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Short communication

Long-term exposure to fine particulate matter and hospitalization in COVID-19 patients

Angelico Mendy [a,*], Xiao Wu [b], Jason L. Keller [c], Cecily S. Fassler [a], Senu Apewokin [d], Tesfaye B. Mersha [e], Changchun Xie [f], Susan M. Pinney [a]

[a] Division of Epidemiology, Department of Environmental and Public Health Sciences, University of Cincinnati College of Medicine, Cincinnati, OH, USA
[b] Department of Biostatistics, Harvard T.H. Chan School of Public Health, Boston, MA, USA
[c] Center for Health Informatics, Department of Biomedical Informatics, College of Medicine, University of Cincinnati, OH, USA
[d] Division of Infectious Diseases, Department of Medicine, University of Cincinnati College of Medicine, Cincinnati, OH, USA
[e] Division of Asthma Research, Department of Pediatrics, Cincinnati Children's Hospital Medical Center, University of Cincinnati, Cincinnati, OH, USA
[f] Division of Biostatistics and Bioinformatics, Department of Environmental and Public Health Sciences, University of Cincinnati College of Medicine, Cincinnati, OH, USA

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ABSTRACT

Background: Ecological evidence suggests that exposure to air pollution affects coronavirus disease 2019 (COVID-19) outcomes. However, no individual-level study has confirmed the association to date.
Methods: We identified COVID-19 patients diagnosed at the University of Cincinnati hospitals and clinics and estimated particulate matter ≤2.5 μm ($PM_{2.5}$) exposure over a 10-year period (2008–2017) at their residential zip codes. We used logistic regression to evaluate the association between $PM_{2.5}$ exposure and hospitalizations for COVID-19, adjusting for socioeconomic characteristics and comorbidities.
Results: Among the 1128 patients included in our study, the mean (standard deviation) $PM_{2.5}$ was 11.34 (0.70) $\mu g/m^3$ for the 10-year average exposure and 13.83 (1.03) $\mu g/m^3$ for the 10-year maximal exposures. The association between long-term $PM_{2.5}$ exposure and hospitalization for COVID-19 was contingent upon having pre-existing asthma or chronic obstructive pulmonary (COPD) ($P_{interaction} = 0.030$ for average $PM_{2.5}$ and $P_{interaction} = 0.001$ for maximal $PM_{2.5}$). In COVID-19 patients with asthma or COPD, the odds of hospitalization were 62% higher with 1 $\mu g/m^3$ increment in 10-year average $PM_{2.5}$ (odds ratio [OR]: 1.62, 95% confidence interval [CI]: 1.00–2.64) and 65% higher with 1 $\mu g/m^3$ increase in 10-year maximal $PM_{2.5}$ levels (OR: 1.65, 95% CI: 1.16–2.35). However, among COVID-19 patients without asthma or COPD, $PM_{2.5}$ exposure was not associated with higher hospitalizations (OR: 0.84, 95% CI: 0.65–1.09 for average $PM_{2.5}$ and OR: 0.78, 95% CI: 0.65–0.95 for maximal $PM_{2.5}$).
Conclusions: Long-term exposure to $PM_{2.5}$ is associated with higher odds of hospitalization in COVID-19 patients with pre-existing asthma or COPD.

Since its occurrence in China in December 2019, the coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has rapidly spread into a pandemic and global health crisis by March 2020 [1]. Ecological studies suggest that exposure to ambient air pollutants such as fine particulate matter with an diameter ≤2.5 μm ($PM_{2.5}$), may contribute to COVID-19 severity and mortality [2,3]. Possible mechanisms include impaired mucociliary clearance and increased susceptibility to infections as well as the exacerbation of existing respiratory and cardiovascular disease [2,3]. However, these ecological studies correlating geographic rates of COVID-19 outcomes with geographic $PM_{2.5}$ levels suffer from ecological fallacy and require individual-level data for validation [4]. Therefore, we performed the first individual-level study on $PM_{2.5}$ exposure and hospitalizations for COVID-19.

1. Methods

1.1. Data sources

We identified all COVID-19 patients diagnosed at the University of

* Corresponding author. Division of Epidemiology, Department of Environmental & Public Health Sciences, The University of Cincinnati College of Medicine, 160 Panzeca Way, Room 335, Cincinnati, OH, 45267.
E-mail address: angelico.mendy@uc.edu (A. Mendy).

