

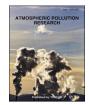
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# Air pollution and COVID-19 mortality and hospitalization: An ecological study in Iran



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ABSTRACT

Exposure to air pollution can exacerbate the severe COVID-19 conditions, subsequently causing an increase in the death rate. In this study, we investigated the association between long-term exposure to air pollution and risks of COVID-19 hospitalization and mortality in Arak, Iran.

Air pollution data was obtained from air quality monitoring stations located in Arak, including particulate matter (PM), nitrogen dioxide (NO<sub>2</sub>), sulfur dioxide (SO<sub>2</sub>), ozone (O<sub>3</sub>) and carbon monoxide (CO). Daily numbers of Covid-19 cases including hospital admissions (hospitalization) and deaths (mortality) were obtained from a national data registry recorded by Arak University of Medical Sciences. A Poisson regression model with natural spline functions was applied to set the effects of air pollution on COVID-19 hospitalization and mortality.

The percent change of COVID-19 hospitalization per 10  $\mu$ g/m<sup>3</sup> increase in PM<sub>2.5</sub> and PM<sub>10</sub> were 8.5% (95% CI 7.6 to 11.5) and 4.8% (95% CI 3 to 6.5), respectively. An increase of 10  $\mu$ g/m<sup>3</sup> in PM<sub>2.5</sub> resulting in 5.6% (95% CI 3.1–8.3%) increase in COVID-19 mortality. The percent change of hospitalization (7.7%, 95% CI 2.2 to 13.3) and mortality (4.5%, 95% CI 0.3 to 9.5) were positively significant per one ppb increment in SO<sub>2</sub>, while NO<sub>2</sub>, O<sub>3</sub> and CO were inversely associated with hospitalization and mortality.

Our findings strongly suggesting that a small increase in long-term exposure to  $PM_{2.5}$ ,  $PM_{10}$  and SO2 elevating risks of hospitalization and mortality related to COVID-19.

## 1. Introduction

Exposure to ambient air pollution in long-term is a major problem for global health worldwide. World Health Organization (WHO) indicated that more than 90% of the world's population live in cities having poor air quality and the concentrations of air pollution in these cities exceeding the WHO air quality guidelines (WHO, 2016). Air pollution was estimated to cause 4.2 million deaths around the world annually (Hosseini et al., 2021; Karimi and Shokrinezhad, 2021b). Exposures to airborne particles with an aerodynamic diameter of  $\leq 2.5 \,\mu m (PM_{2.5})$  and  $\leq 10 \,\mu m (PM_{10})$  and gaseous substances including carbon monoxide (CO), nitrogen dioxides (NO<sub>2</sub>), sulfur dioxide (SO<sub>2</sub>), and ozone (O<sub>3</sub>) are well-known causes of elevating diseases such as respiratory and cardiovascular diseases (Karimi and Samadi, 2019), premature death (Karimi and Shokrinezhad, 2020) and diabetes (Yang et al., 2020). Both short and long-term exposure to air pollution have been linked with

human health effects, more significant health effects associated with long-term exposure (Hales et al., 2021; Karimi and Shokrinezhad, 2021b). Air pollution is also considered to be as a human carcinogen by WHO in 2013 (IARC, 2016; Loomis et al., 2013).

Coronavirus disease (COVID-19) as a contagious disease caused by the SARS-CoV-2 virus (severe acute respiratory syndrome coronavirus-2) is still spreading in the world and subsequently elevating the risk of human deaths (Zheng et al., 2021). The cumulative number of COVID-19 cases has been reached up to 373 million globally in January 2022, with more than 5.6 million deaths (https://covid19.who.int/). Results of an investigation suggested that the majority of COVID-19 deaths occurred in adults aged 60-years old and above (Wu et al., 2020a). Moreover, higher COVID-19 deaths reported among individuals having serious health problems such as cardiorespiratory conditions, diabetes, stroke, hypertension and obesity (Buteau et al., 2018; Garg et al., 2020). Findings of other studies also suggested that exposure to air

