in cumulative 0 to 14- day lags was 1.021 (95% CI: 1.002-1.040), indicating that for a IQR increase in the mean concentration of O_3, the risk of respiratory deaths increases by 2% up to 14 days after exposure to O_3.

O_3 also showed a significant relationship in population subgroups. In the adjusted models in 8- day lags for an IQR increase in the mean concentration of O_3, the risk ratio for respiratory deaths significantly increased in females (RR = 1.019, 95% CI:1.007-1.030) and in those over the age of 60 (RR = 1.011, 95% CI: 1.001-1.022).

Table 1. Number of respiratory deaths and descriptive indices of air pollutants and climate factors in Ahvaz from March 2008 to March 2015

Number of respiratory deaths	> 60 years (%)	18 to 60 years (%)	< 18 years (%)	Males (%)	Females (%)	Overall (%)	
	1180.0(64.7%)	448.0(24.6%)	196.0(10.7%)	1106.0(60.6%)	718.0(39.4%)	1824.0 (100%)	
Variable (Mean per day)	Mean±SE	Minimum	Maximum	25% quartile	Median	75% quartile	Interquartile range
O_3 (ppb)	24.2 ± 18.1	3.0	661.0	18.0	22.0	28.0	10.0
PM_{10} (μ g/m^3)	237.2 ± 289.8	25.0	4498.0	119.2	162.5	249.5	130.3
NO_2 (ppb)	26.4 ± 27.6	1.0	720.0	12.0	21.0	34.0	22.0
CO (ppb)	1141.3 ± 1244.3	100.0	11900.0	500.0	900.0	1300.0	800.0
SO_2 (ppb)	18.6 ± 30.6	1.0	1416.0	10.0	17.0	24.0	14.0
Temperature (° C)	26.7 ± 9.1	11.6	39.5	25.5	27.1	27.8	2.3
Relative humidity (%)	43.1 ± 15.8	19.0	77.0	40.3	41.0	45.9	5.6
Total rainfall (mm)	14.0 ± 23.4	0.0	113.0	11.8	2.4	16.2	4.4
Total sunshine (hours)	256.4 ± 62.6	144.0	374.0	247.7	253.2	263.9	16.2
Total evaporation (mm)	264.7 ± 161.3	41.0	541.0	237.8	255.2	291.8	54.0
Wind speed (m⁄s)	11.5 ± 5.3	7.0	44.0	11.4	10.0	11.9	0.5
Wind direction (º)	227.2 ± 82.6	42.0	350.0	213.4	270.0	236.2	22.8

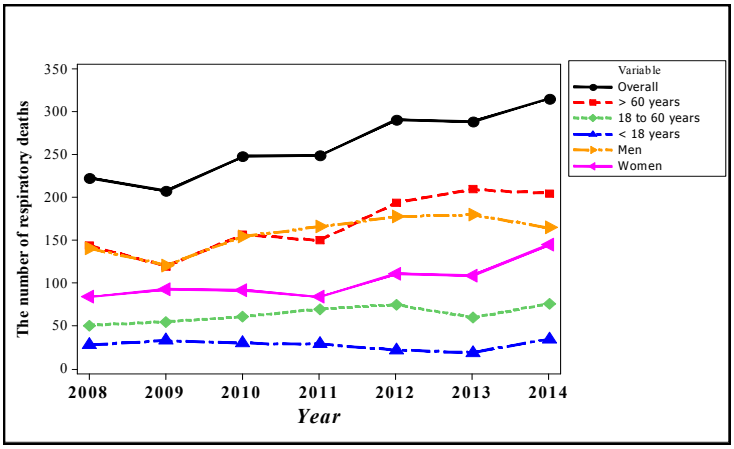

Fig. 2. The trend of respiratory disease mortality from March 2008 to March 2015

*Table 2.*Risk ratio (95% CIs) of respiratory deaths for each IQR increase in pollutants in single and cumulative lag structure models (overall, Males, females)