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Cincinnati healthcare system (UC Health) between March 13, 2020 and July 5, 2020 using the electronic medical record system. UC Health consists of hospitals and clinics located in the greater Cincinnati metropolitan area which has a population of over 2 million people [1]. We identified 1421 COVID-19 patients and after exclusion of 293 patients with missing data (225 for smoking, 65 for zip code, and 3 for sex), 1128 participants were included in our study. The University of Cincinnati Institutional Review Board (IRB) exempted the study from IRB approval since it used a de-identified dataset stripped of all Health Insurance Portability and Accountability Act (HIPPAA) identifiers.

1.2. Hospitalization

Hospitalization defined as admission for a duration of ≥24 h to a hospital or clinic within the UC healthcare system for COVID-19 following the diagnosis of the infection. The delay between COVID-19 diagnosis and hospitalization was no more than a week and the diagnosis of COVID-19 was again confirmed at admission to the hospital.

1.3. Fine particulate matter

$PM_{2.5}$ exposure was estimated on a 0.01 ° × 0.01 ° grid using a validated exposure prediction model merging satellite, modeled, and monitored $PM_{2.5}$ data [5]. Zonal statistics were used to aggregate $PM_{2.5}$ exposure estimates at the patients' residential zip codes over the 10-year period from 2008 to 2017.

1.4. Covariates

Sociodemographic characteristics such as age at COVID-19 diagnosis, sex, race/ethnicity, and smoking were self-reported. The median household income at residential zip code was estimated using 2018 income statistics from the Census Bureau [6]. Comorbidities were defined using the 10th revision of the International Classification of Diseases (ICD10) codes. They included obesity (E66), diabetes (E11), asthma (J45), chronic obstructive pulmonary disease (COPD) (J44), chronic kidney disease (N18), cardiovascular disease (I00–I99), and neoplasm or history of neoplasm (C00-D49).

1.5. Statistical analysis

Descriptive analyses were performed and logistic regression was used to estimate the odds ratios (OR) and corresponding 95% confidence intervals (CI) for hospitalization associated with 1 μg/m^3 increase in average and maximal $PM_{2.5}$ concentrations. The models were adjusted for age and median household income used as continuous variables as well as sex, race/ethnicity, cigarette smoking, and comorbidities (obesity, diabetes, asthma, COPD, cardiovascular disease, chronic kidney disease, and neoplasm or history of neoplasm) used as categorical variables. To identify subgroups of patients vulnerable to COVID-19 hospitalization in relation to $PM_{2.5}$ exposure, we tested each covariate for effect modification with a multiplicative interaction term included in the model one at a time and calculated the interaction *P*-values ($P_{interaction}$). The analyses were performed using SAS Version 9.4 (SAS Institute, Cary, NC) and p-values <0.05 were considered statistically significant.

2. Results

2.1. Description results

The 1128 patients included in our study had median age of 46 years (interquartile range: 32–62 years). They were mostly residents of Ohio (96.6%) and the remaining 3.4% resided in Kentucky, Indiana, New York, South Carolina, West Virginia, and Iowa. The 10-year average $PM_{2.5}$ had a mean (standard deviation) of 11.34 (0.70) μg/m^3 and ranged from 7.70 to 12.73 μg/m^3. The 10-year maximal $PM_{2.5}$ had a mean (standard deviation) of 13.83 (1.03) μg/m^3 and ranged from 9.90 to 15.70 μg/m^3. As shown in Table 1, $PM_{2.5}$ levels were higher in women, in non-Hispanic Blacks, in participants with a median household income below $50,000, and in patients with diabetes, asthma, or COPD.

2.2. Association of $PM_{2.5}$ with hospitalization

2.2.1. Adjusted analysis

In logistic regression analysis adjusted for covariates, the association of long-term exposure to $PM_{2.5}$ with COVID-19 hospitalization was contingent upon the presence of a pre-existing respiratory disease (i.e. asthma or COPD) ($P_{interaction} = 0.030$ for average $PM_{2.5}$ and $P_{interaction} = 0.001$ for maximal $PM_{2.5}$). In COVID-19 patients with respiratory disease, the odds of hospitalization were increased by 62% with 1 μg/m^3 increment in average $PM_{2.5}$ (OR: 1.62, 95% CI: 1.00–2.64) and by 65% with 1 μg/m^3 increase in maximal $PM_{2.5}$ (OR: 1.65, 95% CI: 1.16–2.35) (220 COVID-19 patients, including 88 hospitalized). An inverse relationship was observed between maximal $PM_{2.5}$ and hospitalization among COVID-19 patients without pre-existing respiratory disease (OR: 0.78, 95% CI: 0.65–0.95) (908 COVID-19 patients, including 228 hospitalized) (Fig. 1).

