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ORIGINAL RESEARCH

Air Pollution and Childhood Asthma Hospitalizations in Chengdu, China: A Time-Series Study

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Purpose: Research on the relationship between air pollutants and hospitalization for asthma in children in developing countries remains inadequate. This study aimed to assess the short-term effects of air pollutants, including sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO), ozone (O_3), particulate matter ≤ 2.5 µm ($PM_{2.5}$), and particulate matter ≤ 10 µm (PM_{10}), on children hospitalized for asthma in Chengdu, China, from 2017–2022.

Patients and Methods: During the study period, 5592 children were hospitalized for asthma. A generalized additive model was used to control for seasonality, long-term trends, weather, day of the week, and holidays. The analysis was further stratified by age, sex, and season to estimate the associations.

Results: $PM_{2.5}$, PM_{10}, SO_2, NO_2, and CO were significantly associated with an increased risk of hospitalization due to asthma. A 10 µg/m^3 increase in $PM_{2.5}$, PM_{10}, and CO at lag04 corresponded to an increase of 2.07%, 1.56%, and 0.33% in daily hospital admissions for asthma, respectively. A 10 µg/m^3 increase in SO_2 and NO_2 at lag05 corresponded to an increase of 45.69% and 8.16% in daily hospital admissions for asthma, respectively. Further analysis by age found that PM_{10} and $PM_{2.5}$ had a greater impact on children aged 5–6 years old while NO_2 and CO mainly affected children under 7 years old. Analysis by by sex found that pollutants had a greater impact on hospital admissions in girls. Seasonal analysis revealed that pollutants had a more significant effect on admission during the winter.

Conclusion: Our results suggest that increased concentrations of $PM_{2.5}$, PM_{10}, SO_2, NO_2, and CO in Chengdu lead to hospitalization for asthma in children and that a lag effect was observed, especially with SO_2. These findings highlight the need for stricter air quality controls to reduce childhood asthma hospitalizations.

Plain Language Summary:

- Exposure to air pollutants increases the risk of hospitalization for children with asthma.
- The effect of each studied air pollutant varies according to the age and sex of the child.
- The effect of air pollutants on children with asthma was stronger in the winter.
- Air quality control standards are needed to reduce hospitalizations for asthma in children.

Keywords: pediatric asthma, air pollutants, stratified analysis, in-patient

Introduction

Asthma is a heterogeneous disease with different clinical phenotypes, mainly characterized by chronic airway inflammation,[1] and is the most common chronic inflammatory disease of the respiratory tract in children.[2] It involves reversible expiratory airflow restriction and is often accompanied by recurrent wheezing, shortness of breath, chest tightness, and cough.[3] Without thorough treatment, asthma can continue into adulthood, with severe cases posing life-threatening risks, significantly affecting children's physical and mental health. Asthma is the leading cause of emergency

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hospitalization in children under 5 years of age, with its prevalence increasing over the past 20 years.[4,5] According to the International Study of Asthma and Allergies in Childhood (ISAAC), the global prevalence of asthma symptoms in children increased from 11.1% to 11.6% between phase one and phase three of the study.[2] A doctor confirmed asthma in 6.3% of children across 44 research centers in 16 countries.[1] The prevalence of asthma in children aged 0–14 years in China has also increased from 0.91% in 1990 to 3.02% in 2010.[6]

The pathogenesis of asthma is complex and results from interactions between genetic and environmental factors.[3] With the rapid development of the industrial revolution, the impact of air pollution on asthma has received increasing attention from researchers. Epidemiological and clinical trial studies have found that exposure to air pollutants is not only a significant risk factor for asthma attacks but may also be associated with new-onset asthma.[7–12] An increasing number of studies have linked exposure to air pollutants and acute asthma attacks; however, most of these studies were conducted in developed countries, and the subjects and results were not consistent.[13–17] For example, a New York study revealed no association between pollutants and emergency asthma among children living in neighborhoods with higher asthma prevalence.[13] However, a study showed that increases in ozone and sulfur dioxide(SO_2) concentrations were associated with increased asthma morbidity in children in Indianapolis.[17] Many Asian countries, especially China and India, have significantly higher levels of air pollutants than developed countries did.[18,19] Moreover, meteorological conditions and other factors in these developing countries differ from those in developed countries. In China, where people's lifestyles are different from those in developed countries, a heavy reliance on coal consumption persists, which accounts for 64% of domestic energy consumption, significantly exceeding the world average. Air pollution in China is worsening due to industrial and traffic emissions and natural phenomena (eg, dust, smog).[20]

