Journal of Environmental Health Science and Engineering (2021) 19:1807–1816
https://doi.org/10.1007/s40201-021-00736-4

RESEARCH ARTICLE

Effect of short-term exposure to air pollution on COVID-19 mortality and morbidity in Iranian cities

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Received: 4 April 2021 / Accepted: 30 August 2021 / Published online: 28 October 2021

Abstract

Purpose The association between air pollutant ($PM_{2.5}$, PM_{10}, NO_2, and O_3) concentrations and daily number of COVID-19 confirmed cases and related deaths were evaluated in three major Iranian cities (Tehran, Mashhad, and Tabriz).

Methods Hourly concentrations of air pollutants and daily number of PCR-confirmed cases and deaths of COVID-19 were acquired (February 20th, 2020 to January 4th, 2021). A generalized additive model (GAM) assuming a quasi-Poisson distribution was used to model the associations in each city up to lag-day 7 (for mortality) and 14 (for morbidity). Then, the city-specific estimates were meta-analyzed using a fixed effect model to obtain the overall relative risks (RRs).

Results A total of 114,964 confirmed cases and 21,549 deaths were recorded in these cities. For confirmed cases, exposure to $PM_{2.5}$, NO_2, and O_3 for several lag-days showed significant associations. In case of mortality, meta-analysis estimated that the RRs for $PM_{2.5}$, PM_{10}, NO_2, and O_3 concentrations were 1.06 (95% CI: 0.99, 1.13), 1.06 (95% CI: 0.93, 1.19), 1.15 (95% CI: 0.93, 1.38), and 1.07 (95% CI: 0.84, 1.31), respectively. Despite several positive associations with all air pollutants over multiple lag-days, COVID-19 mortality was only significantly associated with NO_2 on lag-days 0–1 and 1 with the RRs of 1.35 (95% CI: 1.04, 1.67) and 1.16 (95% CI: 1.02, 1.31), respectively.

Conclusion This study showed that air pollution can be a factor exacerbating COVID-19 infection and clinical outcomes. Actions should be taken to reduce the exposure of the public and particularly patients to ambient air pollutants.

Keywords SARS-CoV-2 · Coronavirus · Particulate matter · Nitrogen dioxide · Pandemic

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Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel virus that originated in China and causes coronavirus disease 2019 (COVID-19). COVID-19 can be transmitted through person-to-person pathway, contact with contaminated surfaces, and via airborne particles [1–3]. Globally, over 185 million confirmed cases of this disease have been reported, and about 4 million people have died from COVID-19 (https://www.worldometers.info/coronavirus/#countries). In addition to this remarkable health burden, the disease has caused significant economic losses to the burden [4]. Various pharmaceutical and non-pharmaceutical intervention measures have been proposed and implemented to control the disease.

It is suggested that exposure to air pollution can exacerbate the severe COVID-19 conditions, and possibly causing an increase in the death rate. Several studies have been conducted to investigate the effect of short-term exposure to various air pollutants such as particulate matter (PM_{10} and $PM_{2.5}$), nitrogen dioxide (NO_2), ozone (O_3), etc. on COVID-19 mortality and morbidity [4–7]. Using the multivariate linear regression, Yao et al. (2020) found positive associations between PM_{10} and $PM_{2.5}$ concentrations and case fatality rate (CFR) in 49 Chinese cities. According to their results, the COVID-19 CFR increased by 0.24% (0.01%–0.48%) and 0.26% (0.00%–0.51%) per 10 µg/m^3 increase in $PM_{2.5}$ and PM_{10}, respectively [4]. In a systematic review, Copat et al. (2020) found that $PM_{2.5}$, and NO_2 are two important triggering factors in COVID-19 lethality [8]. In a study in Italy, prolonged exposure to air pollution and fine particulate matter ($PM_{2.5}$) were recognized as the main factor leading to the SARS-CoV-2 effects [5].

Copat et al. (2020) reported that studies conducted on the association between air pollution and COVID-19 mortality and morbidity have used different methods and in some cases, have some serious limitations. Many of these studies have used correlation and linear regression. Another issue is the lack of adjustment for potential confounding factors [8]. Since the virus has spread in a large populations, and more health data has been released over a longer period, there is a need for new relevant analyses with more sophisticated methodologies, especially in countries with no previous studies such as Iran. High concentrations of air pollutants [9–11] and COVID-19 deaths per population are reported in Iran (https://www.worldometers.info/coronavirus/#countries).

In this study, we investigated the associations between four criteria air pollutants ($PM_{2.5}$, PM_{10}, NO_2, and O_3) and the daily number of COVID-19 confirmed cases and deaths in three major Iranian cities, Tehran, Mashhad, and Tabriz.

Methods

Study area and period

Tehran, Mashhad, and Tabriz were included in this study. These cities are among the most populated cities in Iran. Tehran as the capital of Iran and the most populated has about 10 million residents [12]. Mashhad is the second most populated city and has a population of more than 3 million. Due to the religious sites located in this city, millions of people visit Mashhad every year. Tabriz is located in the northeast of the country and has a population of more than 1.5 million. The study period spans from February 20th, 2020 to January 4th, 2021.

Exposure assessment

Hourly concentrations of $PM_{2.5}$, PM_{10}, NO_2, and O_3 measured in three cities of Tehran, Mashhad, and Tabriz were acquired from the Department of Environment of Iran. For Tehran, the measurements from the monitors operated by the Tehran's Air Quality Control Company were also included. First, negative and zero values were removed from the datasets. Then, only the monitors were included in the study that had at least 75% available data, and the rest of the monitors were excluded [13]. For $PM_{2.5}$ and PM_{10}, the 24-h average of concentrations were calculated. In case of NO_2 and O_3, daily maximum 1-h concentration and daily maximum 8-h moving averages were calculated. For averaging, only the days were used that had a minimum of 75% (18 h in 24 h) available data. These criteria were applied to ensure that a representative exposure will be attributed to the population [9, 14]. The number of valid monitors after applying the criteria are presented in the Supplementary Materials (Table S1). No valid monitors remained for NO_2 and O_3 in Mashhad. In addition, the data for the air temperature were acquired from the Iran's Meteorological Organization.