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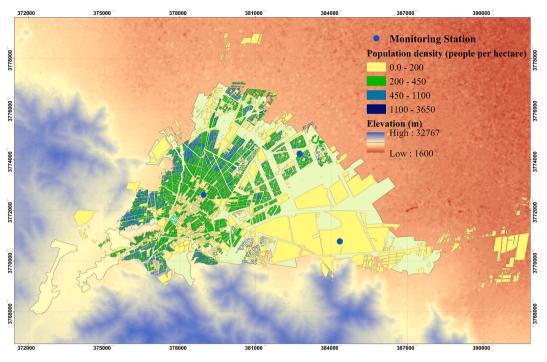


Fig. 1. Population density and sampling points of air pollution over 8 years.

pollution may increase the risk of hospitalization among individuals infected by COVID-19 and subsequently leading to death (Bowe et al., 2021; Wu et al., 2020a). Several pathways explained the connection between hospitalization and death due to COVID-19 with long-term exposure to air pollution (Conticini et al., 2020). The increased risks of diabetes and atherosclerosis are associated with long-term exposure to air pollution (Zhou et al., 2020). The occurrence of such chronic diseases linked with an elevating risk of death rate among infected individuals by COVID-19 (Zhou et al., 2020). Responses of immune systems may influence by exposure to air pollution and respiratory infections (Tsai et al., 2019). Several studies have been demonstrated that the high rates of cardiac arrhythmias, heart damage and thrombosis leading to the severity of hospitalization among COVID-19 patients (Srivastava et al., 2020; Wang et al., 2020; Zheng et al., 2020). Since chronic diseases such as cardiovascular and/or respiratory diseases linked with long-term air pollution and subsequently these diseases may exacerbate the severity of COVID-19 cases, thus we decided to perform this study. The aim of this study was to investigate the long-term effects of air pollution exposure on hospitalization and mortality in patients infected with COVID-19 in Arak, Iran.

#### 2. Materials and methods

#### 2.1. Study information

This study was carried out in Arak ( $34^{\circ}5' 8''$  and  $49^{\circ}41' 2''$ ), which is the capital of Markazi province located in the Northwest of Iran (Fig. 1). The total surface area of this city is about 70 km<sup>2</sup>, with a population of approximately 600,000. The mean annual temperature is about 15 °C, with a maximum temperature up to 42 °C in July and a minimum temperature fall to below freezing point in January. Mean yearly precipitation is about 341.7 mm, with the highest level in January (54.7 mm) and the lowest level in August (0.6 mm). The average elevation of this city is 1700 m above sea level. Arak is classified as one of the most polluted city in Iran. The main air pollution sources of concern are emissions come from industries located around the city and vehicles. Large industries located close to the city grouped into aluminum production, heavy metal manufacturing companies, energy-related equipment manufacturer, mineral industries, petrochemical industry and oil refinery.

# 2.2. Air pollution data

We used air pollution data over the past 8 years (2014–2021) which obtained from air monitoring stations belongs to the Department of Environment located in Arak including  $PM_{10}$ ,  $PM_{2.5}$ ,  $NO_2$ ,  $SO_2$ , maximum 8-h  $O_3$  and CO. The concentrations of air pollutants were measured by beta-attenuation monitoring for  $PM_{10}$  and  $PM_{2.5}$  ( $\mu g/m^3$ ), ultraviolet fluorescence method for  $SO_2$  (ppb), chemiluminescence method for  $NO_2$  (ppb) and maximum daily 8-h  $O_3$  (ppb), and infrared absorption method for CO (ppb). Data processing was conducted in order to an earlier published study (Karimi and Shokrinezhad, 2021a, b). Z-score method was applied to detect and remove outliers from datasets using time series analysis and spatial neighboring stations values. Data with Z-score value greater than four and the ratio of Z-score to moving average of Z-score greater than two were removed.

#### 2.3. Meteorological parameters

Since meteorological parameters have crucial effects in the transmission of COVID-19 virus (Lolli et al., 2020); thus, the influence of meteorological parameters were evaluated. Meteorological parameters obtained from synoptic meteorological station located in the Latitude of 34.07 N and Longitude of 49.76 E including relative humidity (H), precipitation, temperature (T), wind speed (WS) and wind direction (WD).