Variable	Pollutant ($\mu g/m^3$)	Lag 0	Lag 1	Lag 2	Lag 3	Lag 0 to 14	Other Single-Lag
Overall	O_3	1.009 (1.001-1.016)**	0.997 (0.987-1.007)	1.001 (0.991-1.012)	1.001 (0.992-1.010)	1.021 (1.002-1.040)**	lag14 1.009 (1.002-1.017)**
	PM_{10}	1.027 (1.002-1.051)**	0.991 (0.962-1.021)	1.003 (0.974- 1.033)	1.002 (0.975-1.030)	1.065 (1.005-1.128)**	lag14 1.029(1.006-1.052)**
	NO_2	0.993 (0.978-1.008)	1.008 (0.997-1.020)	0.986 (0.963-1.009)	1.001 (0.986-1.017)	0.971 (0.928-1.015)	---
	CO	0.987 (0.947-1.030)	1.009 (0.960-1.060)	0.997 (0.944-1.052)	0.992 (0.940-1.048)	0.979 (0.954-1.005)	lag9 1.058(1.008- 1.111)**
	SO_2	1.007 (0.922-1.1005)	0.950 (0.843-1.077)	0.987 (0.8741-1.113)	1.067 (0.968-1.177)	0.977 (0.931-1.025)	lag9 1.126(1.034-1.220)**
Males	O_3	0.987 (0.961 -1.014)	1.005 (0.992- 1.018)	0.986 (0.954- 1.021)	0.992 (0.966-1.021)	0.950 (0.893-1.011)	---
	PM_{10}	1.019 (0.987-1.052)	1.011 (0.974- 1.047)	0.976 (0.936 -1.018)	0.998 (0.963-1.035)	1.029 (0.956-1.109)	---
	NO_2	1.062 (0.860-1.311)	1.041 (0.852- 1.271)	1.043 (0.854 -1.275)	1.001 (0.821-1.220)	1.080 (0.912-1.280)	---
	CO	1.001 (0.948-1.057)	0.998 (0.937-1.063)	1.007 (0.940-1.078)	0.978 (0.911-1.049)	0.966 (0.933-0.999)	lag9 1.073(1.012-1.137)
	SO_2	1.0101 (0.907-1.125)	0.928 (0.792-1.087)	0.988 (0.841-1.162)	1.108 (0.983-1.249)	1.008 (0.952-1.067)	lag9 1.146(1.046-1.257)
Females	O_3	1.000 (0.983-1.017)	1.009 (0.992-1.027)	0.992 (0.969-1.016)	1.008 (0.993-1.023)	0.904 (0.800-1.020)	lag8 1.019(1.007-1.030)
	PM_{10}	1.032 (0.995-1.070)	0.967 (0.919-1.017)	1.028 (0.987-1.070)	1.013 (0.972-1.056)	1.101 (1.006-1.204)**	lag8 1.037(1.003-1.071)** lag14 1.036(1.002-1.070)**
	NO_2	0.963 (0.752- 1.233)	1.069 (0.856-1.335)	1.1422 (0.910-0.432)	0.939 (0.745-1.185)	1.099 (0.903 -1.339)	---
	CO	0.971 (0.911 -1.035)	1.032 (0.956-1.114)	0.973 (0.893-1.059)	1.024 (0.944-1.111)	0.997 (0.959-1.037)	---
	SO_2	1.021 (0.875-1.192)	0.973 (0.794-1.192)	0.976 (0.806-1.182)	1.022 (0.862-1.213)	0.934 (0.861-1.013)	---