Health data

The daily number of confirmed and deaths of COVID-19 were obtained from the Ministry of Health and Medical Education of Iran. These cases and deaths from COVID-19 were confirmed by the polymerase chain reaction (PCR) tests. The datasets included the number of cases and deaths in each of the three cities (Tehran, Mashhad, and Tabriz) from February 20th, 2020 to January 4th, 2021.

Model

The association between exposure to air pollution and health outcomes are normally assumed to be non-linear.

Therefore, a distributed-lag, nonlinear model (DLNM) and a generalized additive model (GAM) based on the quasi-Poisson distribution were used [14, 15]. We modelled daily number of COVID-19 cases or deaths against one air pollutant at a time ($PM_{2.5}$, PM_{10}, NO_2, or O_3), air temperature, and time variables. The general equation of the model is presented below:

$$Log(E(\mu_t)) = \alpha + \beta * Pollutant + \gamma * Temperature + ns(Time, df_1) + \delta * DOW + \varepsilon * Holiday \quad (1)$$

In this equation, (μ_t) is the expected number of deaths/cases in day t. Pollutant and Temperature are the cross-basis functions which will be explained later. β and γ are the regression coefficients, i.e. the concentration–morbidity (or mortality) rates per unit increase in the levels of air pollutant and temperature, respectively. A natural spline function (ns) was defined for time variable. The time variable (n = 1, 2, 3, …, 299) was included in the model to control for the long- and/or intermediate-term trends of mortality. df1 is the degree of freedom for the natural spline function of time and was set at 3. δ and ε are the regression coefficients for the day of week (DOW) and Holiday as two categorical variables. These two variable were included to adjust for the effect of day of week and holidays on the number of confirmed cases and deaths. Although Ramadan occurred during the study period (April to May), it was not included in the model since prior work showed it had no direct effects on mortality [14].

Two cross-basis functions were developed for the pollutants and temperature. A cross-basis function is a bi-dimensional functional space describing at the same time the dependency along the range of the predictor and in its lag dimension. A cross-basis function incorporates two functions for the concentrations/levels of the variable and also its lag-day value. The degrees of freedom for the levels and lag-day of air pollutant and temperature were similarly set on 2 and 4, respectively. This choice was made after exploring degrees of freedom from 2 to 5 in a model of $PM_{2.5}$ and other variables against COVID-19 mortality/morbidity to obtain an optimum trade-off between Akaike's information criterion (AIC) [16] and relative risk values. Same values were used in all other analyses.

In all analyses, up to a 7-day and 14-day lag-days were employed to investigate the effect of cumulative and non-cumulative exposure to air pollution on the COVID-19 mortality and morbidity, respectively. Cumulative refers to the examining the effect of average concentration during *0-n* days on the day *n*. Non-cumulative refers to the examining the effect of exposure on day *0* to lag-day *n* on the incidence on day *n*. The relative risks (RRs) were estimated for a 10 $\mu g/m^3$ increase in PM_{10}, $PM_{2.5}$, 10 ppb increase in NO_2, and also a 10 ppb increase in O_3 with a threshold of 35 ppb. All the estimates were reported with a 95% confidence interval (95% CI).

Meta-analysis

The relative risk estimates obtained for each of the three cities were pooled using meta-analysis to reach the overall estimates. RR values (with 95% confidence intervals) and sample size (total number of COVID-19 deaths or cases in each city) were required for the meta-analysis. Chi-square and the Higgins I^2 tests were used to assess the heterogeneity among the results of different cities. Due to the low heterogeneity (between 0–25% based on the I^2 index), fixed-effect models were applied to pool the results of the cities. STATA v.12 (STATA Corp., College Station, TX) was used for the meta-analysis. All the analyses were conducted at a significance level of 0.05.

Results and discussion

Descriptive statistics of variables

The effect of air pollution on the exacerbation of COVID-19 conditions were investigated in three major cities in Iran. A total of 114,964 confirmed cases and 21,549 deaths had been recorded in these 3 cities. Numbers of COVID-19 deaths in Tehran, Mashhad, and Tabriz were 13,621, 4140, and 3788, respectively. Table 1 presents the descriptive statistics of COVID-19 cases and deaths, air pollutants, and air temperature during the study period. The ranges of COVID-19 deaths in Tehran, Mashhad, and Tabriz were 1–118, 0–52, and 0–44, respectively, with a daily average of 42.04, 12.94, and 11.84, respectively. The concentrations of all air pollutants ($PM_{2.5}$, PM_{10}, NO_2, and O_3) and values of air temperature in Tehran were higher than those in Mashhad and Tabriz.

Effects of PM on incidence of COVID-19

The effect of exposure to PM on COVID-19 confirmed cases was estimated in each city (Tables S2 and S3 in the Supplementary Materials), and the overall results were obtained using meta-analysis. The association between short-term exposure to PM_{10} and $PM_{2.5}$ and the number of confirmed COVID-19 cases had similar patterns (Fig. 1). The associations in the lag-days longer than lag-day 0–3 (cumulative exposure) and lag-day 2 or 3 (non-cumulative exposure) were positive. In case of PM_{10}, none of the associations were statistically significant ($p < 0.05$). In case of non-cumulative exposure to $PM_{2.5}$, statistically significant associations were found in lag-days 4 (1.03, 95% CI: 1.01, 1.05) to 11 (1.03, 95% CI: 1.01, 1.05) per 10-$\mu g/m^3$ increase in $PM_{2.5}$.