Chengdu is located in southwestern China in the western Sichuan Basin. The elevation difference in the Sichuan Basin region is 5000 m, with significant terrain variations among mountainous, hilly, and plain areas. This region is relatively closed, and the winter wind is weak, making it difficult for air to spread. As a major city in western China, it has a concentration of industrial populations, contributing to heavy air pollution and frequent hazy weather conditions. Chengdu was ranked as the 15th most polluted city in China in 2014 based on its particulate matter ≤ 2.5 μm ($PM_{2.5}$) levels (Greenpeace East Asia, 2014). In addition, we noticed that the prevalence of asthma in children in Chengdu was increasing,[21] and thus we hypothesized whether a correlation exists between air pollution and admission to hospital for acute asthma attacks in children in Chengdu. In southwest China, studies on the relationship between air pollution and acute asthma attacks in children remain lacking. In China, the treatment of acute asthma attacks is usually unscheduled and less affected by factors, such as regular clinical appointments and personal health insurance, making it a good indicator for epidemiological studies.

The purpose of this study was to investigate the effect of air pollutants on hospital admissions for acute asthma attacks in children using a time-series analysis to understand the relationship between air pollution and asthma in Chengdu. This study can guide government personnel in formulating relevant health interventions to reduce the adverse effects of air pollution on children with asthma.

Material and Methods

Study Setting

Chengdu is located in southwest China and is the capital city of Sichuan. Our study location is the metropolitan area of Chengdu, covering an area of 3639.81 km^2, including 14 urban districts namely Jinjiang, Chenghua, Jinniu, Qingyang, Wuhou, Gaoxin, Longquanyi, Shuangliu, Pidu, Xindu, Wenjiang, Tianfu, Qingbaijiang, and Xinjin. Daily admission cases of childhood asthma were obtained from one of the largest pediatric specialist hospitals in the region, which has four wards. This national tertiary Grade A women and children's medical and health institution integrates medical care, health care, scientific research, and teaching with specialized facilities. We systematically retrieved daily asthma admissions of children aged 0–18 years from hospital electronic medical records from January 1, 2017 to December 31, 2022 (2191 days), including admission date, age, sex and International Classification of Diseases (ICD-10). The diagnostic criteria of asthma are based on the recommendations for diagnosis and management of bronchial asthma in children (2020).[22] The diagnosis of asthma in children under 6 years of age remains a challenging clinical problem, suggesting that the main clinical features of asthma in young children include: frequency of wheezing attacks; exercise-related wheezing and coughing; non-specific cough at night or at a fixed time; symptoms persist up to 3 years of age; anti-asthma treatment is effective, repeated after withdrawal. Risk factors such as family history of allergy, personal history of allergic disease and early allergen sensitization were also considered. Asthma was coded according to the ICD-10: asthma (J45) and status asthmaticus (J46).

Pollutant and Weather Data

Daily (24 h) air pollution concentration data were collected by the China National Environmental Monitoring Center from January 2017 to December 2022, including sulfur dioxide (SO_2), ozone (O_3), carbon monoxide (CO), nitrogen dioxide (NO_2), particulate matter ≤ 10 μm (PM_{10}), and $PM_{2.5}$, from seven monitoring stations. Mean levels of SO2, CO, NO_2, PM_{10}, and $PM_{2.5}$ were the average of 24 h values; O_3 was calculated from the mean of 8 h maximum concentration. Additionally, daily weather data, including daily relative humidity (%) and average temperature (°C), were obtained from the Chengdu Meteorological Monitoring Bureau. No data were missing. The average of daily mean levels of air pollutants, from all seven stations (Sanwayao, Shahepu, Junpingjie, Dashixilu, Liangjiaxiang, Jinquanhe, Shilidian) represented the daily exposure of children to asthma during the study period.

