

RESEARCH ARTICLE

Impact of a long-term air pollution exposure on the case fatality rate of COVID-19 patients—A multicity study

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Abstract

Evidence in the literature suggests that air pollution exposure affects outcomes of patients with COVID-19. However, the extent of this effect requires further investigation. This study was designed to investigate the relationship between long-term exposure to air pollution and the case fatality rate (CFR) of patients with COVID-19. The data on air quality index (AQI), PM_{2.5}, PM₁₀, SO₂, NO₂, and O₃ from 14 major cities in China in the past 5 years (2015–2020) were collected, and the CFR of COVID-19 patients in these cities was calculated. First, we investigated the correlation between CFR and long-term air quality indicators. Second, we examined the air pollutants affecting CFR and evaluated their predictive values. We found a positive correlation between the CFR and AQI (1, 3, and 5 years), PM_{2.5} (1, 3, and 5 years), and PM₁₀ (1, 3, and 5 years). Further analysis indicated the more significant correlation for both AQI (3 and 5 years) and PM_{2.5} (1, 3, and 5 years) with CFR, and moderate predictive values for air pollution indicators such as AQI (1, 3, and 5 years) and PM_{2.5} (1, 3, and 5 years) for CFR. Our results indicate that long-term exposure to severe air pollution is associated with higher CFR of COVID-19 patients. Air pollutants such as PM_{2.5} may assist with the prediction of CFR for COVID-19 patients.

KEYWORDS

case fatality rate, COVID-19, long-term air pollution

Abbreviations: AQI, air quality index; CFR, case fatality rate; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; WHO, World Health Organization.

Chang-kai Hou, Ya-fei Qin, Grace Wang, and Quan-lei Liu contributed equally to this work.

1 | INTRODUCTION

The novel coronavirus (COVID-19) was first reported in Wuhan, China, in December 2019,^{1,2} and then spread rapidly worldwide. COVID-19 was declared a pandemic by the World Health Organization (WHO) in March 2020.³ In China, the burden of COVID-19 has recently been curtailed to manageable levels. However, in other countries and regions, the virus is still threatening human life, as indicated by the increasing number of confirmed cases and deaths around the world. According to the data from the WHO, the mortality rate of this epidemic varies in different countries from 0.9% to 18.4%. At present, COVID-19 remains a significant obstacle to the recovery of the world economy and people's everyday lives and functions. Identifying the relevant factors that affect the mortality rate for COVID-19 patients is urgently needed, which may improve the confidence and means available to physicians in the treatment of the COVID-19 infection and reduce public health concerns regarding COVID-19.

Previous studies have found that the morbidity and mortality of COVID-19 patients were related to their general health or presence of comorbidities, such as gender, age, hypertension, diabetes, and obesity.^{4–8} Air pollution can stimulate respiratory and systemic inflammatory responses, and the primary affected organ of both COVID-19 and air pollution is the respiratory system. It has been demonstrated that air pollution increases the incidence of airway inflammation and lung diseases.^{9,10} Recent research has indicated

that short-term exposure to air pollution increases the risk of COVID-19 infection,^{11–13} and the relationship between the long-term air pollution exposure and the outcome of patients with COVID-19 has been investigated but no consensus has been reached.^{14,15} In this study, the objective was to investigate the effects of long-term exposure to air pollution on the case fatality rate (CFR) of patients with COVID-19 in 14 cities in China.

2 | METHODS

2.1 | Data collection

Inclusion criteria: (I) Major cities in China; (II) more than 100 confirmed cases of COVID-19 in the city until April 28th, 2020; and (III) available air quality data of the city on the China Air Quality Online Monitoring and Analysis Platform (<https://www.aqistudy.cn>).

The number of confirmed cases, deaths, and discharges during the epidemic period in the city were archived from the official websites of national or urban Health Commissions (<http://www.nhc.gov.cn>). The CFR of COVID-19 patients in the city was calculated as $CFR = \text{number of deaths} / (\text{number of deaths} + \text{number of discharges})$.

Data of air quality index (AQI), PM_{2.5}, PM₁₀, SO₂, NO₂, and O₃ across the same time period for the 14 cities were collected,