Table 1 Descriptive statistics of COVID-19 deaths and cases, air pollutants, and air temperature during the study period

Parameter	Min	25th	Mean	Median	75th	Max
Tehran						
Cases	33.00	113.25	241.83	236.00	349.75	601.00
Death	1.00	19.25	42.04	39.00	58.00	118.00
$PM_{2.5}$ (μg/m^3)	7.56	21.62	28.90	26.35	33.59	91.98
PM_{10} (μg/m^3)	14.28	54.62	67.91	68.56	81.72	158.28
O_3 (ppb)	11.37	60.38	84.44	84.87	114.41	168.85
NO_2 (ppb)	39.43	72.13	87.21	83.22	97.20	175.69
Temp. (°C)	1.00	11.98	19.62	19.03	27.86	35.05
Mashhad						
Cases	0.00	26.00	53.09	40.00	74.75	169.00
Death	0.00	5.00	12.94	10.00	19.00	52.00
$PM_{2.5}$ (μg/m^3)	4.75	19.68	27.83	26.12	33.04	81.97
PM_{10} (μg/m^3)	5.86	34.23	50.00	46.70	62.07	184.85
Temp. (°C)	-3.95	9.19	16.82	17.13	25.46	32.08
Tabriz						
Cases	0.00	37.50	61.32	57.00	81.00	176.00
Death	0.00	5.00	11.84	9.50	16.00	44.00
$PM_{2.5}$ (μg/m^3)	2.84	10.93	17.51	14.53	20.39	79.25
PM_{10} (μg/m^3)	8.35	28.65	43.20	39.56	53.47	141.91
O_3 (ppb)	10.75	44.89	56.56	57.30	67.99	102.68
NO_2 (ppb)	18.28	33.87	47.05	43.27	58.18	113.33
Temp. (°C)	-8.18	7.88	15.18	15.50	23.66	34.06

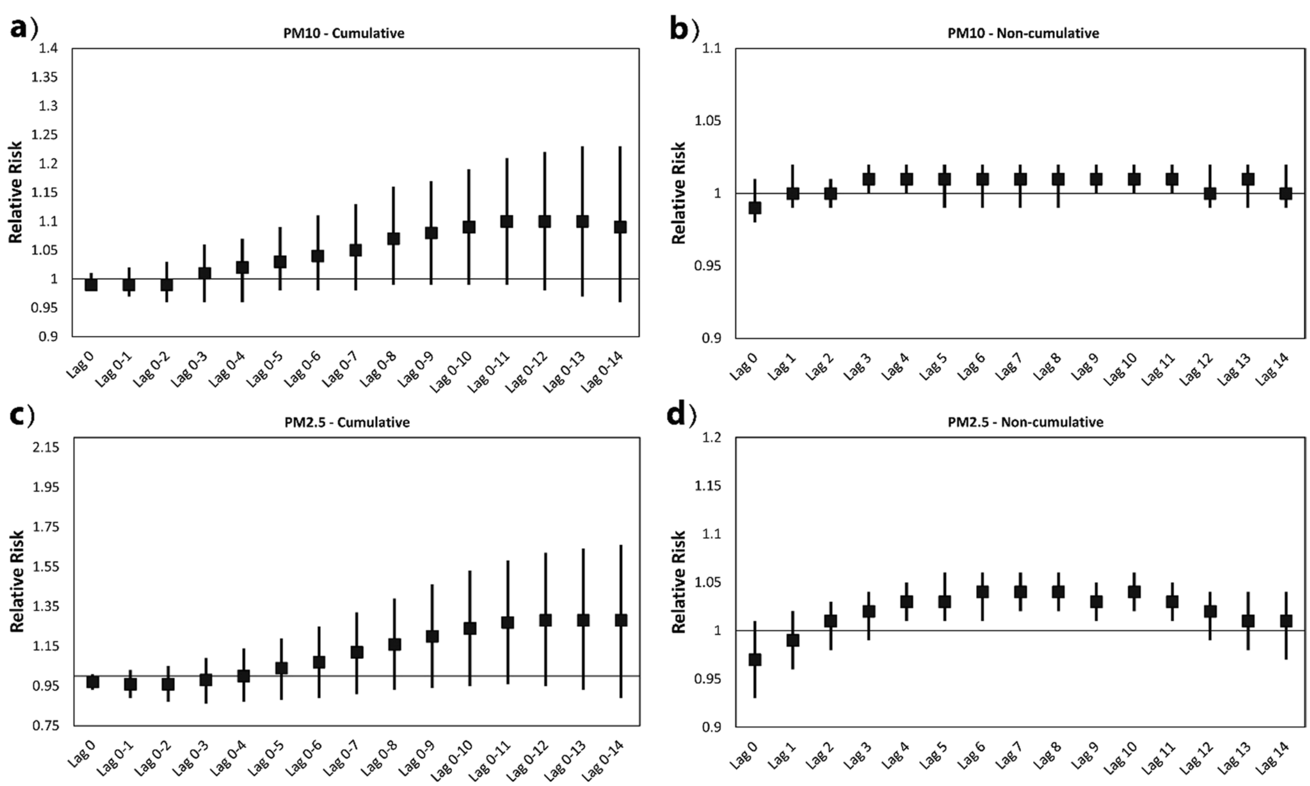

Fig. 1 Results of meta-analysis on the association between daily COVID-19 positive cases and: **a** and **b**) cumulative and non-cumulative exposure to 10 μg/m^3 increase in PM_{10}, **c** and **d**) cumulative and non-cumulative exposure to 10 μg/m^3 increase in $PM_{2.5}$