**P-value is significant at less than 0.05.

Based on the results for PM_{10} in the total population and in adjusted models in 0 to 14- day lags and in cumulative lags of 0 to 14, for an IQR increase in the mean concentration of PM_{10}, which was about 237.3$\mu g/m^3$, the risk ratio for respiratory deaths increased significantly and was, respectively, 1.027 (95% CI: 1.002-1.051), 1.029 (95% CI: 1.006-1.052), and 1.065 (95% CI:1.005-1.128). Also, in females, PM_{10} showed significant associations with respiratory deaths in 8- day (RR = 1.037, 95% CI = 1.003-1.071), 14- day (RR = 1.036, 95% CI = 1.002-1.070), and cumulative 0 to 14 day lags (RR = 1.101, 95% CI = 1.006-1.204). Moreover, PM_{10} showed significant associations with respiratory deaths in under 18 age group in 4- day lags (RR = 1.070, 95% CI = 1.004-1.140), in 18 to 60 age group in 5- day lags (RR = 1.044, 95% CI = 1.002 - 1.088), and in over 60 age group in 14- day lags.

The NO_2 pollutant showed a significant association with respiratory deaths only in 18 to 60 age group and in 9- day

*Table 3.*Risk ratio (95% CIs) of respiratory deaths for each IQR increase in pollutant in single and cumulative lag structure (< 18 years, 18 to 60 years, > 60 years)

Variable	Pollutant ($\mu g/m^3$)	Lag 0	Lag 1	Lag 2	Lag 3	Lag 0 to 14	Other single-lag
< 18 years	O_3	0.995(0.917-1.078)	0.993(0.913-1.080)	0.988(0.932-1.049)	0.993(0.936-1.053)	0.872 (0.721-1.056)	---
	PM_{10}	1.006(0.925 -1.094)	0.983(0.890-1.085)	1.029(0.941-1.126)	0.972(0.876-1.079)	0.935 (0.774-1.128)	lag4 1.070(1.004-1.140)**
	NO_2	1.450 (0.943-2.230)	0.962 (0.614-1.509)	1.356 (0.849-2.165)	0.692 (0.414-1.158	0.926 (0.626-1.371)	---
	CO	0.986 (0.886 -1.098)	1.027 (0.904-1.1667)	0.950 (0.817-1.105)	0.960 (0.836-1.103)	1.071 (1.007-1.140)	---
	SO_2	1.102 (0.960 -1.265)	0.822 (0.636-1.064)	0.987 (0.767-1.272)	1.067 (0.872-1.306)	0.953(0.862-1.054)	---
18 to 60 years	O_3	0.994 (0.958-1.032)	0.994 (0.942-1.046)	0.976 (0.909-1.050)	1.014 (0.998-1.033)	0.866 (0.731-1.026)	---
	PM_{10}	1.033 (0.985-1.083)	0.986 (0.929-1.045)	0.996 (0.935-1.060)	1.023 (0.973-1.077)	1.105 (0.989-1.234)	lag5 1.044(1.002 -1.088)**
	NO_2	0.963 (0.685-1.354)	1.031 (0.750-1.418)	1.064 (0.781-1.448)	0.940 (0.690-1.281)	1.068 (0.820-1.392)	lag9 1.318(1.002-1.733)**
	CO	0.932 (0.845-0.027)	1.028 (0.926-1.141)	1.027 (0.916-1.151)	0.965 (0.863-1.079)	0.981 (0.930-1.035)	---
	SO_2	1.102 (0.960-1.265)	0.822 (0.636-1.063)	0.988 (0.767-1.272)	1.068 (0.872-1.306)	0.953 (0.862-1.054)	---

**P-value was significant at less than 0.05.

Table 3. Cntd

> 60 years	O_3	0.996 (0.982-1.009)	1.010 (0.998-1.021)	0.990 (0.969-1.012)	0.991 (0.969-1.012)	0.978 (0.932-1.026)	lag8 1.011(1.001- 1.022)**
	PM_{10}	1.025 (0.994-1.057)	0.994 (0.956-1.033)	1.003 (0.967-1.040)	0.998 (0.963-1.034)	1.060 (0.984-1.141)	lag14 1.037(1.009- 1.066)**
	NO_2	1.002 (0.815-1.232)	1.060 (0.879-1.279)	1.086 (0.900-1.310)	1.034 (0.858-1.245)	1.130 (0.957-1.333)	---
	CO	1.007 (0.955-1.062)	1.002 (0.939-1.068)	0.996 (0.931-1.067)	1.012 (0.9432-1.085)	0.946 (0.912-0.982)	lag9 1.067(1.004-1.138)**
	SO_2	0.968 (0.856-1.093)	0.993 (0.855-1.156)	0.996 (0.861-1.152)	1.074 (0.951-1.213)	0.990 (0.933-1.050)	lag9 1.165(1.063 -1.276)**