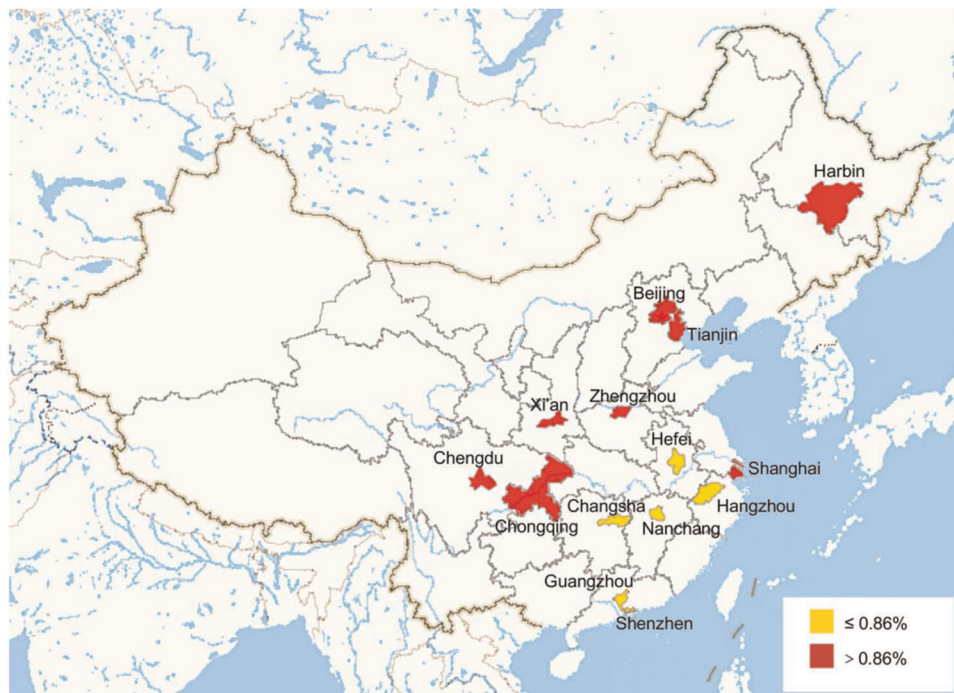


FIGURE 1 Geographic patterns of COVID-19 CFR in the 14 cities in China till April 28th, 2020. CFR, case fatality rate

TABLE 1 Descriptive statistics on COVID-19 case fatality rate and long-term air pollution indicators (AQI, PM2.5, NO₂) in 14 representative cities of China

cities	Total cured	Total death	Case fatality rate (%)	AQI (1 year)	AQI (3 years)	AQI (5 years)	PM2.5 (1 year) $\mu\text{g}/\text{m}^3$	PM2.5 (3 years) $\mu\text{g}/\text{m}^3$	PM2.5 (5 years) $\mu\text{g}/\text{m}^3$	NO ₂ (1 year) $\mu\text{g}/\text{m}^3$	NO ₂ (3 years) $\mu\text{g}/\text{m}^3$	NO ₂ (5 years) $\mu\text{g}/\text{m}^3$
Total	4247	47	1.09	79.28 ± 23.68	80.60 ± 23.79	84.17 ± 27.03	39.45 ± 21.47	42.26 ± 22.08	47.80 ± 25.81	36.40 ± 10.96	39.53 ± 11.82	41.81 ± 12.82
Hangzhou	181	0	0.00	75.75 ± 48.18	77.61 ± 33.77	80.92 ± 36.52	32.91 ± 8.45	37.47 ± 13.15	42.87 ± 16.02	38.42 ± 11.87	40.33 ± 11.89	42.55 ± 11.53
Nanchang	230	0	0.00	70.50 ± 12.01	67.61 ± 12.62	69.92 ± 14.35	35.33 ± 11.71	33.47 ± 13.93	37.18 ± 14.05	32.08 ± 11.04	33.19 ± 10.30	32.9 ± 11.95
Guangzhou	479	1	0.21	73.75 ± 17.44	71.47 ± 13.45	71.12 ± 12.59	27.75 ± 8.96	30.67 ± 10.30	33.17 ± 9.99	42.5 ± 10.88	45.08 ± 9.73	46.1 ± 10.70
Hefei	173	1	0.57	78.67 ± 11.91	82.58 ± 17.71	85.6 ± 20.21	38.83 ± 13.16	45.03 ± 18.96	51.2 ± 21.41	39.17 ± 11.34	41.72 ± 11.93	42.55 ± 12.25
Shenzhen	445	3	0.67	57.42 ± 18.38	53.58 ± 13.76	53.63 ± 13.23	23.25 ± 8.80	24.39 ± 8.87	25.55 ± 8.66	24.67 ± 6.46	26.22 ± 5.30	28.65 ± 5.94
Changsha	240	2	0.83	78.83 ± 15.89	79.22 ± 19.38	80.6 ± 19.24	42.75 ± 16.16	45.81 ± 21.20	49.27 ± 20.54	30.58 ± 10.43	32.67 ± 10.72	24.63 ± 10.71
Chongqing	573	6	1.04	67.83 ± 14.19	71.69 ± 14.44	74.02 ± 14.80	35.33 ± 13.23	37.86 ± 15.53	43.32 ± 16.58	36.83 ± 6.90	40.03 ± 7.17	42.28 ± 7.38
Shanghai	581	7	1.19	70 ± 9.52	74.19 ± 13.36	77.4 ± 13.90	32.42 ± 9.97	34.86 ± 10.56	39.37 ± 13.01	37.92 ± 10.41	40.11 ± 11.41	41.67 ± 11.71
Tianjin	182	3	1.62	97.67 ± 21.46	97.36 ± 17.82	99.8 ± 22.29	49.67 ± 18.87	51.53 ± 16.29	58.77 ± 22.34	40.00 ± 12.37	42.69 ± 11.97	44.33 ± 14.23
Beijing	536	9	1.65	84.42 ± 17.93	88.53 ± 18.71	99.05 ± 25.98	40.33 ± 11.15	45.56 ± 12.12	57.25 ± 25.16	33.00 ± 8.79	37.64 ± 9.31	42.03 ± 12.59
Chengdu	163	3	1.81	74.5 ± 15.81	81.06 ± 18.93	88.35 ± 23.05	40.92 ± 17.74	44.64 ± 19.24	51.27 ± 23.75	38.30 ± 7.27	43.61 ± 9.33	47.53 ± 10.24
Harbin	195	4	2.01	77.33 ± 45.18	78.42 ± 33.77	82.17 ± 36.52	48.25 ± 43.99	47.14 ± 34.93	51.87 ± 36.87	32.08 ± 11.07	36.69 ± 8.65	39.32 ± 12.31
Xi'an	117	3	2.50	99.25 ± 29.32	103.64 ± 32.23	107.75 ± 37.50	54.25 ± 34.19	57.31 ± 34.95	63.07 ± 39.32	43.75 ± 10.72	49.72 ± 13.23	50.83 ± 13.53
Zhengzhou	152	5	3.18	104 ± 21.83	101.39 ± 25.86	108.12 ± 30.13	52 ± 28.62	55.89 ± 28.12	65.07 ± 33.26	40.25 ± 9.87	45.69 ± 11.40	49.93 ± 12.75