# 2.4. COVID-19 data

Daily confirmed COVID-19 cases of hospitalization and mortality were obtained from a national data registry which recorded by Arak University of Medical Sciences. The data registry initiated from the first onset case of COVID-19 (April 22, 2020) until August 11, 2021. All cases of COVID-19 were detected through SARS-CoV-2 swab tests and/or polymerase chain reaction (PCR). Additionally, computed tomography (CT) scan was applied for all cases to confirm the detection of COVID-19.

#### Table 1

Summery statistic of COVID-19 mortality and hospitalization, air pollution and metrological data.

Variables	Variable Obs	Mean	S.d	Min	P <sub>25</sub>	P <sub>50</sub>	P <sub>75</sub>	Max
COVID-19 data								
Outpatient	504	112.22	82.57	0	46.5	109	163	369
Inpatient	504	29.68	24.71	0	10	26	44	155
Total hospitalization	504	151.41	98.97	0	63.5	152	204.5	424
Mortality	626	3.86	1.32	0	1	4	9	14
Air pollution data								
$PM_{10} (\mu g/m^3)$	595	75.5	12.54	24	62	76	93	204
$PM_{2.5} (\mu g/m^3)$	606	35.14	10.32	5.94	22	32	45	71.7
SO2 (ppb)	586	6.7	3.51	3.2	4	6.5	8	25.7
CO (ppb)	598	2.2	0.71	0.2	1	2.2	2.8	9
Ozone (ppb)	582	21.3	11.94	4	16	20.6	34	69
NO	599	61.87	48.11	2	28	49	80	344
NO2	599	49.3	15.32	17	35	48.5	55	114
NOx	599	106.75	59.76	19	64	93	130	454
Meteorological variables								
Temperature (°C)	625	17.5	10.04	-7.6	7.9	18	25.7	36.3
Maximum temperature (°C)	625	24.05	11.94	-3.6	14.4	25.4	33.4	116
Minimum temperature (°C)	625	8.45	8.26	-14	2	9	15	52
Relative humidity (%)	620	42.23	24.69	18	23	35	57	97
Average wind speed (Km/h)	573	12.94	5.75	0	9.3	12.2	15.4	78
Average precipitation (mm)		340.7	23.22	0.6	158.6	329.5	361.6	425

SD: Standard deviation; CO: Carbon monoxide; NO<sub>2</sub>: Nitrogen dioxide; O<sub>3</sub>: Ozone; SO<sub>2</sub>: Sulfur dioxide; PM<sub>2.5</sub>: Particulate matter less than 2.5 µm; PM<sub>10</sub>: Particulate matter less than 10 µm.

(1)

## 2.5. Statistical analysis

(precipitation) +  $\beta_5$  (time, df<sub>1</sub>)

Spearman test was applied to examine the correlation between air pollutants with hospitalization and mortality due to COVID-19. A generalized additive model (GAM) and non-linear distributed lag model (DLNM) with a quasi-likelihood Poisson regression were applied to investigate the non-linear relationship between air pollutants and meteorological variables with hospitalization and morality (Karimi and Shokrinezhad, 2021a). We modeled the daily hospitalization and mortality against one air pollutant at a time and meteorological variables (temperature, relative humidity, precipitation, time) using equation (1):

 $Log(\mu(Y)) = \beta_0 + \beta_1 \text{ (pollutant)} + \beta_2 \text{ (temperature)} + \beta_3 \text{ (humidity)} + \beta_4$ 

Where  $\mu(Y)$  is hospitalization or mortality as a response variable,  $\beta_1$  is

the regression coefficient of hospitalization or mortality per unit increment of air pollutant concentration,  $\beta_2$  to  $\beta_5$  are the regression coefficients of meteorological variables. Cubic spline function was applied to control the effects of long-term trends and seasonality as time variable. The degree of freedom (df<sub>1</sub>) was set at 3 (Karimi and Shokrinezhad, 2021a).