**P-value was significant at less than 0.05

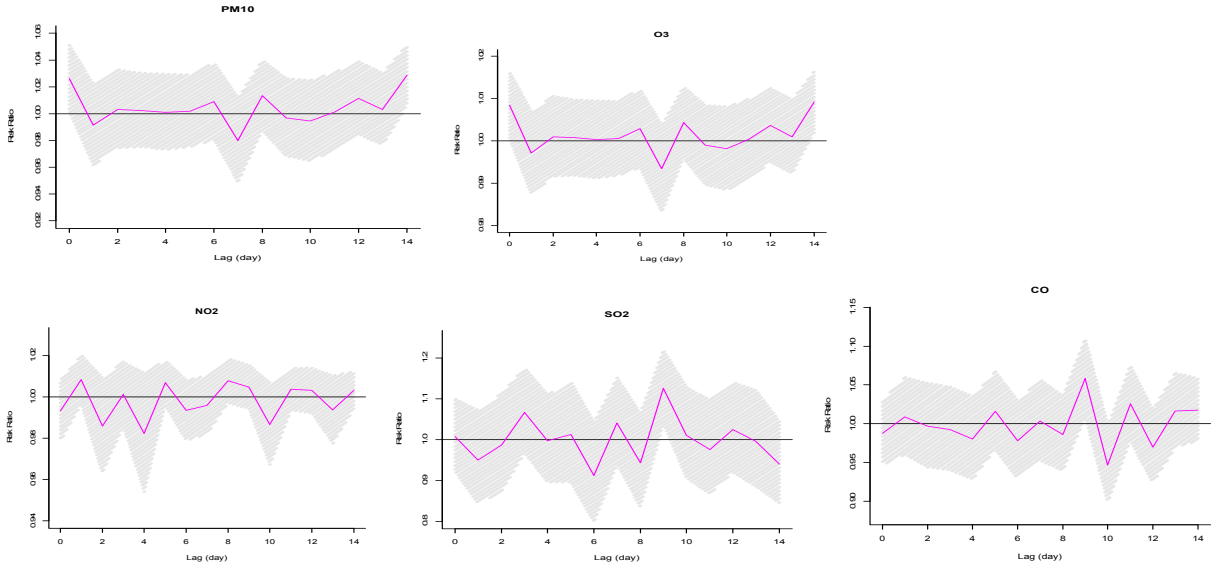

*Fig. 3.*Risk ratio (95% CIs) of respiratory deaths for each IQR increase in pollutant in single 0 to 14- day lag in the total population

lags; and for an IQR increase in the mean concentration of NO_2,which was about 61.3µg/m^3, RR was 1.318 (95% CI: 1.002-1.733).

The results indicated that for an IQR increase (about 1.12µg/m^3) in the mean concentration of CO, the adjusted RR for respiratory deaths in 9- day lags in the total population was 1.058 (95% CI:1.008- 1.111), it was 1.073 (95% CI:1.012-1.137) in males, and 1.067 (95% CI:1.004-1.138) in over 60 age group. Also, the association between the mean CO concentration and respiratory deaths in cumulative 0 to 14 lags was significant in the population under 18 years (RR = 1.071, 95% CI: 1.007-1.140).

In the adjusted model, in 9- day lags, for an IQR increase in the concentration of SO_2, which was about 62.2µg/m^3, the adjusted RR for respiratory deaths in the total population, males, and the over 60 age group was, respectively, 1.126 (95% CI: 1.034-1.220), 1.146 (95% CI: 1.046-1.257), and 1.165 (95% CI: 1.063 -1.276). (Tables 2, 3, and Fig. 3).