Statistical Methods

A time-series regression analysis was used to investigate the short-term relationship between daily hospitalizations for asthma and exposure to air pollutants (SO_2, O_3, CO, NO_2, $PM_{10,}$ and $PM_{2.5}$).[23] Because the number of daily hospitalizations for asthma is a low-probability event that roughly follows a Poisson distribution, we utilized a generalized additive model (GAM) to model the time-series data and control for the effects of seasonality, long-term trends, weather, workdays, and holidays.[24]

The model is as follows:

$Y_t \sim$ Poisson (μ_t)

Log (μ_t) = βX_t+ s (t,dft)+ s (Zt,dft)+ Holiday + DOW+ α

Where t represents the day of observation; Y_t represents the number of hospitalizations due to asthma on day t; μt represents the expected number of hospitalizations on day t; X_t represents the concentration of atmospheric pollutants on day t (including SO_2, O_3, CO, NO_2, $PM_{10,}$ and $PM_{2.5}$); β is the regression coefficient; *s* represents natural smooth splined function; Zt represents the meteorological factor of day t (including average temperature, relative humidity); dft is the degree of freedom of a non-parametric smoothing function; Holiday is a binary variable for national holidays in China; DOW is a day of the week (value ranges from 1 to 7 on Sunday to Saturday); α is intercept. For adjustment of the delayed and non-linear confounding effects of temperature and humidity, we adjusted the degrees of freedom (DOF) several times in the model, and combined with previous studies, applied the distributed lag non-linear models with three degrees of freedom in the natural smooth splined function.[24,25] According to the Partial Autocorrelation Function (PACF), the DOF of the model's summary non-parametric smoothing function was determined to be 6 years to control seasonal, long-term trends in the time-series dataset.

We used a single-day lag (from lag0 to lag5) and a multi-day cumulative lag (from lag01 to lag05) to estimate the lag effect of air pollutants. Single-day lag is expressed as lag0, lag1... lag5, where lag0 represents the day of exposure; The cumulative lag is expressed as lag01, lag02... lag05, where lag01 represents the cumulative effect on the day of exposure and 1 day of lag. Our choice of lag days was based on the fact that asthma's response to environmental factors is acute and does not extend for a long time. After establishing the basic model, air pollutants were sequentially introduced into single models to explore their correlation with asthma hospitalization. Moreover, to investigate possible effect modification by season (spring: March through May; summer: June through August; autumn: September through November; winter: December through February), sex, and age (0–4 years old; 5–6 years old; 7–18 years old) group, we performed separate analysis stratified by these potential modifiers.

For sensitivity analysis, the cumulative lag day with the most significant exposure effect was selected in the single pollutant model as the research object, while controlling for other confounding factors. The robustness of the model was tested by establishing a two-pollutant model to see if the effects of pollutants remain have statistical significance.

SPSS 22.0 was used for descriptive analysis of weather data and air pollutant concentration. The indicators included mean, standard deviation, minimum, maximum, and percentile (P5, P25, P50, P75, P95), and Spearman rank correlation method was used for the correlation analysis. Using the software package "dlnm" in R software, a generalized additive Poisson regression model was used for time-series analysis. The results were expressed as the rate of daily increase in asthma hospitalization (excess risk, ER) and 95% confidence interval (CI) per 10 μg/m^3 increase in air pollutant concentration.

Results

Table 1 summarizes the primary statistical data of the study participants. In our study area, from 2017 to 2022, the total number of hospitalizations for asthma was 5592, with an average daily admission of 2.55. Most patients (67.06%) were boys. Children aged 0–4, 5–6, and 7–18 years accounted for 81.56%, 9.91%, 8.53% of cases, respectively. A total of 1384 (24.75%) patients hospitalized in spring (March–May),1303 (23.30%) patients hospitalized in summer (June–August), 1689 (30.20%) patients hospitalized in autumn (September–November), and 1216 (21.75%) patients hospitalized in winter (December–February), were recorded.

