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Ambient Air Quality and Fatal Asthma Exacerbations among Children in North Carolina

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Abstract

Background: Little is known about the role of air quality in fatal asthma exacerbations among children.

Methods: We collected information about 80 deaths that occurred in North Carolina from 2001 through 2016, among children aged 5–17 years, with asthma identified as the primary cause of death. We linked information about each death with county-level estimates of particulate matter ≤2.5 μm ($PM_{2.5}$) and ozone (O_3). Using the linked data, we conducted a case–crossover analysis of associations between $PM_{2.5}$ and O_3 lagged by 3–5 days with the odds of fatal asthma exacerbations.

Results: In the highest tertile of $PM_{2.5\ lag(3–5)}$, the odds of a fatal exacerbation of asthma were more than twice the odds in the lowest tertile (odds ratio = 2.2; 95% confidence interval = 1.1, 4.6).

Conclusion: These findings from North Carolina provide evidence to support the hypothesis that ambient air pollution increases the risk of fatal exacerbations of asthma among children.

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The authors do not have permission to share the analytic dataset. The case data and environmental data are publicly available. The computing code used to generate the results may be requested from the corresponding author.

Keywords

Air pollution; Asthma; Child; Epidemiology; Mortality

Death is a rare but devastating outcome of asthma. In 2020, an estimated 6% of children in the United States had current asthma, and 204 deaths among children under the age of 18 years were attributed to asthma.[1] Despite this burden, little is known about environmental risk factors for fatal exacerbations of asthma, especially among children.[2] Air quality is a well-recognized trigger of asthma symptoms in children.[3,4] To date, however, to our knowledge, only a few epidemiologic studies are available that describe the role of air quality in fatal asthma exacerbations. We conducted this study to investigate associations between particulate matter ≤2.5 μm in aerodynamic diameter ($PM_{2.5}$) and ozone (O_3), two ambient air pollutants associated with airway hyperresponsiveness, airway inflammation, and oxidative stress,[3] with fatal exacerbations of asthma among children.

METHODS

For this analysis, we analyzed data collected for a parent study of fatal exacerbations of asthma among children in North Carolina.[5] For the parent study, records from the North Carolina Office of the Chief Medical Examiner were reviewed to identify deaths that occurred in North Carolina from 1 January 1999 to 31 December 2012, among individuals under 19 years of age, and for whom asthma (International Statistical Classification of Diseases and Related Health Problems, Tenth Revision:[6] J45 and J46) was identified as the primary cause of death.[5] For the present analysis, we collected additional data to identify deaths through 2016 and excluded deaths in 1999–2000, resulting in a final study period of 1 January 2001 to 31 December 2016. We restricted our analysis to children 5–17 years of age to exclude deaths that occurred at the youngest ages when asthma diagnoses are most difficult. As a result, we identified 80 decedents and recorded the following data elements: county of occurrence, date of birth, date of death, race, and sex.

For all dates during the study period, we used daily predictions of 24-hour average $PM_{2.5}$ in micrograms per cubic meter ($\mu g/m^3$) and daily maximum 8-hour average O_3 concentrations in parts per billion at 2010 US census tract centroid locations using a Bayesian space-time Downscaler fusion model.[7] We used 2010 US census tract population counts to determine spatial weights to generate weighted daily, county-level estimates of $PM_{2.5}$ and O_3.[8]

We estimated associations between $PM_{2.5}$ and O_3 with the odds of fatal asthma exacerbations using a case–crossover analysis in which we compared exposure estimates for each decedent's county and date of death to those on matched comparison days.[9,10] For each day on which a fatal exacerbation of asthma occurred (i.e., case day), we selected as comparison days all noncase days that occurred on the same day of the week in the same month and year and in the same county as the case (mean: 3.4 matched comparison days per case).[10,11] We regressed case and comparison day status against $PM_{2.5}$ and O_3 using a conditional logistic regression model. $PM_{2.5}$ and O_3 were each parameterized as 3-day averages, where averages were calculated using values 3–5 days before the case or comparison day (i.e., lag days 3–5). This lag period is consistent with existing literature

showing associations between ambient air pollution exposure and respiratory morbidity among children.[12] $PM_{2.5\ lag(3–5)}$ and $O_{3\ lag(3–5)}$ were both included in the final model as tertiles of the distributions of the 271 comparison days.