Note: "(1 year)" is the abbreviation of "Average in the past year"; "(3 years)" is the abbreviation of "Average in the past 3 years"; "(5 years)" is the abbreviation of "Average in the past 5 years."

and the average values in the past 1-, 3-, and 5-year period were calculated.

2.2 | Statistical analysis

SPSS software Version 25.0 (IBM; Armonk) was used for all the statistical analyses. Shapiro–Wilk test was used to analyze whether the indicator conformed to the normal distribution. A simple scatter plot was used to illustrate the relationship between air quality indicators of 1, 3, and 5 years and the CFR. The Pearson correlation or the Spearman test was performed for normally distributed variables. The average CFR of the recorded Chinese population (excluding Hubei Province) is 0.86%. This cohort was divided into a low CFR group (CFR <0.86%; *n* = 6) and a high CFR group (CFR >0.86%; *n* = 8). All continuous variables were presented as the mean ± *SD*, and were compared with an

independent *t* test for normally distributed variables. In addition, the receiver operating characteristic curve (ROC) was determined. A *p* value of less than .05 was considered statistically significant.

3 | RESULTS

A total of 14 cities were included in this study (Figure 1 and Table 1). Of all the participants, 4247 COVID-19 patients recovered and 47 died. The overall CFR was 1.09%. The average daily concentrations of AQI, PM2.5, PM10, SO₂, NO₂, and O₃ in the past 5 years were 84.17 μg/m³, 47.80 μg/m³, 75.88 μg/m³, 12.36 μg/m³, 41.81 μg/m³, and 90.59 μg/m³, respectively (Table 1 and Table S1). The trend of several air pollution indicators in these 14 cities over the past 5 years is shown in Figure 2A–F.