Table 2 summarizes the descriptive statistical data for the air pollutants and meteorological conditions. During the study period, the average daily concentrations of SO_2, NO_2, O_3, $PM_{2.5}$, and PM_{10} were 7.35, 39.29, 96.52, 46.05, and 71.99 μg/m^3, respectively. The average daily CO concentration was 0.83 mg/m^3. The daily relative humidity and average temperature were 80.44% and 16.88°C, respectively.

Figure 1 shows raw time-series plots for each air pollution variable. $PM_{2.5}$, PM_{10}, O_3, CO, and NO_2 showed a certain degree of seasonal fluctuation, whereas SO_2 exhibited a declining trend over the six years.

Table 1 Summary Statistics of Children Hospitalized for Asthma by Sex, Age, and Season, 2017–2022

Characteristics	Number of Patients	Percentage %
Sex		
Boys	3750	67.06
Girls	1842	32.94
Age (years)		
0–4	4561	81.56
5–6	554	9.91
7–18	477	8.53
Season		
Spring	1384	24.75
Summer	1303	23.30
Autumn	1689	30.20
Winter	1216	21.75
Total	5592	100.00

Notes: Spring: March–May; Summer: June–August; Autumn: September–November; Winter: December–February.

Table 2 Summary Statistics for Air Pollutants Concentrations and Weather Conditions in Chengdu, 2017–2022

	Mean	SD	Percentiles					Max	Min	Days Exceeded WHO AQG
			5	25	50	75	95			
$PM_{2.5}$ (μg/m^3)	46.05	31.94	12.500	24.00	38.00	60.00	106.20	292.50	4.00	1477 (67.41)
PM_{10} (μg/m^3)	71.99	45.70	22.500	39.50	60.50	94.00	155.50	465.00	8.50	1992 (90.92)
CO (mg/m^3)	0.83	0.27	0.49	0.65	0.79	0.96	1.35	2.71	0.31	0 (0)
SO_2 (μg/m^3)	7.35	3.86	3.00	5.00	6.50	9.00	14.50	60.00	1.50	1 (0.04)
NO_2 (μg/m^3)	39.29	16.18	16.50	27.00	37.50	50.00	67.50	114.50	7.00	1735 (79.19)
O_3 (μg/m^3)	96.52	56.80	23.00	52.00	84.00	135.00	208.40	294.00	4.00	887 (40.48)
Temperature (°C)	16.88	7.41	5.31	9.98	16.99	23.34	27.49	32.36	0.75	
Humidity (%)	80.44	9.00	65.25	74.25	80.86	87.25	94.13	99.00	39.88	

Abbreviations: WHO, World Health Organization; AQG, air quality guidelines; PM, particulate matter; CO, carbon monoxide; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; O_3, ozone; SD, standard deviation.

Table 3 shows the relationship between the air pollutant levels and meteorological conditions. $PM_{2.5}$, PM_{10}, SO_2, and NO_2 were positively correlated, with PM_{10} and $PM_{2.5}$ having the closest correlation ($R = 0.959$, $P < 0.01$). O_3 had no obvious correlation with SO_2, and was negatively correlated with the other three pollutants, which were positively correlated. Temperature was negatively correlated with all pollutants except O_3, and humidity was negatively correlated with all pollutants except CO.