Following our main analysis, we conducted sensitivity analyses to assess the impacts on our results of adjusting our final model for continuous measures of daily, county-level mean temperature and relative humidity on the case and matched comparison days (sensitivity analysis 1) and on lag days 3–5 (sensitivity analysis 2). Daily, county-level estimates of mean ambient air temperature in degrees Fahrenheit (°F) and mean relative humidity in percentage (%) were generated using predictions from the North American Land Data Assimilation System Phase 2 model[13] at 0.125° spatial resolution. We conducted additional sensitivity analyses in which we replaced tertiles of the $PM_{2.5\ lag(3–5)}$ and $O_{3\ lag(3–5)}$ distributions used in the main model and sensitivity analyses 1 and 2, with continuous measures of each pollutant (sensitivity analyses 3–5).

We conducted all analyses using SAS version 9.4 (SAS Institute, Inc., Cary, North Carolina) and present results as odds ratios (ORs) with 95% confidence intervals (CIs). This study was reviewed by the Wake Forest University School of Medicine Institutional Review Board and determined not to have met the federal definition of research involving human subjects research; it was not subject to Institutional Review Board review at the Centers for Disease Control and Prevention.

RESULTS

Ages of the decedents (n = 80) ranged from 5 to 17 (mean: 11.4) years. Decedents were predominantly male (n = 44, 55%) and Black (n = 64, 83%). Deaths occurred most frequently in February (n = 9), June (n = 10), and December (n = 11).

Table 1 shows $PM_{2.5}$, O_3, temperature, and relative humidity on case and comparison days and $PM_{2.5}$ and O_3 for lag days 0–2 and 3–5. In our final model, the odds of a fatal exacerbation of asthma in the highest tertile of $PM_{2.5\ lag(3–5)}$ were more than twice the odds in the lowest tertile (OR = 2.2; 95% CI = 1.1, 4.6) and $O_{3\ lag(3–5)}$ in the highest tertile, compared to the lowest tertile, was associated with a 60% increase in odds (OR = 1.6; 95% CI = 0.6, 4.8), though the 95% CI was imprecise (Table 2).

Table 3 shows the results of the five sensitivity analyses. Results of sensitivity analysis 1, in which we adjusted our final model for same-day temperature and relative humidity, were similar in direction, magnitude, and precision to those of our main analysis for both $PM_{2.5\ lag(3–5)}$ (middle tertile: OR = 0.7; 95% CI = 0.3, 1.5; highest tertile: OR = 2.5; 95% CI = 1.2, 5.2) and $O_{3\ lag(3–5)}$ (middle tertile: OR = 1.4; 95% CI = 0.7, 2.8; highest tertile: OR = 1.7; 95% CI = 0.6, 5.1). When same-day temperature and relative humidity were replaced with lag day 3–5 averages in sensitivity analysis 2, the ORs were slightly attenuated but again similar in direction and precision for both $PM_{2.5\ lag(3–5)}$ and $O_{3\ lag(3–5)}$.

Sensitivity analysis 3, in which we replaced tertiles of $PM_{2.5\ lag(3–5)}$ and $O_{3\ lag(3–5)}$ with continuous measures of each, generated ORs of 1.0 (95% CI = 0.9, 1.1) per $\mu g/m^3$ increase in $PM_{2.5\ lag(3–5)}$ and 1.0 (95% CI = 1.0, 1.1) per parts per billion increase in $O_{3\ lag(3–5)}$. ORs

for each unit increase in $PM_{2.5\ lag(3–5)}$ and $O_{3\ lag(3–5)}$ were nearly identical in sensitivity analysis 4, in which we adjusted for same-day temperature and relative humidity, and sensitivity analysis 5, in which we replaced same-day temperature and relative humidity with lag day 3–5 averages of each (Table 3).