Different lag models were applied to investigate the relationships between exposure to air pollutants and outcomes. In single lag models, different lags have been fitted one at a time. Since different lag effects in single lag models were not adjusted for each other; thus, distributed lag models were also applied. Additionally, non-linear distributed-lag models (NDLM) was used because collinearity in this approach is declined and greater precision can be estimated (Bhaskaran et al., 2013). We estimated the relative risks (RRs) of COVID-19 hospitalization and mortality for each 10-unit increase in  $PM_{2.5}$  and  $PM_{10}$ , and 1-unit

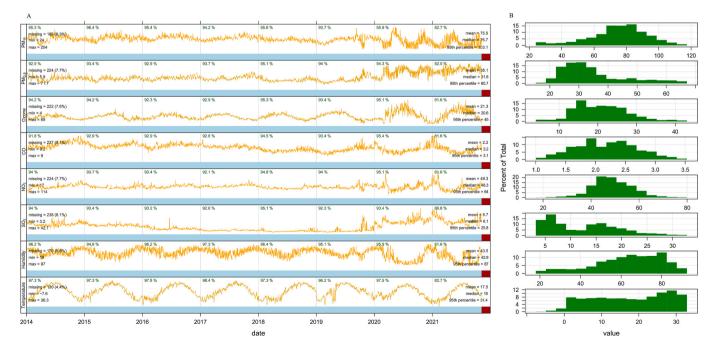
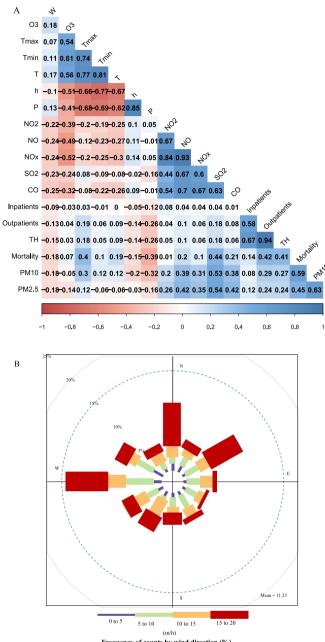


Fig. 2. Time-series trends of air pollutants with overall summary statistics (A), and the distribution of each pollutant using a histogram plot (B).



Frequency of counts by wind direction (%)

**Fig. 3.** Correlations between air pollutants, hospitalization, mortality and meteorological data (A) and mean wind rose direction in studied area during 2014–2021 (B).

increase in concentrations of  $SO_2$  (ppb),  $O_3$  (ppb),  $NO_2$  (ppb) (Karimi and Shokrinezhad, 2021a). The percent changes in hospitalization and mortality were calculated by following equation (2):

Percent change of hospitalization and mortality  $(\%) = (RR-1) \times 100\%$  (2)

We applied several packages in R version 3.2.3 for statistical analyses. We used splines, dlnm, Epi, foreign, and tsModel packages for modeling and analysis.

## 3. Results

Summary statistic data of hospitalization and mortality due to COVID-19, concentrations of air pollutants and meteorological data are presented in Table 1. Hospital admissions due to COVID-19 occurred in 75,382 cases, of which 1089 were passed away (mortality). On average,

daily hospital admissions and mortality occurred in 151.5 and 4 cases, respectively. The mean concentrations of  $PM_{2.5}$ ,  $PM_{10}$ ,  $SO_2$ , CO,  $NO_2$  and  $O_3$  during the study period were 35.14 µg/m<sup>3</sup>, 75.5 µg/m<sup>3</sup>, 6.7 ppb, 2.2 ppm, 49.3 ppb, and 21.3 ppb; respectively. The temporal pattern of air pollutants and meteorological data are illustrated in Fig. 2.

Daily mortality was positively correlated with  $PM_{2.5}$  ( $R^2 = 0.59$ ),  $PM_{10}$  ( $R^2 = 0.45$ ),  $SO_2$  ( $R^2 = 0.44$ ) and temperature ( $R^2 = 0.4$ ); and negatively correlated with precipitation (-0.39), relative humidity ( $R^2 = -0.15$ ) and wind speed ( $R^2 = -0.18$ ) (Fig. 3A). Similarly, positive correlations were found between hospitalization with  $PM_{2.5}$  ( $R^2 = 0.34$ ),  $PM_{10}$  ( $R^2 = 0.28$ ) and  $SO_2$  ( $R^2 = 0.21$ ); and negatively associated with wind speed ( $R^2 = -0.18$ ), relative humidity ( $R^2 = -0.61$ ) and precipitation ( $R^2 = -0.18$ ) (Fig. 3A). The concentrations of  $PM_{2.5}$  and  $PM_{10}$  were negatively correlated with wind speed, temperature, relative humidity and precipitation. Correlations between air pollutants are illustrated in Fig. S1. The dominant direction of wind rose is from the northeast to east (Fig. 3B). Using polar plots, the effects of wind direction and speed on the distribution of  $PM_{2.5}$ ,  $PM_{10}$ ,  $SO_2$ , NO<sub>2</sub>, temperature and relative humidity display in Fig. S3A–F.