A comprehensive study was conducted in China on the effect of exposure to PM_{10} and $PM_{2.5}$ on daily number of confirmed cases of COVID-19. The results showed that a 10-µg/m^3 increase (lag0–14) in $PM_{2.5}$ and PM_{10} was associated with a 2.24% (95% CI: 1.02 to 3.46) and 1.76% (95% CI: 0.89 to 2.63) increase in the daily counts of confirmed cases, respectively [17]. A study in seven metropolitan cities Korea showed that exposure to PM_{10} was not associated with daily cases of COVID-19 in any investigated lag-days. However, exposure to $PM_{2.5}$ had significant associations with daily counts of COVID-19 cases in lag-days 0, 0–7, 0–14, and 0–21 [18]. In a study in California by Bashir et al. (2020), the authors using the Kendall correlation coefficient and Spearman correlation coefficient found that particulate matter including PM_{10}, $PM_{2.5}$, had a significant correlation with the COVID-19 confirmed cases [19]. In Italy, the daily average concentration of $PM_{2.5}$ and daily average and maximum concentrations of $PM_{2.5}$ were positively associated with daily new cases of COVID-19 [7].

Effects of NO_2 and O_3 on incidence of COVID-19

The effect of exposure to NO_2 and O_3 on COVID-19 confirmed cases was estimated in each city (Tables S4 and S5 in the Supplementary Materials), and the overall results were obtained using meta-analysis (Fig. 2). Results of meta-analysis showed that there are similar patterns in the associations between exposure to NO_2 and O_3 and COVID-19 confirmed cases. In case of NO_2, the lag-days longer than lag-day 0–4 (cumulative exposure) and lag-day 2 (non-cumulative exposure) showed positive relationships. The RRs were significant in the lag-days 4 (1.04, 95% CI: 1.01, 1.08) to 9 (1.03, 95% CI: 1.00, 1.06). For O_3, also the lag-days 4 (1.05, 95% CI: 1.01, 1.09) to 9 (1.05, 95% CI: 1.01, 1.09) were statistically significant.

Frontera et al. (2020) raised a hypothesis that NO_2 may have a significant role in incidence of severe forms of COVID-19. Long-term exposure to PM leads to overexpression of ACE-2 receptor in lungs. This may exacerbate the viral load of SARS-CoV-2, deplete ACE-2 receptors, and weaken immune system's defense. Finally, short-term exposure to NO_2 provide a second hit causing a severe form of COVID-19 [20]. In 120 Chinese cities with an average (± SD) NO_2 concentrations of 19.28 (± 11.87), it was reported that 10-µg/m^3 increase (lag0–14) in NO_2 is associated with 6.94% (95% CI: 2.38 to 11.51) increase in the daily counts of confirmed cases, respectively [17]. This percentage is much lower than those values found in the present study. In addition to the higher concentrations in the present study, this difference can be due to the different lag-days considered in the model. A study in seven metropolitan cities Korea showed that 10 ppm increase in NO_2 (lag 0-7,