DISCUSSION

Overall, we found higher odds of fatal asthma exacerbations in association with higher $PM_{2.5}$ and O_3 3–5 days before death. These findings extend our understanding of risk factors for fatal asthma exacerbations by providing evidence suggesting that ambient air pollution might increase the risk of fatal exacerbations of asthma among children in North Carolina. In combination with the results of our sensitivity analyses, in which we considered continuous metrics of exposure to $PM_{2.5}$ and O_3, our main findings suggest that the increased risks of fatal asthma exacerbations among children observed in our study might not be constant across the range of air pollutant concentrations considered.

Despite the high prevalence of asthma among children, pediatric deaths due to asthma are rare. Consistent with findings of the parent study from which these cases were selected,[5] decedents were disproportionately Black, and deaths occurred largely in Piedmont (n = 35, 44%) and coastal (n = 37, 46%) regions of North Carolina. With a case series of 80 decedents, we were unable to assess heterogeneity in the associations across demographic categories or within regions. We were also unable to assess the influence of weather events (e.g., heat waves and thunderstorms), pollen, or other potential asthma triggers. A larger case series, such as what might have been drawn from a larger geographic area or a longer study period, might have allowed us to examine the role of seasonality. Our study, for example, does not account for ozone season, which extends from approximately March or April through October in North Carolina.[14] Our study also does not account for decedents' behaviors, activities, or health status in the days before the fatal exacerbations, and our analyses were limited to the use of county-level ambient air pollution. If decedents did not spend the days preceding their death in the county where they died, then the metrics we used might be misclassified compared to the true ambient air quality. Although we are unable to assess the impact of such exposure misclassification on our results, we do not expect that our results were affected by systematic differences in the misclassification of air quality in the case and comparison exposure windows. Despite these potential limitations, our study provides novel insights into the potential role of air quality in fatal exacerbations of asthma among children.

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TABLE 1.

Metrics of $PM_{2.5}$, O_3, Temperature, and Relative Humidity for Case and Comparison Days for Children with Fatal Exacerbations of Asthma in North Carolina, 2001–2016

	Lag Period, in Days	Mean (SD)	Minimum	25th[a]	Median	75th[a]	Maximum
Case days, n = 80							
$PM_{2.5}$, in μg/m^3	0	10.3 ± 5.0	2.5	6.3	9.6	13.2	26.2
	3–5	11.2 ± 4.2	2.9	8.3	11.4	13.6	25.4
O_3, in ppb	0	39.9 ± 13.2	18.6	29.7	37.2	47.1	70.3
	3–5	42.0 ± 12.7	15.6	32.3	40.5	50.1	79.8
Temperature, in °F	0	55.8 ± 15.2	25.0	45.2	57.1	69.3	79.1
	3–5	56.1 ± 14.3	29.3	43.0	57.9	68.3	79.1
Relative humidity, in %	0	75.2 ± 12.6	35.5	68.8	75.3	83.8	95.9
	3–5	73.0 ± 8.7	45.1	66.0	73.6	80.5	91.5
Comparison days, n = 271							
$PM_{2.5}$, in μg/m^3	0	11.5 ± 5.6	1.3	7.4	10.7	14.6	37.1
	3–5	10.7 ± 4.5	3.8	7.7	9.7	12.9	35.6
O_3, in ppb	0	41.8 ± 13.5	14.8	31.6	40.2	48.9	80.9
	3–5	39.8 ± 12.6	12.9	30.6	36.9	47.6	92.4
Temperature, in °F	0	56.3 ± 16.6	15.6	42.5	57.3	71.6	81.2
	3–5	56.1 ± 16.0	14.2	44.4	56.8	71.6	82.1
Relative humidity, in %	0	73.6 ± 10.1	42.7	66.9	75.3	81.1	94.8
	3–5	74.4 ± 9.4	49.9	68.1	75.7	82.3	93.6

[a]Percentile.

$PM_{2.5}$, particulate matter ≤2.5 μm; ppb, parts per billion; O_3, ozone.

TABLE 2.