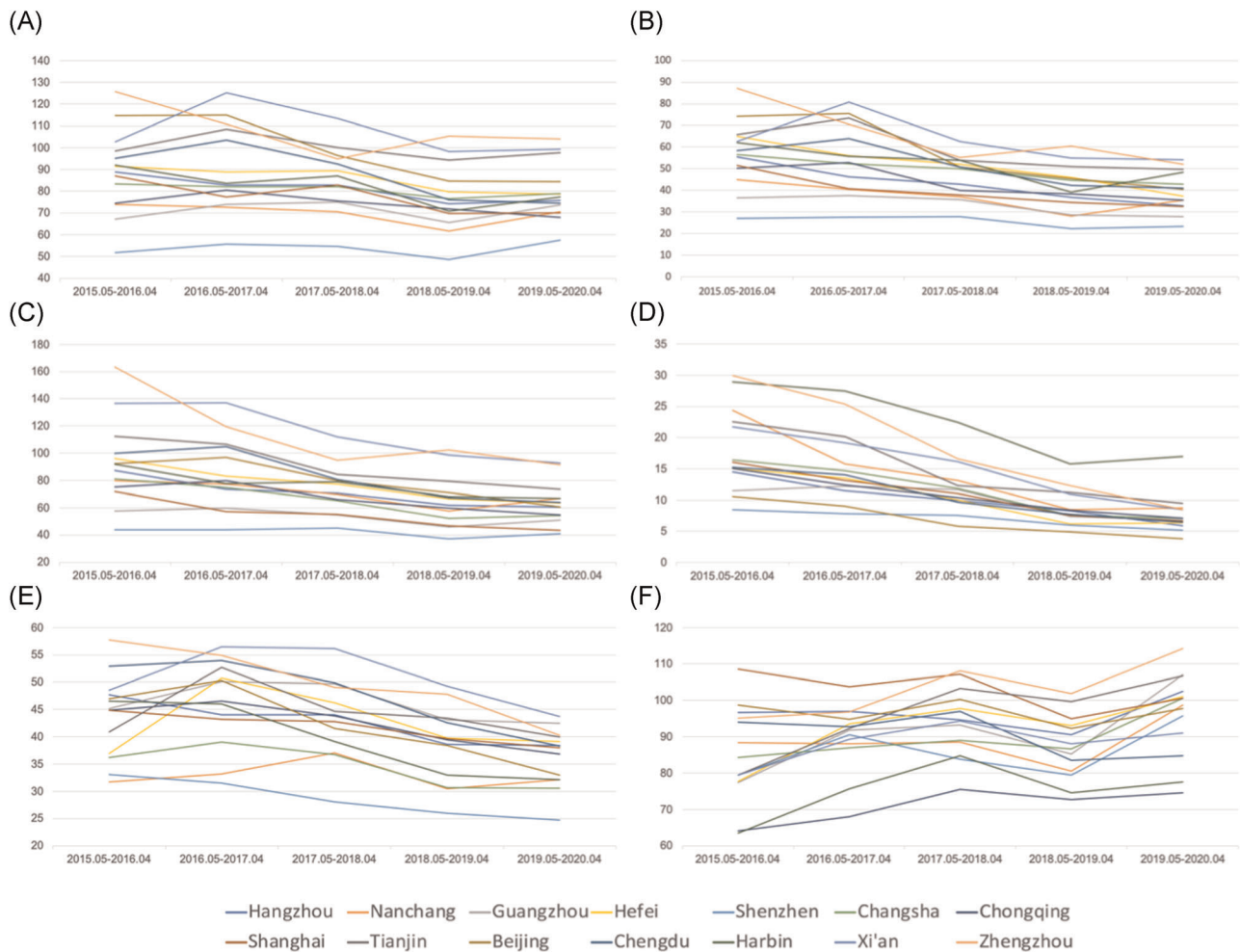


FIGURE 2 The changes of air quality indicators in these 14 cities over the past 5 years. (A) AQI; (B) PM2.5; (C) PM10; (D) SO₂; (E) NO₂; (F) O₃. AQI, air quality index