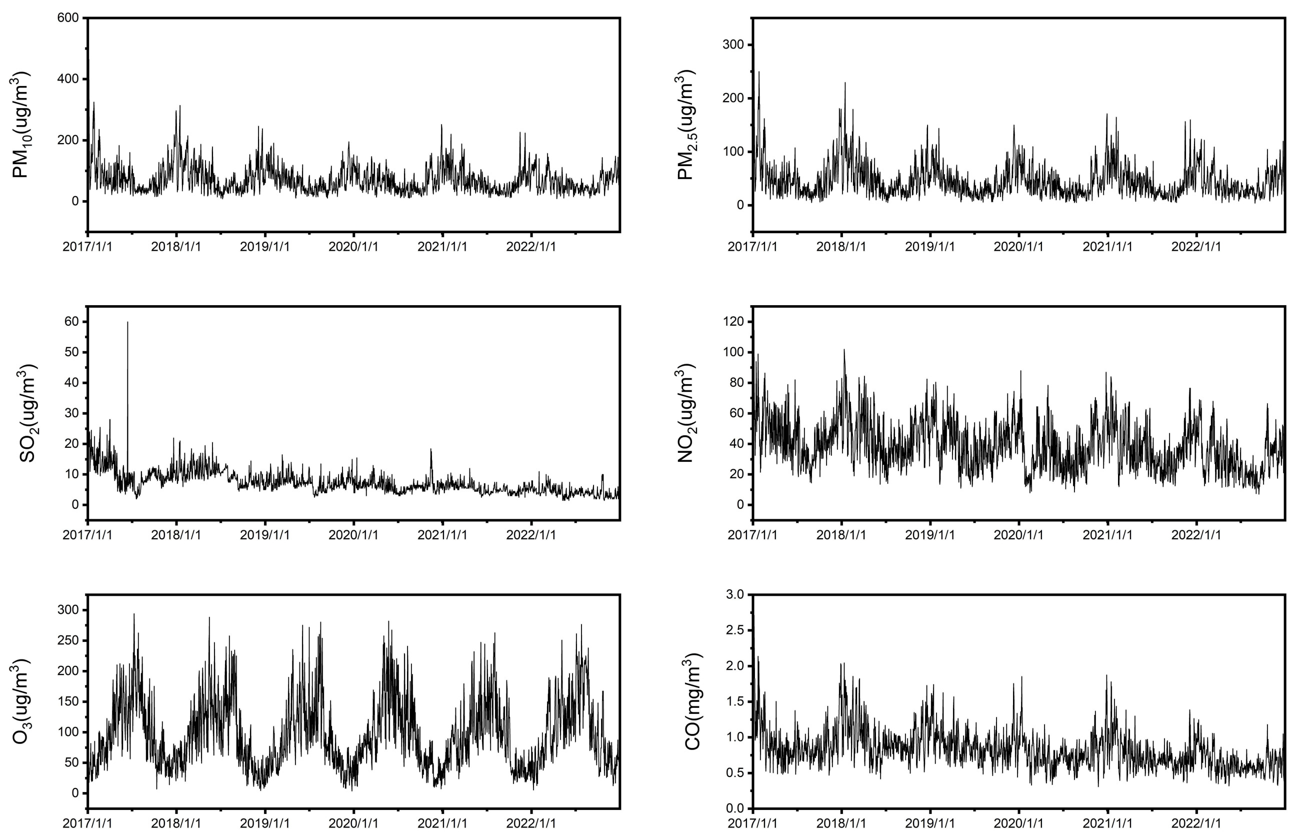

Figure 1 Time-series plots of air pollutant variables in Chengdu, 2017–2022.
Abbreviations: PM, particulate matter; CO, carbon monoxide; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; O_3, ozone.

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Table 3 Pearson's Correlation Matrix Between Air Pollutant Concentrations and Weather Conditions in Chengdu, 2017–2022

	$PM_{2.5}$	PM_{10}	CO	SO_2	O_3	NO_2	Temperature	Humidity
$PM_{2.5}$	1.000	**0.959****	**0.664****	**0.424****	**−0.219****	**0.729****	**−0.460****	**−0.142****
PM_{10}		1.000	**0.616****	**0.454****	**−0.189****	**0.772****	**−0.442****	**−0.235****
CO			1.000	**0.559****	**−0.160****	**0.665****	**−0.267****	**0.066****
SO_2				1.000	0.004	**0.555****	**−0.161****	**−0.186****
O_3					1.000	**−0.205****	**0.778****	**−0.440****
NO_2						1.000	**−0.365****	**−0.180****
Temperature							1.000	**−0.050***
Humidity								1.000

Notes: *$P < 0.05$; **$P < 0.01$; bold: significant p-values.
Abbreviations: PM, particulate matter; CO, carbon monoxide; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; O_3, ozone.