Fig. 4 shows the estimated percent change of hospitalization and mortality linked with exposures to  $PM_{2.5}$  and  $PM_{10}$  following the adjustment of long-term trend, seasonality and temperature. The percent change of daily mortality per 10 µg/m<sup>3</sup> increment in  $PM_{2.5}$  and  $PM_{10}$  were, respectively; 5.6% (95% CI 3.1 to 8.2) and 3.1% (95% CI -0.95 to 4.8) and for hospitalization were 8.5% (95% CI 7.6 to 11.5) and 4.8% (95% CI 3 to 6.5) (Fig. 4).

The estimated percent change of hospitalization and mortality in lagdays 0-7 per 10  $\mu$ g/m<sup>3</sup> increment in PM<sub>2.5</sub> and PM<sub>10</sub> following the adjustment of long-term trend, seasonality and temperature are illustrated in Fig. 5A and D. PM<sub>2.5</sub> in lag-days 3-6 was significantly associated with mortality using lag-stratified models (Fig. 5A). The percent change of hospitalization per 10  $\mu$ g/m<sup>3</sup> increment in PM<sub>2.5</sub> in lag-days 1-6 was significant applying lag-stratified models (Fig. 5B). Per 10  $\mu$ g/m<sup>3</sup> increment in PM<sub>10</sub> in lag-days 2-6 using non-linear lag models, the percent change in daily deaths was 1.3–1.7% (Fig. 5C). PM<sub>10</sub> in lag-days 2-7 was significantly associated with hospitalization using lag-stratified models (Fig. 5D).

Estimated percent changes in hospitalization and mortality per 1 ppb increment in SO<sub>2</sub> exposure after adjusting for long-term trend, temperature and seasonality were 4.5% (95% CI 0.3 to 9.5) and 7.7% (95% CI 2.2 to 13.3), respectively. Per 1 ppb increment in CO (4.3, 95% CI -3.5 to 8.6), NO<sub>2</sub> (4.7%, 95% CI -4.2 to 14.4) and O<sub>3</sub> (1.2%, 95% CI -5.6 to 8.8) were not significantly associated with mortality. The highest estimated percent change in hospitalization per 1 ppb increment was related to NO<sub>2</sub> (7.3%, 95% CI -1.6 to 16.3), the second highest associated with CO (6.6, 95% CI -4.7 to 16.5) and followed by O<sub>3</sub> (2.9%, 95% CI -7.3 to 12.5).

Mortality in non-linear distributed lag model was significantly associated with SO<sub>2</sub> exposure in lag-day 2 (2.25, 95% CI 0.66 to 3.45), lag-day 3 (2.38, 95% CI 1.05 to 3.92) and lag-day 4 (1.31, 95% CI 0.56 to 2.35) (Table 2). Similarly, significant positive relationship was obtained between 1 ppb increase in SO<sub>2</sub> exposure and hospitalization in lag-day 3 (1.06, 95% CI 0.24 to 1.76), lag-day 4 (1.25, 95% CI 0.43 to 1.93) and lag-day 5 (1.24, 95% CI 0.2 to 2.1). Hospitalization and mortality in non-linear distributed lag model were not significant with exposures to NO<sub>2</sub>, CO and O<sub>3</sub> (Table S1). The estimated relative risk per one ppb increment in NO, NO<sub>2</sub>, CO and O<sub>3</sub> related to hospitalization and mortality are presented in supplementary Fig. S4.