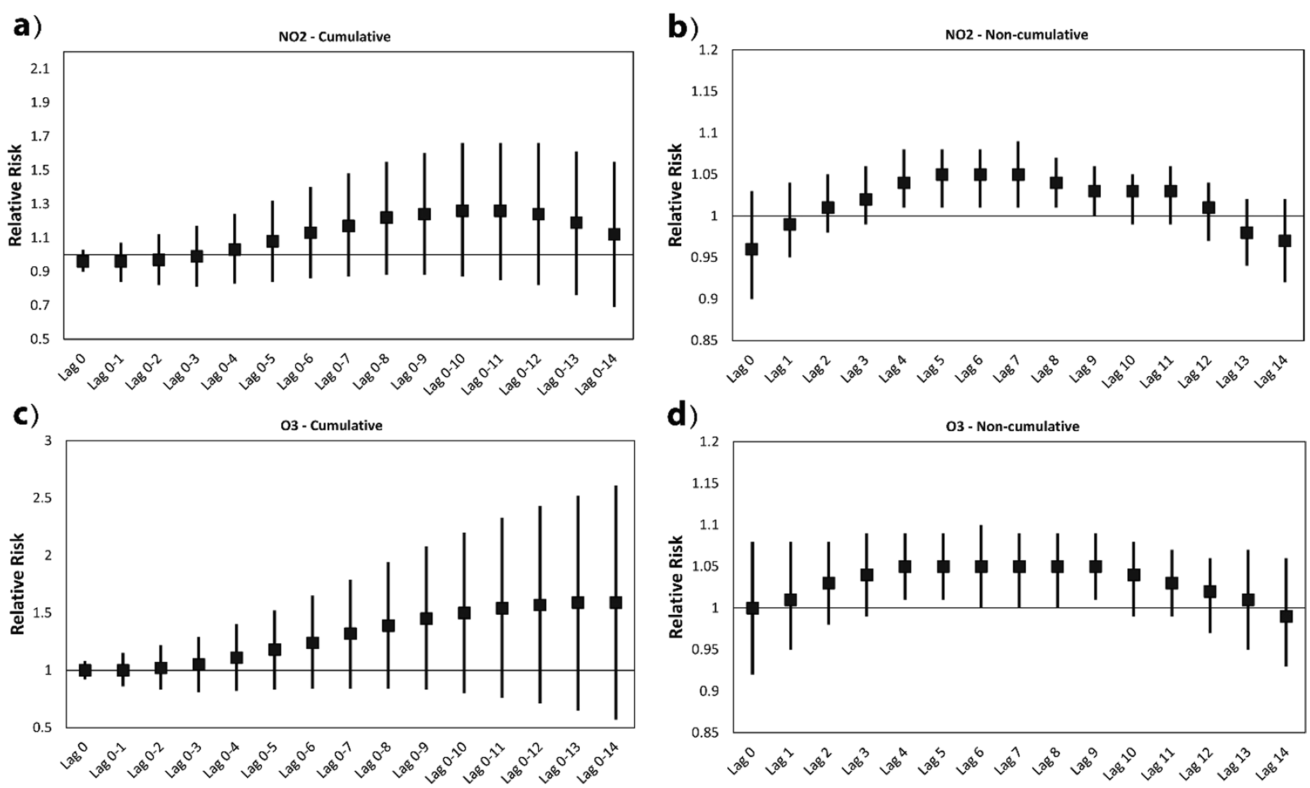

Fig. 2 Results of meta-analysis on the association between daily COVID-19 positive cases and: **a** and **b**) cumulative and non-cumulative exposure to 10 ppb increase in NO_2, **c** and **d**) cumulative and non-cumulative exposure to 10 ppb increase in O_3

lag 0–14, and lag 0-21) was significantly associated with increases of COVID-19 cases, with odds ratios (95% CIs) of 1.13 (1.02-1.25), 1.19 (1.09-1.30), and 1.30 (1.19-1.41), respectively. None of the associations for O_3 were positive and/or significant [18]. Bashir et al. (2020) investigated the correlation (using the Kendall correlation coefficient and Spearman correlation coefficient) between air pollution and COVID-19 morbidity and mortality in California, and reported that air pollutants such as SO_2, NO_2, and CO had a significant correlation with the COVID-19 confirmed cases [19]. The correlation between air quality index (AQI) and daily new cases of the disease due to SARS-CoV-2 in Italy was found to be positive [7]. In another study in New York, ozone concentrations were correlated with COVID-19 positive cases [21].

Effects of PM on mortality

Figure 3 (and Table S6 in Supplementary Materials) illustrates the effect of cumulative and non-cumulative exposure to PM_{10} in three cities of Tehran, Mashhad, and Tabriz on the daily deaths due to COVID-19. The RRs in Mashhad were mainly larger than those found in Tehran and Tabriz. In Tehran, cumulative exposure from lag-day 0–1 to lag-day 0–4 and also non-cumulative exposure in lag-days 0 and 1 were positively associated with COVID-19 deaths. However, none of the RRs were statistically significant. In case of Mashhad, an increasing trend of positive associations were observed in cumulative exposure from lag-day 0–1 (1.00, 95% CI: 1.20–1.44) to lag-day 0–7 (0.81, 95% CI: 1.51–2.54) per 10 μg/m^3 increase in PM_{10}. Contrary, the trend of RRs in non-cumulative exposure to PM_{10} was decreasing from lag-day 1 (1.01, 95% CI: 1.14–1.30) to lag-day 7 (0.89, 95% CI: 1.01–1.15). In Mashhad, effect of PM_{10} only in lag-day 0 and lag-day 0–1 were statistically significant. In Tabriz, cumulative exposure to PM_{10} in all lag-days and non-cumulative exposure to PM_{10} in lag-days 0 to 4 were positively related to COVID-19 deaths. However, none of the estimates were statistically significant. The differences between the cities could be due to the several factors such as the distribution of air pollution concentrations, clinical facilities and medications, availability of diagnostic tests, etc. [22].

The relative risks for $PM_{2.5}$ in Tabriz were found to be greater than those in Tehran and Mashhad (Table S7). In Tehran, cumulative exposure from lag-day 0–1 to lag-day 0–3 and also non-cumulative exposure in lag-days 1, 2 and 7 were positively associated with COVID-19 deaths. However, only the association in lag-day 1 was statistically significant (1.19, 95% CI: 1.00, 1.41 per 10 μg/m^3 increase in $PM_{2.5}$).