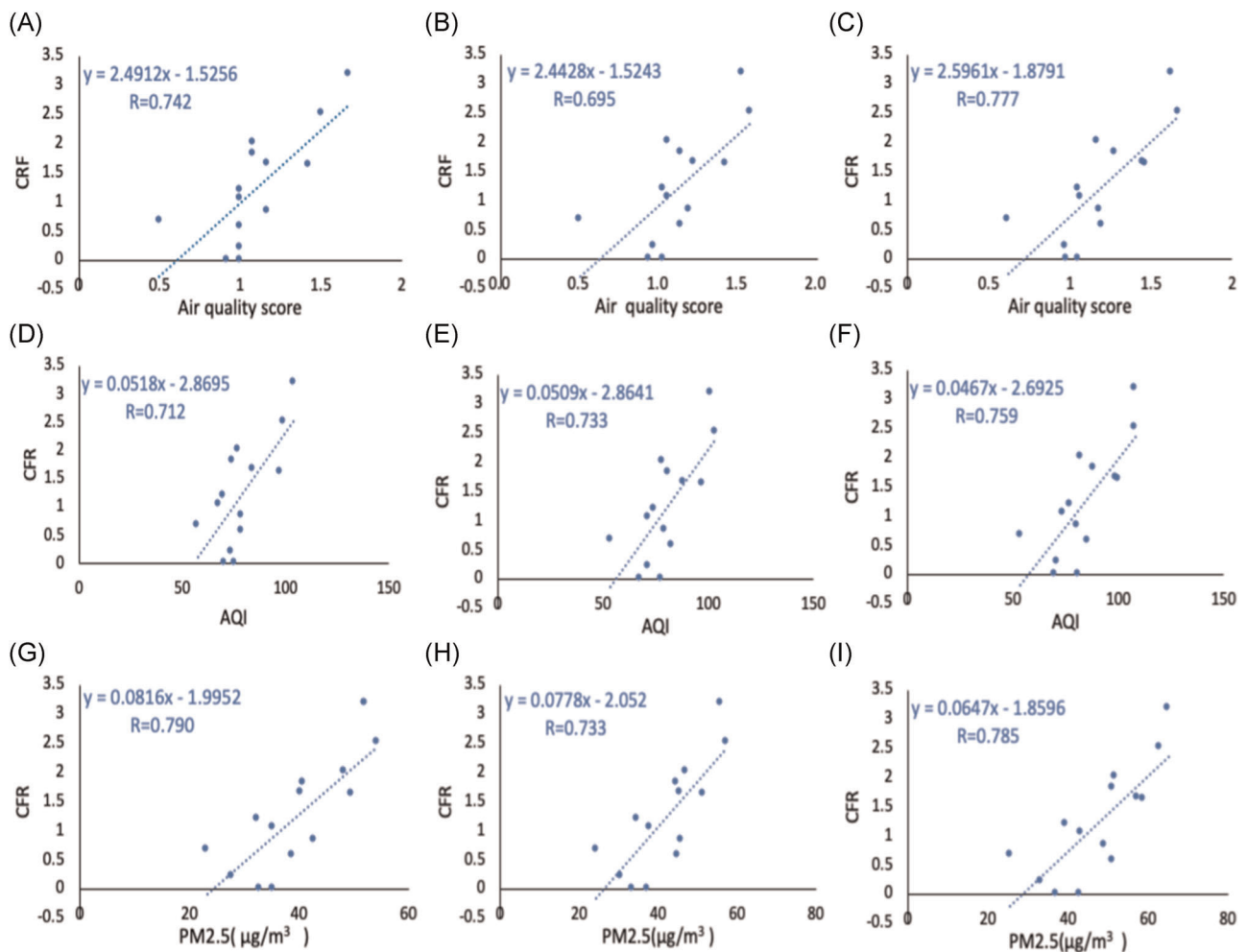


FIGURE 3 Scatterplots showing the relationships between CFR and air quality indicators. (A–C) Air quality score in the past 1, 3, and 5 years, respectively. (D–F) AQI in the past 1, 3, and 5 years, respectively. (G–I) PM2.5 in the past 1, 3, and 5 years, respectively. AQI, air quality index; CFR, case fatality rate

3.1 | Correlation test between CFR and long-term air quality indicators

As shown in Figure 3 and Table 2, there was a moderate positive correlation between the CFR and AQI (1, 3, and 5 years), PM2.5 (1, 3, and 5 years), and PM10 (1, 3, and 5 years). The CFR of COVID-19 patients increased where the levels of long-term AQI, PM2.5, and PM10 were higher. However, the correlation between the CFR and the levels of SO_2 , NO_2 , and O_3 were not statistically significant.

3.2 | Comparison of air quality between high CFR group and low CFR group

As of April 28th, 2020, 13,962 cases were recovered in China (excluding Hubei Province), with a total of 121 deaths.

This resulted in a national CFR (excluding Hubei Province) of 0.86%. Based on this number, our cohort was divided into a low CFR group ($\text{CFR} \leq 0.86\%$; $n = 6$) and a high CFR group ($\text{CFR} > 0.86\%$; $n = 8$). The list and geographical distribution of each group is shown in Figure 1.

As compared with the low CFR group, the AQI (3 and 5 years) and PM2.5 (1, 3, and 5 years) were significantly higher in the high CFR group ($p < .05$) (Table 3). However, there was no significant difference in the PM10, SO_2 , NO_2 , and O_3 between these two groups ($p > .05$).

3.3 | Predictive values of various indicators for CFR

ROC curve was used to calculate the predictive value of air pollutants to CFR, and it showed the area under the curve of

TABLE 2 Correlation test results of various air pollution indicators and case fatality rate