Figure 2 shows the results from the single-lag day models (lag0–lag5) and multi-day cumulative lag models (lag01–lag05) for the percentage increase in hospitalization per 10 μg/m^3 increase in pollution. The single-day lag effect of $PM_{2.5}$ was significant only at lag2 [RR = 1.002 (95% CI: 1.000–1.003)], with the risk of asthma admission increasing by 1.51% (95% CI: 0.25–2.79%) per 10 μg/m^3 increase. The cumulative lag effect of $PM_{2.5}$ was significant at lag02–lag05, with the largest effect observed at lag04, where a 10 μg/m^3 increase in $PM_{2.5}$ increased the risk of

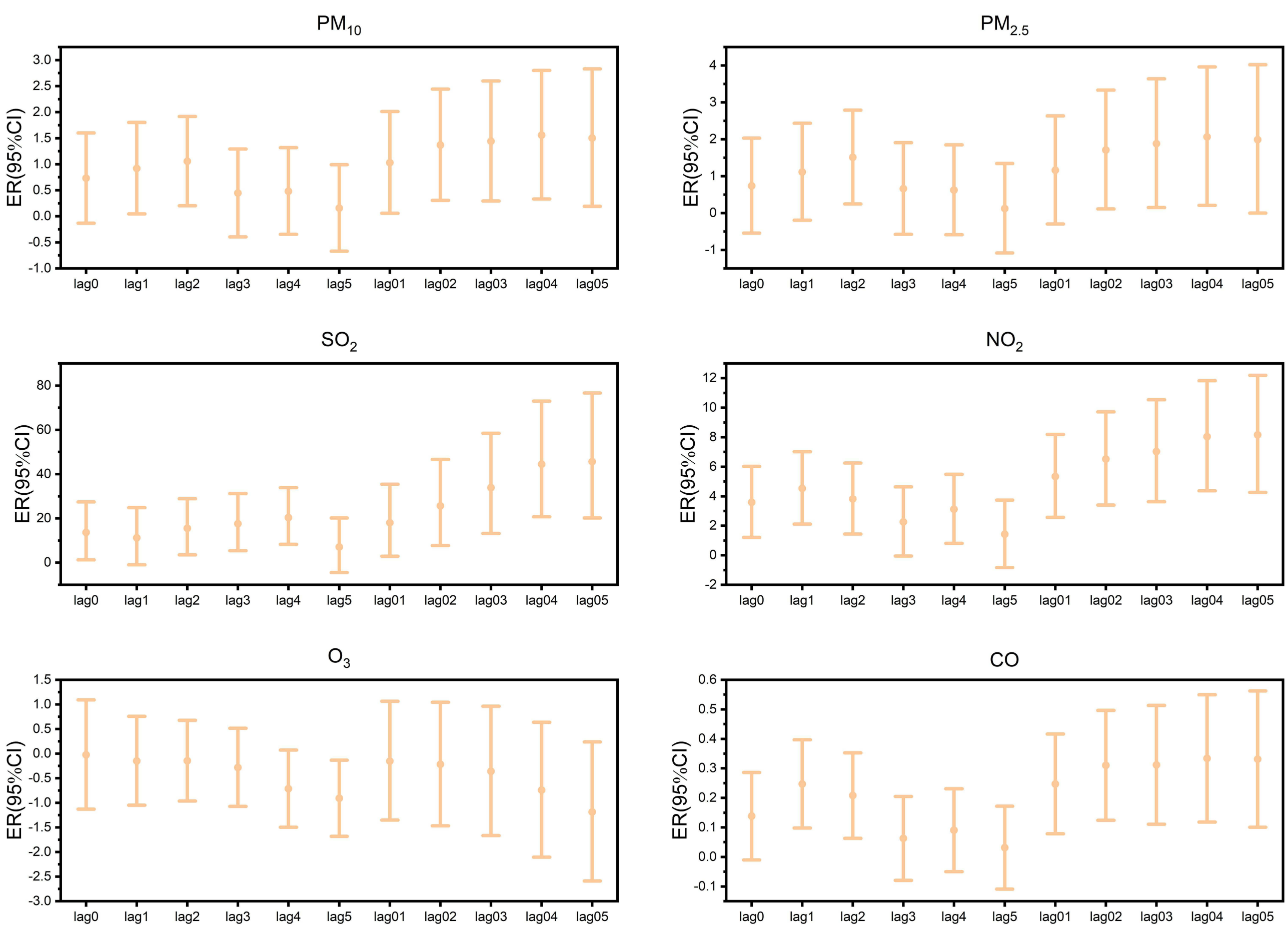

Figure 2 In single-lag models (lag 0, 1, 2, 3, 4, and 5) and cumulative lag models (lag 01, 02, 03, 04, and 05), a 10 μg/m^3 increase in air pollutants corresponds to a percentage increase in daily asthma hospitalizations (with 95% CI).
Abbreviations: PM, particulate matter; CO, carbon monoxide; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; O_3, ozone; ER, excess risk.