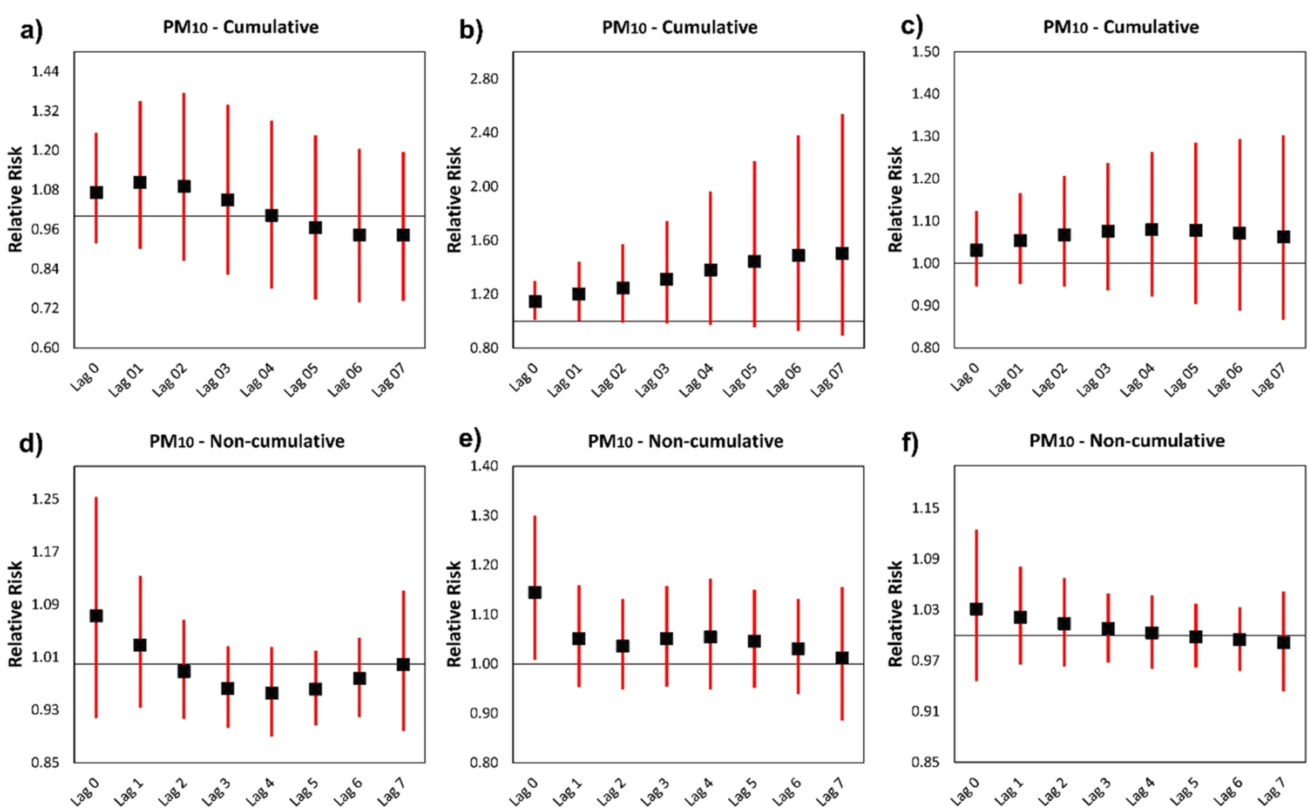

Fig. 3 Association of daily COVID-19 deaths with cumulative exposure to 10 μg/m^3 PM_{10} in (**a**) Tehran, (**b**) Mashhad, and (**c**) Tabriz, and non-cumulative exposure to PM_{10} in (**d**) Tehran, (**c**) Mashhad, and (**f**) Tabriz

In Mashhad and Tabriz, no significant associations were observed. In both cities, the estimates decreased in middle lag-days, and then increased in longer lag-days.

Figure 4 depicts the results of meta-analysis on the association between daily COVID-19 deaths and cumulative and non-cumulative exposure to PM_{10} and $PM_{2.5}$. Both fractions of particulate matter did not show any significant association with death due to COVID-19. In case of PM_{10}, all lag-days in cumulative exposure and lag-days 0 to 3 were positive. For $PM_{2.5}$, the relationships in lag-days 0–1 to 0–3 (for cumulative exposure) and lag-days 0, 1, 2, and 7 (for non-cumulative exposure) were positive. For both PM_{10} and $PM_{2.5}$, the associations in cumulative exposure increased from shorter lag-days up to lag-days 0–2, and then weakened. The inverse trends were observed for non-cumulative exposure. The RRs for same-day exposure to 10 μg/m^3 increase in PM_{10} and $PM_{2.5}$ were 1.06 (95% CI: 0.99, 1.13) and 1.06 (95% CI: 0.93, 1.19), respectively.

Zhu et al. (2020) reported that short-term exposure to $PM_{2.5}$ and PM_{10} in lag-day 0–14 can cause 2.24% (95% CI: 1.02 to 3.46) and 1.76% (95% CI: 0.89 to 2.63) increase in daily number of COVID-19 deaths [17]. Using linear regression, Yao et al. (2020) found that per 10 μg/m^3 increase in $PM_{2.5}$ and PM_{10} concentrations, the fatality rate of COVID-19 increased by 0.24% (0.01%-0.48%) and 0.26% (0.00%-0.51%), respectively [4]. In Italy, COVID-19 infection was more reported in areas with higher number of days exceeding the limits set for PM_{10} [23]. Copat et al. (2020) by conducting a systematic review concluded that $PM_{2.5}$ and with a less extent PM_{10} can be considered as the triggering factors for increasing the rate of CIVID-19 mortality [8].

Effects of NO_2 and O_3 on mortality

Tables S8 and S9 present the effects of cumulative and non-cumulative exposure to NO_2 and O_3 on COVID-19 deaths in two cities of Tehran and Tabriz. Table S8 in the Supplementary Materials shows that greater associations between NO_2 and COVID-19 deaths with wider confidence intervals can be observed in Tabriz. In Tehran, the associations in lag-days 0–1, 0–2, 0, 1, 2, and 7 were positive; but only the relationship in the lag-day 1 was statistically significant (1.20, 95% CI: 1.00, 1.45 per 10 ppb increase in NO_2). In Tabriz, the association between COVID-19 mortality and cumulative exposure in all lag-days and non-cumulative exposure in lag-days 0, 1, 6, and 7 were positive. However, only the RRs in lag-days 0–1 and 0–2 were statistically significant. Table S9 in the Supplementary Materials indicates the associations for O_3 in Tehran are greater than those in Tabriz. In Tehran, most of the associations were positive, but only non-cumulative exposure in lag-days 4 (1.22, 95% CI: 1.02, 1.46) and 5 (1.18, 95% CI: 1.01, 1.39) per 10 ppb increase in O_3