Variables	Correlation coefficient	p Value
AQI (1 year)	R = .712	.004 ^a
AQI (3 years)	R = .733	.003 ^a
AQI (5 years)	R = .759	.002 ^a
PM2.5 (1 year, $\mu\text{g}/\text{m}^3$)	R = .790	.001 ^a
PM2.5 (3 years, $\mu\text{g}/\text{m}^3$)	R = .733	.001 ^a
PM2.5 (5 years, $\mu\text{g}/\text{m}^3$)	R = .785	.001 ^a
PM10 (1 years, $\mu\text{g}/\text{m}^3$)	R = .686	.007 ^a
PM10 (3 years, $\mu\text{g}/\text{m}^3$)	R = .744	.002 ^a
PM10 (5 years, $\mu\text{g}/\text{m}^3$)	R = .686	.007 ^a
SO ₂ (1 year, $\mu\text{g}/\text{m}^3$)	rs =0.328	.252
SO ₂ (3 years, $\mu\text{g}/\text{m}^3$)	R = .469	.091
SO ₂ (5 years, $\mu\text{g}/\text{m}^3$)	R = .559	.038 ^a
NO ₂ (1 year, $\mu\text{g}/\text{m}^3$)	R = .280	.332
NO ₂ (3 years, $\mu\text{g}/\text{m}^3$)	R = .471	.089
NO ₂ (5 years, $\mu\text{g}/\text{m}^3$)	R = .523	.055
O ₃ (1 year, $\mu\text{g}/\text{m}^3$)	R = -.074	.800
O ₃ (3 years, $\mu\text{g}/\text{m}^3$)	R = .200	.493
O ₃ (5 years, $\mu\text{g}/\text{m}^3$)	R = .129	.659

Abbreviation: AQI, air quality index.

^aIndicates that this data is statistically significant; "(1 year)" is the abbreviation of "Average in the past year"; "(3 years)" is the abbreviation of "Average in the past 3 years"; "(5 years)" is the abbreviation of "Average in the past 5 years"; R is the result of Pearson correlation test; rs is the result of Spearman correlation test.

AQI (1, 3, and 5 years) and PM2.5 (1, 3, and 5 years) were 0.688, 0.81, 0.854, and 0.823, 0.833, 0.896, respectively. The cut-off values of AQI (5 years) and PM2.5 (1, 3, and 5 years) were 86.98, 39.58, 37.67, and 51.57 $\mu\text{g}/\text{m}^3$, respectively (Table 4 and Figure 4).

4 | DISCUSSION

In this multicity study, we have estimated the association between long-term exposures to common air pollutants and COVID-19 CFR, and have calculated the predictive values for the CFR of COVID-19 patients in these cities. The results show that the levels of AQI, PM2.5, and PM10, but not NO₂ and O₃, are significantly positively correlated with the CFR. Meanwhile, the levels of AQI and PM2.5 were significantly higher in the high CFR

group than those in the low CFR group. Furthermore, ROC curve analysis indicates the most predictive value for CFR is long-term PM2.5. These findings may explain the differences in COVID-19 outcomes between regions. Public health authorities should focus more on these vulnerable populations, who are exposed to severe long-term air pollution.

Previous studies have shown that living environments play an important role in the transmission and outcomes of major viral diseases, namely severe acute respiratory syndrome¹⁶ and H1N1 influenza.¹⁷ The role of the atmospheric environment in COVID-19 cases is not yet fully understood.¹⁸ Frontera et al¹⁹ have reported that the outbreak of COVID-19 may be associated with climate and air pollutants. Other researchers have also found that air pollutants are substantially associated with an increased risk of COVID-19.^{11,13,20–22} Another study has investigated COVID-19 infection in 120 cities in China, indicating that it is closely related to the short-term exposure to PM2.5, PM10, CO, NO₂, and O₃.¹¹ However, the relationship of COVID-19 outcomes with long-term air pollutants is in the early stages of the investigation. The results from this study suggested the significant positive associations between the long-term PM2.5 levels and COVID-19 CFR. Previous studies highlight PM2.5 affecting the airways and the cardiovascular system by penetrating deep into the lung tissue and causing an immune-mediated inflammatory response.^{23–25} Long-time exposure to the PM2.5 has been correlated with increased risks of chronic diseases, including COPD that can progress into lung cancer.^{26,27} In addition, short-term exposure to PM2.5 significantly increases the mortality from various cardiopulmonary diseases, as indicated by a nationwide analysis of 272 Chinese cities.²⁸ Given the close relationship between COVID-19 and the respiratory system, PM2.5 may affect the CFR of COVID-19 patients by eliciting the local immune or inflammatory response.

Despite the lack of observed associations between NO₂ levels with severe outcomes of COVID-19, probably due to the limited numbers of cases in our research, this pollutant may impact COVID-19 outcomes. Dr. Ogen's research team²⁹ found that long-term exposure to NO₂ may be an important cause of death in COVID-19 patients in both Italy and Spain. Liang and Shi¹⁴ conducted a cross-sectional nationwide study to estimate the association between the long-term county-levels of exposure to NO₂, PM2.5, and O₃ and the county-levels of COVID-19 case-fatality and mortality rates in the United States; they found that long-term exposure to NO₂ may enhance the susceptibility to severe COVID-19 outcomes.