asthma admission by 2.07% (95% CI: 0.21–3.96%). The single-day lag effect of PM_{10} was significant at lag1 and lag2, and the cumulative lag effect of PM_{10} was significant at lag01–lag05, with the largest effect observed at lag04. For every 10 μg/m^3 increase in PM_{10}, the risk of asthma admissions increased by 1.56% (95% CI: 0.33–2.80%). The single-day lag effect of SO_2 was the largest at lag 4 (*RR* = 1.019 [95% CI: 1.008–1.030]), and its cumulative lag effects were all significant, showing a gradually increasing trend. The cumulative lag effects of NO_2 were similar to those of SO_2. A 10μg/m^3 increase in SO_2 and NO_2 at lag05 was associated with 45.69% (95% CI: 20.17–76.62%) and 8.16% (95% CI: 4.26–12.20%) increments in daily admission for asthma, respectively. The single-day lag effects of CO were significant at lag1 and lag2, with the largest effect at lag1 (RR = 1.280 [95% CI: 1.103–1.486]). The cumulative lag effect was significant, and the most prominent effect was observed at lag04. For every 10 μg/m^3 increase in CO, the risk of asthma hospitalization increased by 0.33% (95% CI: 0.12–0.55%). The single-day lag effect of O_3 was negative and significant only at lag5 (*RR* = 0.999 [95% CI: 0.998–1.000]). A 10 μg/m^3 increase in O_3 reduced the risk of asthma admission by 0.91% (95% CI: 1.68–0.13%), with the cumulative effect not being significant.

Figure 3 shows the effects of six air pollutants on acute asthma attacks in children of different ages. The effect of $PM_{2.5}$ on asthma admissions in children aged 5–6 years was similar to that in the total study population. The cumulative lag effect was significant at lag04–lag05, and the largest effect was observed at lag05. The risk of hospitalization for asthma was increased by 8.18% (95% CI: 1.57–15.21%). However, the effects on admission rates for children aged 0–4 years and 7–18 years were not statistically significant. The effect of PM_{10} on asthma in different age groups was similar