In analysis stratified by asthma and COPD, the odds hospitalization for COVID-19 associated with 1 μg/m^3 of maximal $PM_{2.5}$ was 82% higher in patients with asthma (OR: 1.82, 95% CI: 1.13–2.93) (169 COVID-19 patients, including 55 hospitalized) ($P_{interaction} = 0.008$ for effect modification by asthma) and 65% higher in those with COPD (OR: 1.65, 95% CI: 1.05–2.60) (107 COVID-19 patients, including 57 hospitalized) ($P_{interaction} = 0.017$ for effect modification by COPD) (Fig. 1). $PM_{2.5}$ association with COVID-19 hospitalization did not differ by the other covariate.

2.2.2. Unadjusted analysis

The unadjusted estimates for the association between exposure to $PM_{2.5}$ and COVID-19 hospitalization overall and by pre-existing respiratory disease are reported in Supplementary Tables 1 and 2 Average and maximal $PM_{2.5}$ was associated with higher odds of hospitalization in COVID-19 patients with respiratory disease (OR: 1.81, 95% CI: 1.18–2.78 for average $PM_{2.5}$ and OR: 1.62, 95 CI: 1.21–2.17 for maximal $PM_{2.5}$). However, they were not associated with increased hospitalization in those without the respiratory conditions (OR: 0.83, 95% CI: 0.67–1.02) ($P_{interaction} = 0.001$) for average $PM_{2.5}$ (OR: 0.82, 95% CI: 0.71–0.95) ($P_{interaction}<0.001$) for maximal $PM_{2.5}$.

3. Discussion

This is the first individual-level study on $PM_{2.5}$ and COVID-19 outcomes. The results suggest that long-term exposure to $PM_{2.5}$ is associated with higher odds of hospitalization in COVID-19 patients with pre-existing asthma or COPD.

These results are consistent with reports that $PM_{2.5}$ exposure may exacerbate asthma and COPD by causing airway inflammation through the release of proinflammatory cytokines and free radicals from activated alveolar macrophages [3,7,8]. In addition to causing airway oxidative stress and mucosal damage, $PM_{2.5}$ can impair mucociliary clearance of pathogens and natural killer cell response and increase susceptibility to COVID-19 and COVID-19 severity [3,7,8]. The reason for the inverse association between maximal $PM_{2.5}$ and hospitalization in COVID-19 patients without respiratory disease is unclear and should be further investigated. It is possible that in this population, healthier patients who had lower risk of COVID-19 hospitalization tended to live in areas of higher $PM_{2.5}$ exposure or that we were unable to account for unmeasured potential confounders. Limitations of our study include the estimation of $PM_{2.5}$ exposure at the residential zip-code level and from 2008 to 2017 since data for more precise locations and for the years

Table 1
$PM_{2.5}$ levels by characteristics of study participants.