In the 14 cities researched in this study, the levels of the most air pollutants, such as NO₂, PM2.5, and PM10, gradually decreased over the past five years (Figure 3), which may be attributed to the increased awareness of environmental protection in China. However, considering that the impact

Variables	Low CFR group	High CFR group	t Value	p Value
AQI (1 year)	72.49 ± 8.021	84.28 ± 14.196	1.832	.092
AQI (3 years)	72.01 ± 10.530	87.04 ± 12.541	2.368	.036*
AQI (5 years)	73.63 ± 11.533	92.08 ± 13.442	2.694	.020*
PM2.5 (1 year, µg/m ³)	33.47 ± 7.152	44.15 ± 8.030	2.575	.024*
PM2.5 (3 years, µg/m ³)	36.14 ± 8.360	46.85 ± 7.966	2.438	.031*
PM2.5 (5 years, µg/m ³)	39.87 ± 9.828	53.75 ± 9.085	2.733	.018*
PM10 (1 year, µg/m ³)	56.15 ± 9.383	68.39 ± 17.208	1.565	.144
PM10 (3 years, µg/m ³)	57.81 ± 10.492	74.64 ± 17.454	2.084	.059
PM10 (5 years, µg/m ³)	66.04 ± 16.174	85.34 ± 20.209	1.855	.088
SO ₂ (1 year, µg/m ³)	6.68 ± 1.220	8.42 ± 3.842	1.059	.311
SO ₂ (3 years, µg/m ³)	8.23 ± 1.315	10.44 ± 4.034	1.280	.225
SO ₂ (5 years, µg/m ³)	10.46 ± 2.320	13.78 ± 5.013	1.497	.160
NO ₂ (1 year, µg/m ³)	34.57 ± 2.702	34.77 ± 1.358	-1.143	.275
NO ₂ (3 years, µg/m ³)	36.54 ± 2.868	42.02 ± 1.529	-1.811	.095
NO ₂ (5 years, µg/m ³)	36.23 ± 3.561	44.74 ± 1.489	-2.205	.065
O ₃ (1 year, µg/m ³)	100.92 ± 3.820	93.41 ± 14.008	-1.446	.185
O ₃ (3 years, µg/m ³)	92.66 ± 4.259	92.72 ± 11.835	0.015	.988
O ₃ (5 years, µg/m ³)	90.65 ± 3.574	90.54 ± 12.019	-0.024	.982

Abbreviations: AQI, air quality index; CFR, case fatality rate.

*Indicates that this data is statistically significant; "(1 year)" is the abbreviation of "Average in the past year"; "(3 years)" is the abbreviation of "Average in the past 3 years"; "(5 years)" is the abbreviation of "Average in the past 5 years".

TABLE 4 ROC curve analysis of case fatality rate

Variables	Cut-off value	AUC	p Value
AQI (1 year)	NA	0.688	.245
AQI (3 years)	NA	0.813	.053
AQI (5 years)	86.98	0.854	.028 ^a
PM2.5 (1 year, µg/m ³)	39.58	0.823	.045 ^a
PM2.5 (3 years, µg/m ³)	37.67	0.833	.039 ^a
PM2.5 (5 years, µg/m ³)	51.57	0.896	.014 ^a

Abbreviations: AQI, air quality index; ROC, receiver operating characteristic curve.

^aIndicates that this data is statistically significant; "(1 year)" is the abbreviation of "Average in the past year"; "(3 years)" is the abbreviation of "Average in the past 3 years"; "(5 years)" is the abbreviation of "Average in the past 5 years."

of air pollutants on human health is mainly mediated by the stimulation of immune and inflammatory responses, it is expected that long-term exposure to air pollutants may cause cumulative adverse effects. Therefore, only investigating the

TABLE 3 Independent sample t test results of various air pollution indicators between high CFR Group and low CFR group

effects of short-term air pollution may not adequately capture the full impact of environmental pollution on COVID-19 prognosis.

This study has several limitations. First, specific patient comorbidities, ethnic characteristics, and social factors, such as population density and access to care, all of which may affect the CFR were not analyzed as this was a population-level study. Second, although our study provided a reference for studying the relationship between long-term air pollution and CFR, it was limited to China and further research with an expanded geographic scope is needed. Finally, as this was a retrospective cohort study with relatively small sample size, there is a risk for sampling error.

5 | CONCLUSION

Long-term exposure to an environment with severe air pollution is associated with increased CFR of COVID-19 patients. Air quality indicators such as PM2.5 may have the potential to predict the CFR of COVID-19 patients.