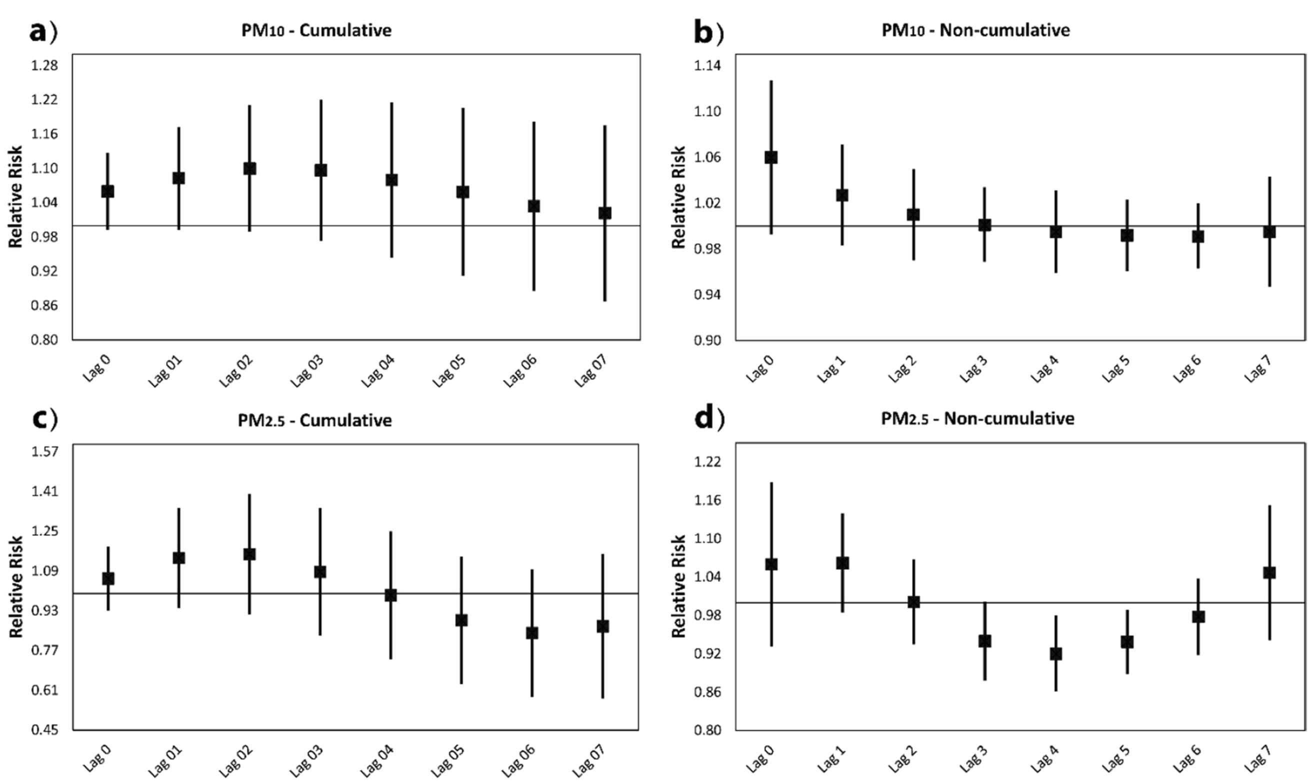

Fig. 4 Results of meta-analysis on the association between daily COVID-19 deaths and: **a** and **b**) cumulative and non-cumulative exposure to PM_{10}, **c** and **d**) cumulative and non-cumulative exposure to $PM_{2.5}$ per 10 μg/m^3 increase in PM concentrations

had statistically significant effects on COVID-19 mortality. In case of Tabriz, none of the associations were significant. The differences between the cities could be due to the distribution of air pollution concentrations, clinical facilities and medications, availability of diagnostic tests, etc. [22].

The results of meta-analysis for NO_2 and O_3 are presented in Fig. 5. The effect of NO_2 in shorter lag-days were positive. COVID-19 mortality in lag-days 0–1 (cumulative exposure) and 1 (non-cumulative exposure) were significantly associated to NO_2 with the RRs of 1.35 (95% CI: 1.04, 1.67) and 1.16 (95% CI: 1.02, 1.31) per 10 ppb increase in the average of NO_2, respectively. This means that cumulative and non-cumulative exposure to NO_2 in these lag-days can increase the risk of death due to COVID-19 by 35% and 16%, respectively. Ogen et al. (2020) reported that exposure to NO_2 can be a contributing factor for higher rates of death due to COVID-19 [24]. In the Zhu et al. study, lower lag-days (0–7) showed weak, non-significant associations [17]. Copat et al. (2020) conducted a review that concluded that NO_2 is a triggering factor for lethality of COVID-19 [8]. In India, high correlation coefficients were found between NO_2 concentration and the absolute number of COVID-19 deaths ($r = 0.79$, $p < 0.05$) and case fatality rate ($r = 0.74$, $p < 0.05$) [25]. These findings are consistent with the present study.

No statistically significant associations were found for O_3. The strongest association was found in lag 0 by an RR of 1.07 (95% CI: 0.84, 1.31) per 10 ppb increase in O_3 concentrations. In case of non-cumulative exposure, the estimates increased after lag-day 2 and positive associations were found. Ozone therapy has been suggested as a potential method of treatment for COVID-19 [26]. This suggestion was put forward at the same time that this and other studies show that ozone can exacerbate the patients' clinical conditions. Zhu et al. (2020) found that COVID-19 daily mortality increased by 4.76% (95% CI: 1.99 to 7.52) per 10 μg/m^3 increase in O_3 concentrations [17]. Zoran et al. (2020) in Italy reported that ozone concentrations were positively correlated with total number of deaths due to COVID-19 [6]. In Italy, COVID-19 infection was reported to be higher in areas with higher number of days exceeding the air quality limits set for ozone [23]. However, another study has suggested that ozone as a natural disinfectant can be the influential factor behind the lower possibility of developing severe effects COVID-19 in residents of high-altitude areas [27]. Although more studies are required to understand the exact mechanisms on interaction between ozone and SARS-CoV-2, the results of epidemiological studies cannot be neglected.