Associations of $PM_{2.5}$ and O_3 With Fatal Exacerbations of Asthma Among Children in North Carolina, 2001–2016

Pollutant	Lag Period, in days	Tertile Range	OR (95% CI)
$PM_{2.5}$, in μg/m^3	3–5	3.84–8.55	Referent
		8.57–11.27	0.7 (0.3, 1.5)
		11.30–35.61	2.2 (1.1, 4.6)
O_3, in ppb	3–5	12.92–32.51	Referent
		32.66–43.95	1.4 (0.7, 2.8)
		43.99–92.40	1.6 (0.6, 4.8)

CI indicates confidence interval; $PM_{2.5}$, particulate matter ≤2.5 μm; ppb, parts per billion; O_3, ozone; OR, odds ratio.

TABLE 3.

Associations of $PM_{2.5}$ and O_3 With Fatal Exacerbations of Asthma Among Children in North Carolina, With Results Generated From Five Sensitivity Analyses

	Lag Period, in Days	OR (95% CI)
Sensitivity analysis 1: Main model, adjusted for continuous measures of same-day temperature and relative humidity		
$PM_{2.5}$, in μg/m^3	3–5	Referent
		0.7 (0.3, 1.5)
		2.5 (1.2, 5.2)
O_3, in ppb	3–5	Referent
		1.4 (0.7, 2.8)
		1.7 (0.6, 5.1)
Temperature, in °F	0	1.0 (0.9, 1.0)
Relative humidity, %	0	1.0 (1.0, 1.1)
Sensitivity analysis 2: Main model, adjusted for continuous measures of temperature and relative humidity, lagged by 3–5 days		
$PM_{2.5}$, in μg/m^3	3–5	Referent
		0.7 (0.3, 1.4)
		2.1 (1.0, 4.5)
O_3, in ppb	3–5	Referent
		1.2 (0.6, 2.6)
		1.2 (0.4, 4.2)
Temperature, in °F	3–5	1.0 (1.0, 1.1)
Relative humidity, %	3–5	1.0 (0.9, 1.0)
Sensitivity analysis 3: Main model, with tertiles replaced by continuous measures of $PM_{2.5}$ and O_3		
$PM_{2.5}$, in μg/m^3	3–5	1.0 (0.9, 1.1)[a]
O_3, in ppb	3–5	1.0 (1.0, 1.1)[a]
Sensitivity analysis 4: Sensitivity analysis 1, with tertiles replaced by continuous measures of $PM_{2.5}$ and O_3		
$PM_{2.5}$, in μg/m^3	3–5	1.0 (0.9, 1.1)[b]
O_3, in ppb	3–5	1.0 (1.0, 1.1)[b]
Temperature, in °F	0	1.0 (0.9, 1.0)
Relative humidity, %	0	1.0 (1.0, 1.1)
Sensitivity analysis 5: Sensitivity analysis 2, with tertiles replaced by continuous measures of $PM_{2.5}$ and O_3		
$PM_{2.5}$, in μg/m^3	3–5	1.0 (0.9, 1.1)[c]
O_3, in ppb	3–5	1.0 (1.0, 1.1)[c]
Temperature, in °F	3–5	1.0 (1.0, 1.1)
Relative humidity, %	3–5	1.0 (0.9, 1.0)

[a] ORs shown are per unit increase. Converting to ORs per 10-unit increase generates an OR per 10 μg/m^3 of $PM_{2.5}$: 1.0 (95% CI = 0.4, 2.3) and an OR per 10 ppb of O_3: 1.5 (95% CI = 1.0, 2.3).

[b] ORs shown are per unit increase. Converting to ORs per 10-unit increase generates an OR per 10 μg/m^3 of $PM_{2.5}$: 1.1 (95% CI = 0.5, 2.5) and an OR per 10 ppb of O_3: 1.5 (95% CI = 1.0, 2.3).

[c] ORs shown are per unit increase. Converting to ORs per 10-unit increase generates an OR per 10 μg/m^3 of $PM_{2.5}$: 1.0 (95% CI = 0.4, 2.2) and an OR per 10 ppb of O_3: 1.4 (95% CI = 0.9, 2.4).

CI indicates confidence interval; $PM_{2.5}$, particulate matter ≤2.5 μm; ppb, parts per billion; O_3, ozone; OR, odds ratio.