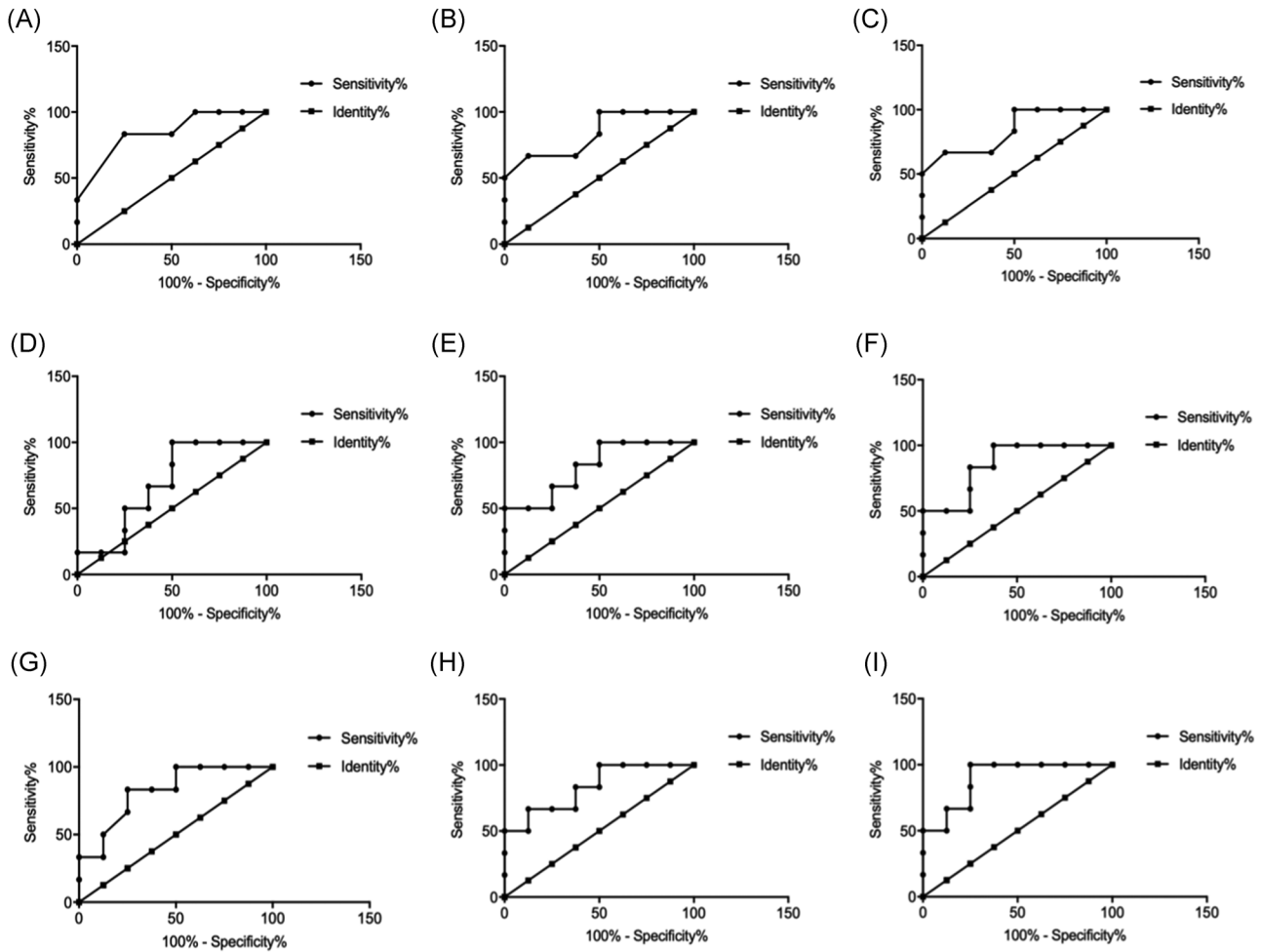


FIGURE 4 ROC curves showing the ability of air quality indicators to predict the CFR. (A–C) Air quality score in the past 1, 3, and 5 years, respectively. (D–F) AQI in the past 1, 3, and 5 years, respectively. (G–I) PM_{2.5} in the past 1, 3, and 5 years, respectively. AQI, air quality index; CFR, case fatality rate

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Conception and design: Hao Wang and Xin-yu Yang; Data analysis and interpretation: Chang-kai Hou and Quan-lei Liu; Collection and

assembly of data: Chang-kai Hou and Ya-fei Qin; Manuscript writing: Chang-kai Hou; Manuscript revision and polishing: Grace Wang; Final approval of manuscript: All authors.

PEER REVIEW

The peer review history for this article is available at <http://publons.com/publon/10.1002/jmv.26807>.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

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SUPPORTING INFORMATION

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