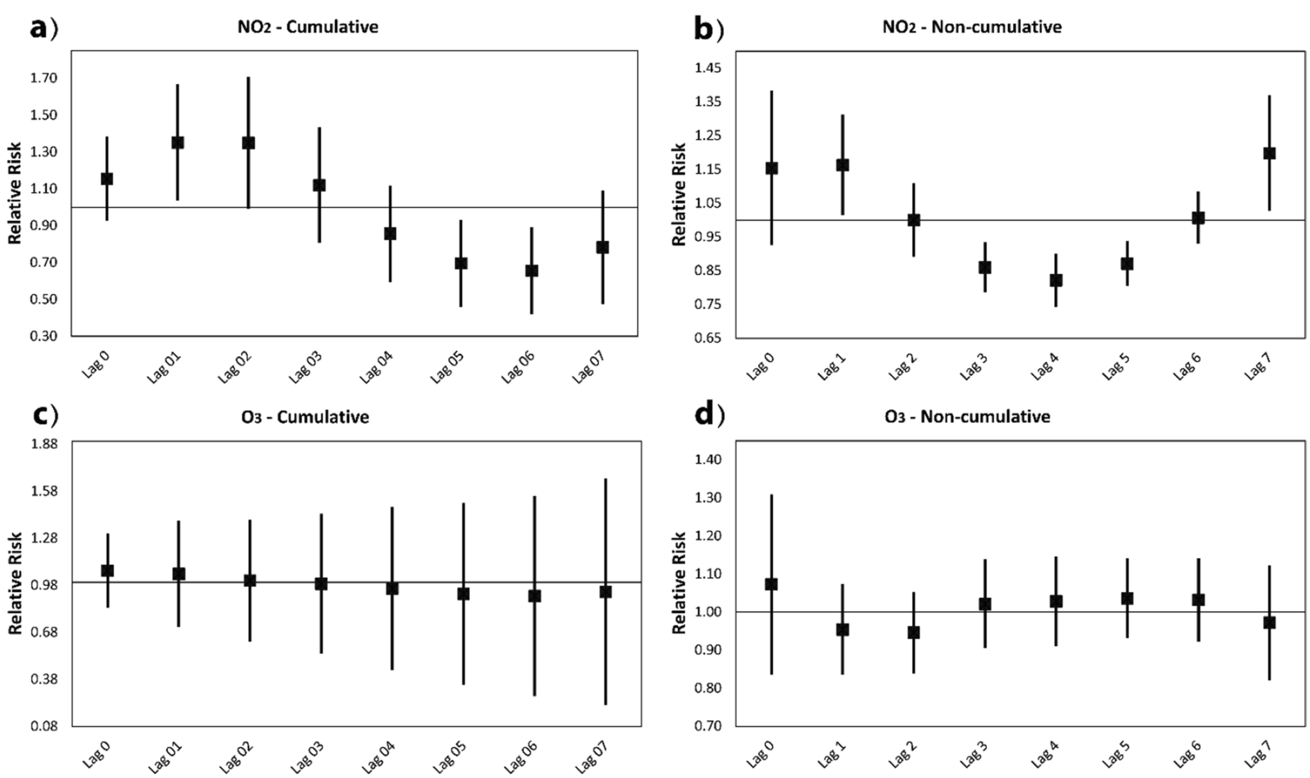

Fig. 5 Results of meta-analysis on the association between daily COVID-19 deaths and: **a** and **b**) cumulative and non-cumulative exposure to 10 ppb increase in NO_2, **c** and **d**) cumulative and non-cumulative exposure to 10 ppb increase in O_3

Strength and limitations

This study provides more evidence that short-term exposures to air pollution influence COVID-19 confirmed cases and daily deaths, especially for the higher air pollutant concentrations are normally observed in Iran comparing to developed countries. Compared to most previous studies, the present study employed a more sophisticated methodology. The use of data from three cities could increase the certainty of the estimates. However, this study has some limitations. First, the study period is short although almost all the period since the emergence of COVID-19 in Iran was included. Second, this study has only included the data for PCR-confirmed cases of death and morbidity. Air pollution affects all COVID-19 patients. However, there are likely to have been many cases that were not considered in the present study because they were not confirmed by a PCR test. Third, the use of data from more cities would be more robust. However, due to the limited data accessibility, only these three locations could be analyzed.

Conclusions

This study aimed to evaluate the association between exposure to air pollution ($PM_{2.5}$, PM_{10}, NO_2, and O_3) and COVID-19 confirmed cases and deaths in three Iranian cities. The associations were separately estimated for each city, and the meta-analyzed to obtain the overall estimates. In case of mortality, particulate matter fractions as well as ground level ozone for several lag-days showed positive but not statistically significant associations. Nitrogen dioxide on lag-day 1 (non-cumulative exposure) and during 0–1 (cumulative exposure) was significantly associated with COVID-19 mortality. For confirmed cases, exposure to $PM_{2.5}$, NO_2, and O_3 over several lag-days showed significant associations. This study showed that air pollution can be a factor leading to exacerbation of COVID-19 incidence and mortality. However, more studies with longer study periods are needed for better quantification of the effect size. Actions should be taken to reduce the exposure of general population and patients to high concentrations of ambient pollutants. Implementing lockdown in cities could reduce the concentration of air pollution, and also the number of COVID-19 cases through decreased population contacts.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40201-021-00736-4.

Acknowledgements The authors want to thank Shahid Beheshti University of Medical Sciences, Tehran, Iran for their full support of this study (grant number #25200).

Funding This study was funded by Shahid Beheshti University of Medical Sciences, Tehran, Iran (grant number #25200).

Data availability For access the data and associated metadata and calculation tools, please contact corresponding author.

Code availability Not applicable.

Declarations

Ethics approval This study was ethically approved by Shahid Beheshti University of Medical Sciences, Tehran, Iran (Ethics code: #IR.SBMU.PHNS.REC.1399.112).

Consent to participate All participants signed a written consent for participation in this study.

Consent for publication Not applicable.

Conflicts of interest/Competing interests The authors declare no conflict of interests.

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