#### 4. Discussion

In the present study, significant and positive associations were found between exposure to  $PM_{2.5}$  and  $PM_{10}$  with elevating risk of hospitalization and mortality. The percent changes of hospitalization and mortality were positively associated with one ppb increment in exposure to

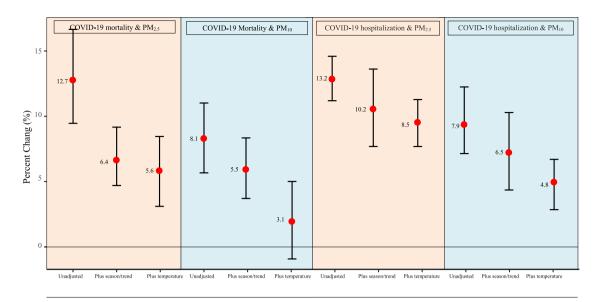


Fig. 4. Percent change of hospitalization and mortality per  $10 \ \mu g/m^3$  increment in exposure to  $PM_{2.5}$  and  $PM_{10}$ .

 $SO_2$ , while  $NO_2$ ,  $O_3$  and CO were inversely associated with hospitalization and mortality.

We observed positive associations between the percent changes in hospitalization with  $PM_{2.5}$  (8.5%, 95% CI 7.6 to 11.5) and  $PM_{10}$  (4.8%, 95% CI 3 to 6.5) per 10 µg/m<sup>3</sup> increase. The same results were reported by earlier studies conducted in Italian and Chinese cities (Wang et al., 2020; Zoran et al., 2020). Our results were to somewhat higher than those findings reported by a study performed in 120 Chinese cities for  $PM_{2.5}$  (2.24%, 95% CI 1.02 to 3.46) and  $PM_{10}$  (0.76%, 95% CI 0.89 to 2.63) per 10 µg/m<sup>3</sup> increment (Zhu et al., 2020). In contrast to our results,  $PM_{10}$  in seven metropolitan cities of Korea and  $PM_{2.5}$  in 28 geographical areas of Japan were not significantly associated with hospitalization and mortality relevant to Covid-19 (Azuma et al., 2020; Hoang and Tran, 2021).

The percent change of mortality per 10  $\mu$ g/m<sup>3</sup> increase in PM<sub>2.5</sub> in present study was 5.6% (95% CI 3.1–8.3%). Findings of studies investigating association between mortality with PM<sub>2.5</sub> and/or PM<sub>10</sub> with mortality conducted in China (Zhu et al., 2020), Italy (Bianconi et al., 2020), the United States (US) (Bashir et al., 2020; Wu et al., 2020b), Japan (Azuma et al., 2020), Netherlands (Cole et al., 2020), UK (Travaglio et al., 2021), and Spain (Ogen, 2020) were in consistent with our results. Our results were lower than those the percent change (8%, 95% CI 2 to 15) reported by a cross-sectional study conducted in the US (Wu et al., 2020a). The findings of two studies showed that mortality was not significantly associated with long-term exposure to air pollution (Goldberg and Villeneuve, 2020; Stieb et al., 2020). Moreover, airborne dust has also led to very poor air quality and serious human health impacts, notably in southeastern and southwestern Iran (Mesbahzadeh et al., 2020).

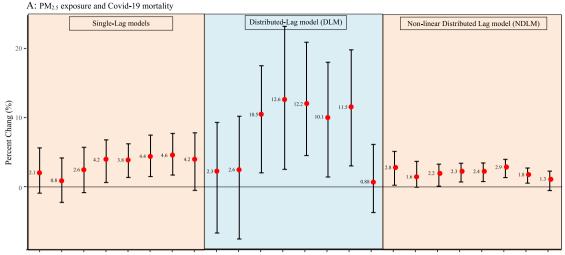
The distribution of air pollutants and COVID-19 virus differed in diverse countries and locations depending on population density and local meteorological parameters (Wang et al., 2021). Since COVID-19 virus can be detected in various environments particularly in houses, buses, hospitals and subways (Azuma et al., 2020; Hoang and Tran, 2021); thus, particulates perhaps can act as COVID-19 virus carriers leading to an increasing the human vulnerability to COVID-19.