Discussion

Air pollution is one of the important problems of large industrial cities. In Iran, there is evidence about the relationship between air pollutants and deaths from cardiovascular and respiratory diseases in Kerman, Shiraz, and Arak (8, 34-36). However, no similar study was conducted in Ahvaz. The present study was conducted to estimate the acute effects of air pollutants (O_3, PM_{10}, NO_2, CO, and SO_2) on respiratory mortalities.

The major air pollutant in Ahvaz was particulate matter smaller than 10 micrometers, and the daily average of PM_{10} during 2008 and 2015 was higher than the acceptable level. Dust storms are one of the main natural hazards that have affected the West and Southwest of Iran and Ahvaz in Khuzestan province in recent years; and besides numerous social and economic problems, dust storms have jeopardized people's health (37). Several factors are involved in this regard, the most important of which are bordering Khuzestan province with Iraq and the increased number of dust days and reduced precipitation in Iraq. Also, Turkey and Syria built dams on the Tigris and Euphrates in 1977, which led to drying Hvralzym Marshes and Shadegan wetlands in Ahvaz (38). Actions, such as watering the Hvralzym Marshes and Shadegan wetlands and their mulching, have reduced the amount of the dust in recent years (37).

The present study revealed a significant positive relationship between the concentrations of ambient air O_3 and respiratory deaths in the total population in 0 and 14- day lags and cumulative 0 to 14 day lags. O_3 also showed a significant positive relationship with respiratory deaths in population subgroups, in females, and in over 60 age group on 8- day lags.

O_3 was related to death due to respiratory diseases in other studies as well. In a study done in Taiwan, a signifi-

cant association was observed between daily respiratory disease mortality and O_3 among people over 65 years and all ages in the winter. Also, results showed that this pollutant was related to daily respiratory disease mortality among people over 65 years only in the summer (39). In Lipsett et al.'s study in California, the relationship between O_3 and non-cancerous respiratory mortality was significant as well (40).

However, some studies have reported non-significant relationships between O_3 and respiratory mortality. Jerrett et al. reported a positive correlation between respiratory mortality and long-term exposure to O_3 throughout California. Nonetheless, after geographical analysis in Southern (RR = 1.01, 95% CI: 0.96 to 1.07), Northeast (RR = 0.99, 95% CI: 0.92 to 1.07), and Southeastern (RR = 1.12, 95%CI 1.05-1.19) California, no relationship was found between O_3 and respiratory mortality (41). In a study in China, after adjusting for other pollutants, O_3 had no significant relationship with mortality due to respiratory diseases (42).

The scientific aspects of ozone's adverse effects are still under question. Issues such as its acute or chronic effects, confounders, or its interaction with climate variables and other pollutants are still not well understood (43). Nevertheless, its adverse effects are important because nowadays the levels of ozone are much higher than the pre-industrial times (43).