Characteristics	N (%)	Average $PM_{2.5}$ ($\mu g/m^3$)		Maximal $PM_{2.5}$ ($\mu g/m^3$)	
		Mean (SD)	P-value	Mean (SD)	P-value
All participants	1128 (100)	11.34 (0.70)		13.83 (1.03)	
Age groups			0.17		0.94
<60 years	800 (70.9)	11.32 (0.66)		13.83 (0.96)	
≥60 years	328 (29.1)	11.39 (0.79)		13.83 (1.17)	
Sex			0.04		0.11
Men	525 (46.5)	11.29 (0.68)		13.78 (1.02)	
Women	603 (53.5)	11.38 (0.71)		13.87 (1.04)	
Race/ethnicity			<0.001		<0.001
Non-Hispanic Whites	304 (27.0)	11.11 (0.83)		13.27 (1.18)	
Non-Hispanic Blacks	505 (44.8)	11.50 (0.64)		14.17 (0.92)	
Hispanics	242 (21.5)	11.30 (0.56)		13.91 (0.69)	
Other	77 (6.8)	11.32 (0.59)		13.61 (0.83)	
Median household income			<0.001		<0.001
< $50,000	459 (40.9)	11.50 (0.73)		14.25 (0.97)	
≥ $50,000	664 (59.1)	11.23 (0.65)		13.54 (0.97)	
Cigarette Smokers			0.10		0.056
Never	771 (68.4)	11.31 (0.66)		13.78 (0.95)	
Past & current	357 (31.6)	11.39 (0.78)		13.92 (1.17)	
Obesity			0.34		0.571
No	844 (74.8)	11.33 (0.67)		13.82 (1.00)	
Yes	284 (26.2)	11.38 (0.78)		13.86 (1.26)	
Diabetes			0.01		0.013
No	833 (73.8)	11.31 (0.68)		13.78 (1.00)	
Yes	295 (27.2)	11.42 (0.74)		13.96 (1.09)	
Asthma			<0.001		<0.001
No	959 (85.0)	11.31 (0.70)		13.77 (1.03)	
Yes	169 (15.0)	11.52 (0.65)		14.14 (0.98)	
COPD			<0.001		<0.001
No	1021 (90.5)	11.32 (0.69)		13.79 (1.01)	
Yes	107 (9.5)	11.56 (0.72)		14.23 (1.12)	
Cardiovascular disease			0.38		1.00
No	538 (47.7)	11.32 (0.65)		13.83 (0.97)	
Yes	590 (52.3)	11.36 (0.74)		13.83 (1.08)	
Chronic kidney disease			0.54		0.36
No	982 (87.1)	11.33 (0.68)		13.82 (1.01)	
Yes	146 (22.9)	11.38 (0.80)		13.91 (1.18)	
Neoplasm/history of neoplasm			0.30		1.00
No	873 (77.4)	11.33 (0.70)		13.83 (1.01)	
Yes	255 (22.6)	11.38 (0.70)		13.83 (1.08)	
COVID-19 hospitalization			0.90		0.85
No	818 (72.5)	11.34 (0.66)		13.83 (0.97)	
Yes	310 (27.5)	11.34 (0.79)		13.82 (1.17)	

Abbreviations: $PM_{2.5}$, Particulate matter ≤ 2.5 μm; SD, standard deviation; COPD, Chronic Obstructive pulmonary disease; COVID-19, Coronavirus disease 2019. P-values for difference in $PM_{2.5}$ calculated using *t*-test or analysis of variance.

2018 and 2019 was not available. However, if exposure misclassification exists from estimating $PM_{2.5}$ exposure at the zip-code level, it is expected to be non-differential, attenuating the associations [9].

In conclusion, long-term exposure to $PM_{2.5}$ was associated with higher odds of hospitalization in COVID-19 patients with pre-existing asthma or COPD. Independent replications are needed to confirms these results. If the observed associations are confirmed in future studies and are indeed causal, appropriate measures to prevent SARS-CoV-2 infection particularly in patients with asthma or COPD residing in high $PM_{2.5}$ exposure areas could reduce COVID-19 hospitalization and morbidity.

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Disclosures

The authors have no disclosure related to the submitted manuscript.

AM takes full responsibility for the integrity of the dataset and the analysis results. The SAS codes and datasets without patients' identifiable information will be made available for the sole purpose of reproducing the findings upon reasonable request.

CRediT authorship contribution statement

Angelico Mendy: Conceptualization, Formal analysis, Writing – original draft, Writing – review & editing, contributed to the study concept and design, analysis and interpretation of data, and writing of the manuscript, reviewed the manuscript for intellectual content. **Xiao Wu:** Writing – original draft, contributed to the interpretation of data and writing of the manuscript, contributed to the collection of the dataset. **Jason L. Keller:** contributed to the collection of the dataset. **Cecily S. Fassler:** Writing – original draft, contributed to the interpretation of data and writing of the manuscript. **Senu Apewokin:** Writing –