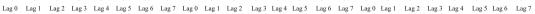
Researchers discovered that long-term exposure to  $PM_{2.5}$  associated with cardiorespiratory diseases such as chronic obstructive pulmonary disease (Guo et al., 2021), ischemic heart disease (Nirel et al., 2021) and lung cancer (Hvidtfeldt et al., 2021). Peoples with chronic diseases are more susceptible to COVID-19 virus and poor air quality may also exacerbate the COVID-19 clinical symptoms (Al-Kindi et al., 2021). Airborne particulates on a dry surface may act as a carrier for COVID-19 virus (Borisova and Komisarenko, 2021). Maleki et al. (2021), in a systematic review, indicates that ambient particulate matter did not relate to the COVID-19 transmission, but the reduction of resistance to infection in the long term was confirmed (Maleki et al., 2021). Moreover, exposure to PM<sub>2.5</sub> in the long time can increase the protein expression of ACE-2 in A549 cells (Du et al., 2020; Miyashita et al., 2020). The ACE-2 receptor could raise the viral RNA entering lungs cells and exacerbate the viral load of the COVID-19 virus (Baildya et al., 2021; Watzky et al., 2021).

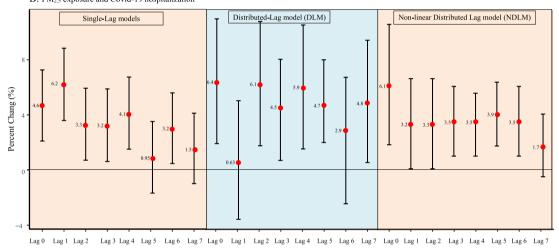
Results of other studies in consistent with our findings reported that hospitalization and mortality were associated with SO<sub>2</sub> exposure (Jiang and Xu, 2021; Lembo et al., 2021; Wang et al., 2021). Liu et al. (2021) in China reported that the dispersion speed of COVID-19 infection increased with SO<sub>2</sub> exposure (Liu et al., 2021). In parallel to our results, the incidence of COVID-19 was significantly associated with all ambient air pollutants except NO<sub>2</sub> (Jiang et al., 2020). In contrast to our results, Zhu et al. (2020) did not find a positive association between exposure to SO<sub>2</sub> and hospitalization (-7.79%, 95% CI: -14.57 to -1.01) (Zhu et al., 2020).

In the present study, there is a lag time or delay association between hospitalization and mortality with exposure to particles. To confirm this, Lopez-Feldman was reported robust evidence between mortality and long-term exposure to  $PM_{2.5}$  while negative association was found in short-term exposure (López-Feldman et al., 2021).

The role of meteorological parameters in the transferring of the COVID-19 virus has been widely studied (Hoang and Tran, 2021; Jain et al., 2021). In hot-season with high temperature and sunlight, the longevity of COVID-19 virus decreases, while in the cold season with low temperature the mortality rate of respiratory disease increases. Under these conditions, the susceptibility may be increased due to the reduction of immune function and slower clearance of mucociliary (Ficetola and Rubolini, 2021). Moreover, the potential transportation of pathogens raised in the cold season with high relative humidity and moisture (Aidoo et al., 2021). Similar conclusions to our results were reported in Italy, Ghana, and India, and a negative correlation between COVID-19 mortality and the air temperature was confirmed (Aidoo et al., 2021; Kulkarni et al., 2021; Lolli et al., 2020). A negative correlation between atmospheric pressure and temperature with COVID-19 mortality was also suggested by Jain et al. (2021), and Sharma et al. (2021) (Jain et al.,







B: PM2.5 exposure and Covid-19 hospitalization

Fig. 5. Estimated percent change of hospitalization and mortality linked to PM<sub>2.5</sub> and PM<sub>10</sub>: (A) mortality and PM<sub>2.5</sub>, (B) hospitalization and PM<sub>2.5</sub>, (C) mortality and PM<sub>10</sub>, (D) hospitalization and PM<sub>10</sub>.

2021; Sharma et al., 2021). However, a study conducted by Crema (2021) suggested a strong influence of air humidity with COVID-19 mortality, but temperatures do not important (Crema, 2021).

The estimates derived results from this study could be applied to the health assessment of airborne particles and sulfur dioxide with COVID-19 hospitalization and mortality in various lag times. However, the influence of age, sex, personal behaviors and hygiene, social distancing, mean travel time to work, smoking, and chronic diseases, including diabetes, cardiovascular, hypertension, obesity, and chronic respiratory illnesses, which increase the COVID-19 mortality, were not considered in this study (Bang et al., 2021; Luo et al., 2021; Magnan et al., 2021). Finally, in the current study, we only regarded as COVID-19 data in the Arak city. Similar research is needed in the neighboring regions to test the model performance in other high incidence areas.