In this study, PM_{10} showed a significant relationship with respiratory deaths in some lags and some subgroups. Similar to these results in New Zealand, in an adjusted statistical model, a significant association was found between increased mean PM_{10} levels and respiratory deaths (excluding lung cancer) (44). In a study conducted in California among never smokers, both PM_{10} and $PM_{2.5}$ were related to non-cancerous respiratory deaths (40). In another study done in California on both genders, there was a significant association between PM_{10} and respiratory mortality (45). In the city of Wuhan in China, each 10 mg increase in the daily concentration of PM_{10} (at lag 0) was related to 71% increase in respiratory mortality (46). Jonidi et al. also showed a weak but significant association between PM_{10} and respiratory and cardiac deaths in Tehran (47). Also, in a study in Kerman, Iran, after adjusting for temperature and humidity, there was a significant direct association between male respiratory death and PM_{10}, but this significant relationship was not seen among females (9). Braga et al.'s study (2001) conducted in 10 cities in the US, found that in respiratory deaths, exposure to PM_{10} after a one day lag (for death from pneumonia) and a 2-day lag (for death from COPD) had a greater impact than exposure on the same day. However, cardiovascular deaths were more affected by PM_{10} concentrations on the same day (48). Another study by Kim et al. (2003) found no association between exposure to PM_{10} and increase in respiratory mortalities caused by COPD on the same day, but this relationship was significant in the lagged model (increased mortality= 12.2%, 95% CI: 2.5% - 22.9%) (49). Zeka et al. (2005) showed that deaths from respiratory diseases were associated with concentration of PM_{10} on the previous day (% increase in respiratory mortalities was related to one unit increase in the concentration of PM_{10} (0.52%, 95% CI: 0.15% -0.89 %.), 2 days before (0.51%, CI 95%: 0.16% - 0.86%), and 3 days before (0.87%, CI 95%: 0.38% -1.36%). These researchers stated that considering only one time lag leads to underestimation of the effects of PM_{10} on all mortalities and cardiopulmonary mortality (50). Analitis et al. (2005) showed that for every 10 $\mu g/m^3$ increase in PM_{10} in the 0 and 1 lag time, a 0.58% increase in respiratory deaths was seen (CI 95%: 0.21% - 0.95%) (12). The majority of researchers in this field believe that cardiovascular and respiratory mortality lag patterns are different, but it seems that like cardiovascular mortalities, they are more influenced by pollutants on the same day, while respiratory deaths are more affected by pollutants in earlier days (48, 51, 52).

In this study, a strong significant relationship was found between the mean concentration of NO_2 and respiratory deaths in the 18 to 60 age group and in 9- day lags. A study by Cesaroni et al. (2013) on those older than 30 in Rome showed a significant positive relationship between respiratory mortality and NO_2 (Hazard Ratio: 1.03, CI 95%: 1.00- 1.06) after adjustment for confounding variables including gender, marital status, place of birth, education, and social/economic status (53). In another study by Beelen et al. (2008) using data from the Netherlands diet and cancer Cohort, a significant positive correlation was observed between NO_2 pollution and respiratory mortality;and after adjustment for age, gender, smoking habits, and socioeconomic status, for each 10 µg/m3 increase in the concentration of NO_X, the relative risk for respiratory mortality was 1.37 (95% CI: 1.00-1.87)(54). Gehring et al. (2006) conducted a study on 4800 (50-59 year- old) females using the Cox's proportional hazards model adjusted for smoking and socioeconomic status, and they reported a positive relationship between increase in NO_2 concentration and death from cardiopulmonary disease (Hazard Ratio: 1.57, 95% CI: 1.23 - 2.00) as well (55). Also, in a cohort study by Heinrich et al. (2012) on 4800 (55 year-old) females in Germany, the adjusted results showed that an increase of 16 $\mu g/m^3$ in the concentration of NO_2 is associated with increased all- cause mortality (Hazard Ratio: 1.18, 95% CI: 1.07- 1.30) from cardiopulmonary disease (Hazard Ratio: 1.55, 95% CI: 1.30 - 1.84) (56). Finally, in Dong et al. (2011) in Shenyang, China (57), Yorifuji et al. (2010) in Shizuoka, Japan (58), and Filleul et al. (2005) in 7 cities in France (59), the hazard ratio for every 10 micrograms per cubic meter increase in NO_2 for respiratory related deaths was 2.97 (95% CI: 2.69 - 3.27), 1.19 (95% CI: 1.02-1.38), and 1.27 (95% CI: 1.04-1.56), respectively.