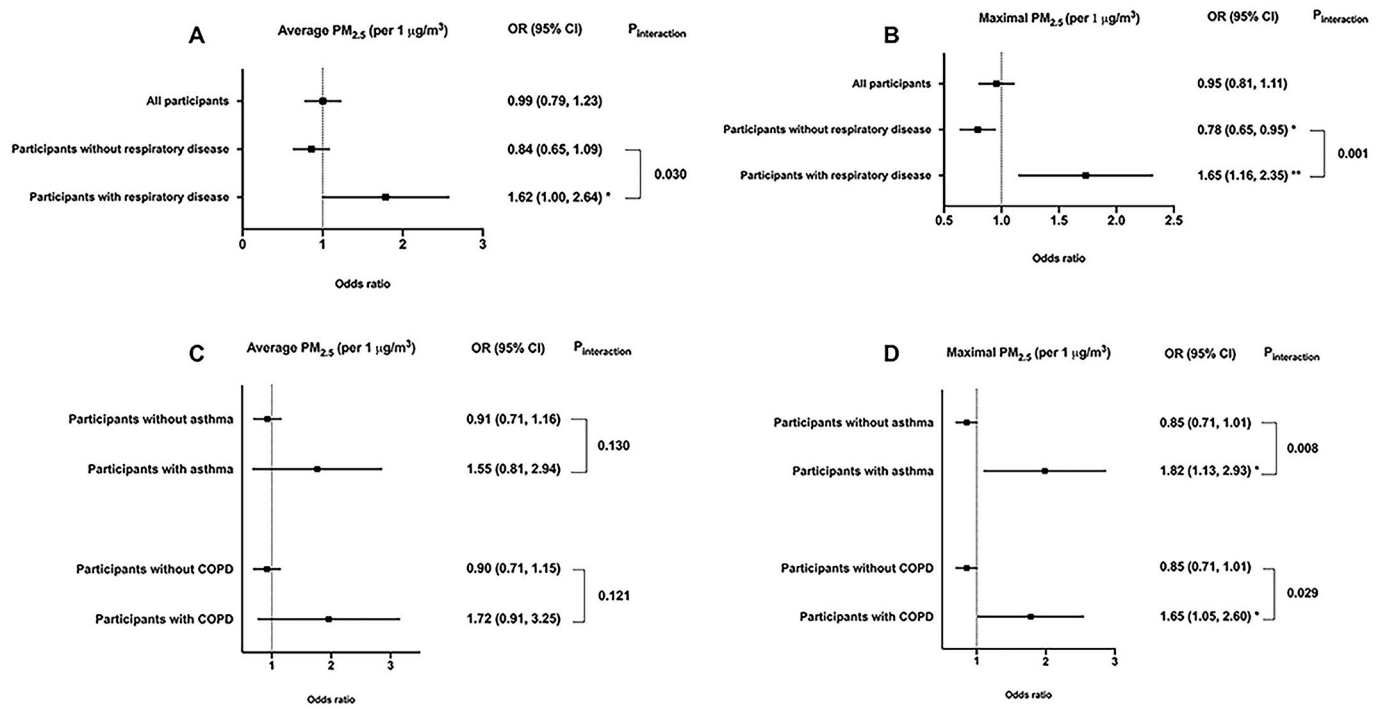

Fig. 1. Odds ratios (OR) and 95% confidence interval (CI) for association of 1 μg/m^3 increase in average and maximal $PM_{2.5}$ exposure with COVID-19 hospitalization. In Panels A and B, OR (95% CI) reported for 1 μg/m^3 increase in average (panel A) and maximal (panel B) $PM_{2.5}$ in all participants and in participants with and without respiratory disease. In Panels C and D, OR (95% CI) reported for 1 μg/m^3 increase in average (panel C) and maximal (panel D) $PM_{2.5}$ in participants with and without asthma or with and without COPD. $PM_{2.5}$ association with COVID-19 hospitalization was different by respiratory disease for average $PM_{2.5}$ (panel A) and for maximal $PM_{2.5}$ (panels B and D). Models adjusted for age, sex, race/ethnicity, median household income, cigarette smoking, and comorbidities (obesity, diabetes, asthma, COPD, cardiovascular disease, chronic kidney disease, and neoplasm or history of neoplasm). *P < 0.05 **P < 0.01.

original draft, contributed to the interpretation of data and writing of the manuscript. **Tesfaye B. Mersha:** Writing – original draft, contributed to the interpretation of data and writing of the manuscript. **Changchun Xie:** Writing – original draft, contributed to the interpretation of data and writing of the manuscript. **Susan M. Pinney:** Writing – original draft, contributed to the interpretation of data and writing of the manuscript.

Declaration of competing interest

The authors have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmed.2021.106313.

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