## 5. Conclusion

Air pollution play a significant role in the severity of disease and mortality among individuals infected by COVID-19. We obtained positive and significant associations between  $PM_{2.5}$ ,  $PM_{10}$ , and  $SO_2$  with the onset of disease and mortality due to COVID-19. Additionally, air

pollutants including NO<sub>2</sub>, CO and  $O_3$  were inversely related to hospitalization and mortality. Meteorological data including precipitation, relative humidity and wind speed were inversely linked. Our findings suggesting that applying of control measures for air pollution may reduce the severity of COVID-19 disease.

### **Research** ethics

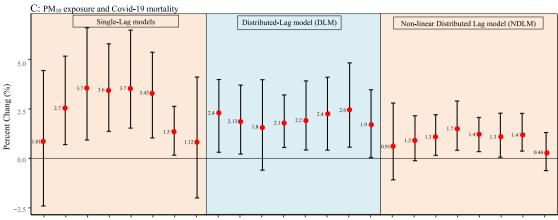
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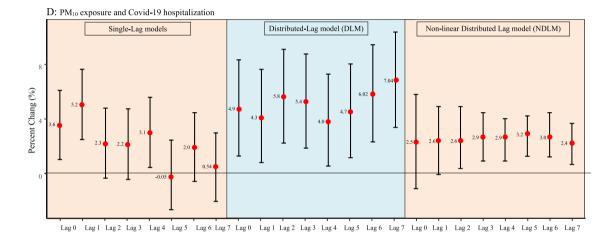
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# Credit author statement

B.K. designed the study, participated in the data collection and wrote the main manuscript. B.K. and B. Sh. performed the statistical analysis and assisted in the data collection and approved the final version.







#### Fig. 5. (continued).

## Table 2

Hospitalization and mortality associated to SO2 exposure after adjustment of long-term trend, seasonality and temperature using single-lag models, distributed lag model (DLM), and non-linear distributed lag model (NDLM).

	Single-Lag 1	nodels		Distributed-Lag model (DLM)			Non-linear Distributed Lag model (NDLM)					
Mortality	Mortality and SO <sub>2</sub>											
lag0	-0.43	-3.41	2.47	-1.16	-4.27	2.38	1.2	-0.49	2.8			
lag1	-0.51	-3.15	3.12	-0.56	-4.08	3.09	0.63	$^{-1}$	2.07			
lag2	0.67	-2.45	3.14	0.32	-3.12	3.88	2.25	0.66	3.45			
lag3	2.04	0.47	3.95	0.53	-2.20	4.22	2.38	1.05	3.92			
lag4	2.94	0.35	7.02	1.06	0.16	2.79	1.31	0.56	2.46			
lag5	2.63	0.51	4.45	1.55	-1.51	4.04	-0.4674	-1.95	0.97			
lag6	3.18	1.37	6.28	1.76	0.59	3.20	-0.12	-1.69	1			
lag7	0.58	-1.49	2.24	2.12	0.16	3.53	-0.36	-1.54	0.95			
Total Adn	nission and SO <sub>2</sub>											
lag0	1.12	-1.41	3.69	2.34	-2.08	6.96	1.05	-0.2	1.83			
lag1	0.71	-1.57	3.4	0.29	-2.82	3.06	0.75	-0.33	1.87			
lag2	1.89	-1.18	4.66	2.17	-2.24	6.78	0.67	-0.55	1.64			
lag3	3.26	1.35	5.42	2.12	0.47	4.03	1.06	0.24	1.76			
lag4	3.46	0.85	7.35	3.76	0.68	6.8	1.25	0.43	1.93			
lag5	3.39	1.73	5.67	2.61	0.84	4.86	1.24	0.22	2.15			
lag6	4.4	2.27	7.5	-1.94	-6.42	2.75	0.63	-0.32	1.46			
lag7	1.69	-1.18	4.16	0.88	-3.45	5.41	0.18	-0.61	0.85			

# Declaration of competing interest

# Appendix A. Supplementary data

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. Supplementary data to this article can be found online at https://doi.org/10.1016/j.apr.2022.101463.

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