Despite the laboratory, clinical, and epidemiological studies, the health effects of exposure to NO_2 in humans are not understood well. NO_2 is a hardly water-soluble, highly reactive, and nitrogen-centered gas with free radicals that resides in the lung tissue. NO_2 penetrates the respiratory system, but studies have shown that terminal bronchioles are the main place for their reaction. The main destructive mechanism of NO_2 in the respiratory tract is lipid peroxidation in cell membranes and involvement in various free radical reactions that effect the cell structure

and function (60). NO_2 causes inflammation of the airways, particularly the terminal bronchioles (61). It has been shown in human studies that the main effect of NO_2 in inducing airway reactivity was in concentrations ≥1800 $\mu g/m^3$ in healthy individuals and in concentration of 200 to 500 $\mu g/m^3$ in patients with asthma (62) and patients with chronic obstructive pulmonary disease (63). Also, NO_2 has a reinforcing effect on asthmatic response to allergens. Evidence suggests that 15 to 30 minutes exposure to 500 $\mu g/m^3$ NO_2 activates asthmatic reactions (15). Some studies suggest that 15 minutes of exposure to 500 $\mu g/m^3$ NO_2 in high traffic locations could cause inflammatory allergic reactions in airways without causing symptoms or lung defects (64). NO_2 in concentrations present in the atmosphere are potentially irritating and associated with chronic obstructive pulmonary diseases. It also increases airway reaction in asthmatics and can cause severe acute respiratory symptoms such as cough, chest pain, shortness of breath, and bronchopneumonia (65). Also, toxicological evidence suggest that increased sensitivity to infection, functional impairment of the airways, and worsening health status of people with chronic respiratory conditions are among the potential health impacts of NO_2(15).

With regards to CO, this study showed that this pollutant was related to respiratory deaths after 9- day lags in the total population, in males, and in older than 60 age group. Also, in the population under 18, there was a significant association between the mean of CO and respiratory deaths in the cumulative 0 to 14- day lags. In a study done in Tehran, CO was directly related to respiratory deaths and the correlation was about 0.7 (66). In another study from Tehran, in the months that CO increased, the rate of respiratory mortality in children under 12 years increased as well(67). In a study from Shiraz, Iran, the results of multivariate analysis showed that CO is directly related to respiratory death in the total population, males, females, and those aged 18 to 60 years (8).

Finally, the present study found a significant positive relationship between the concentrations of ambient air SO_2 and respiratory deaths in the total population, males, and older than 60 age group in 9- day lags. Similar to this, in Wong et al.'s study in China, SO_2 was directly and significantly related to respiratory death (42). In another study from California, SO_2 showed a strong relationship with increased mortality from lung cancer in both genders (45). In a study from Kerman, Iran, after adjusting for temperature and humidity, a significant association was observed between increased respiratory mortality among males (but not females) and ambient air SO_2(9). However, several studies that have shown a non-significant association between SO2 and respiratory mortality, such as a study from Beijing (68). In a study on the long-term effects of air pollution on adult mortality in 18 areas in 7 cities in France, the relationship between SO_2 and cardiopulmonary disease was not significant (59), and in the study conducted by Liang in Taiwan, SO_2 had no significant association with respiratory mortality (39).

Several mechanisms explain the effects of air pollution on the respiratory system. The most acceptable and basic explanation is that in exposure of the respiratory epithelium to air pollutants, high concentrations of oxidants and pro-oxidants in these pollutants form oxygen and nitrogen- free radicals that cause oxidative stress in the respiratory system. In other words, an increase in free radicals initiates an inflammatory response and release of inflammatory cells and mediators (cytokines, chemokines, and adhesion molecules) to the circulatory system, which creates a subclinical inflammation that not only has a negative impact on the respiratory system, but also causes systemic effects (2, 69, 70).

One of the limitations of this study was that exposure measurement was done by air pollution stations that do not accurately represent exposure at the individual level. Nevertheless, this method is the most practical and affordable method to measure exposure in air pollution studies (71). Another limitation of this study was lack of socioeconomic information on the deceased, which prevented us from adjusting this variable.

Conclusion

Air pollutants in Ahvaz were associated with respiratory mortality on the same day and multi-day lags. Due to the increasing trend of respiratory deaths in this city, it is necessary to implement interventions to reduce air pollution sources and adopt policies to reduce exposure to air pollution in Ahvaz.

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Conflict of Interests

The authors declare that they have no competing interests.

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