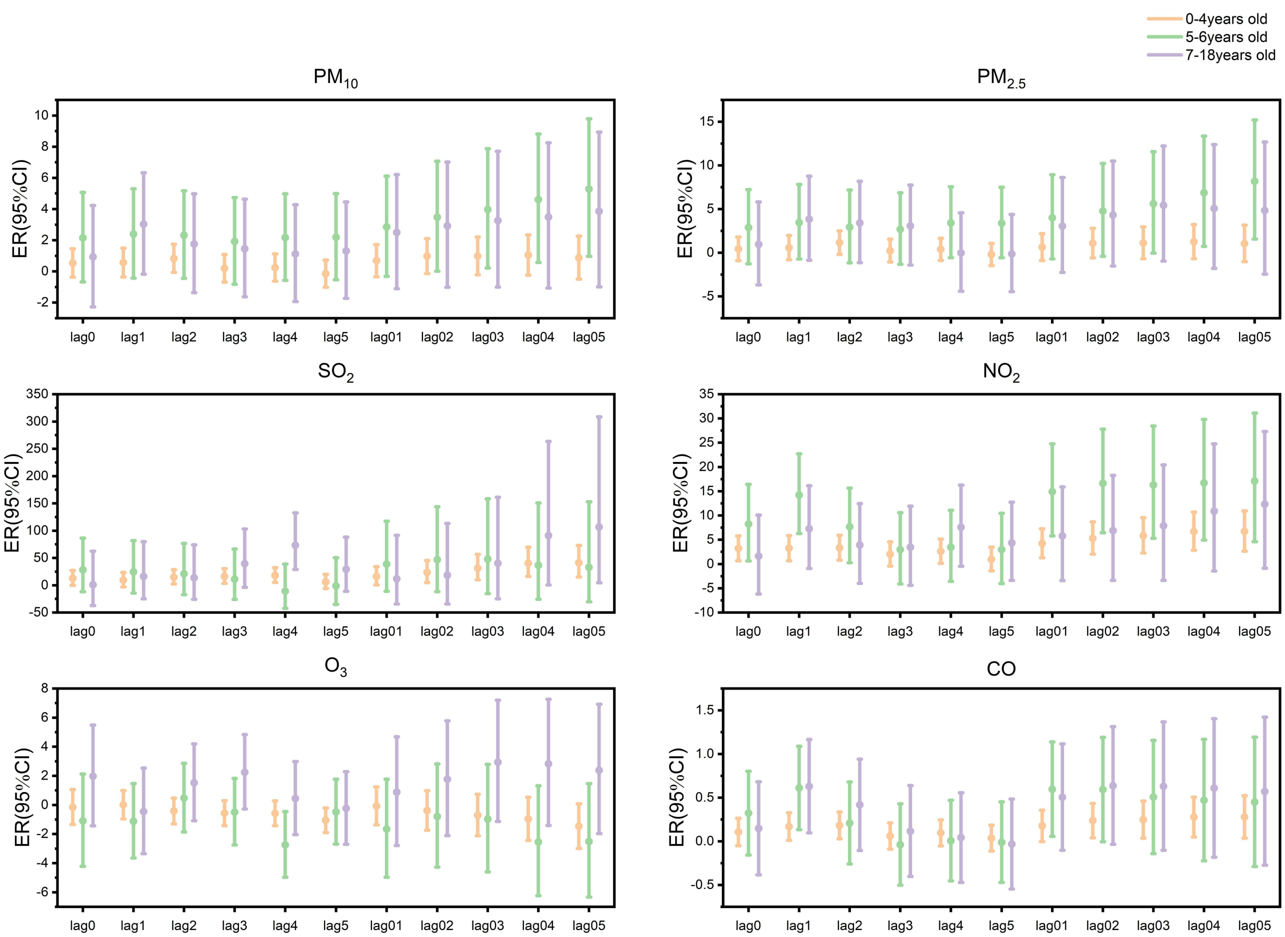

Figure 3 In single-lag models (lag 0, 1, 2, 3, 4, and 5) and cumulative lag models (lag 01, 02, 03, 04, and 05) stratified by age group, a 10 μg/m^3 increase in air pollutants corresponds to a percentage increase in daily asthma hospitalizations (with 95% CI).

Abbreviations: PM, particulate matter; CO, carbon monoxide; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; O_3, ozone; ER, excess risk.

to that of $PM_{2.5}$, and the cumulative lag effect in children aged 5–6 years old reached a maximum at lag05, with the risk of asthma admission increasing by 5.29% (95% CI: 0.98–9.79%). The effects of SO_2 on asthma admissions in children aged 0–4 years was similar to that in the total study population. The single-day lag effect reached a maximum at lag4, with the risk of hospitalization increasing by 17.94% (95% CI: 5.34–32.05%) per 10μg/m3 increase in SO_2. The cumulative lag effect was significant in lag01-lag05 and reached a maximum at lag05, with the risk of hospitalization increasing by 41.10% (95% CI: 15.10–72.97%) per 10μg/m3 increase in SO_2. The single-day lag effect of SO_2 on admission for asthma in children aged 7–18 years was significant only at lag4, while the cumulative lag effect was significant at lag04 and lag05; however, the effect on admission rates for children aged 5–6 years was not statistically significant. The effect of NO_2 on admission for asthma in children aged 0–4 years and 5–6 years was similar to that in the total study population, with cumulative lag effect reaching its maximum at lag05 for both age groups, while the effect on admission for asthma in children aged 7–18 years was not statistically significant. The effect of CO on asthma admissions in children aged 0–4 years was similar to that in the total study population, with significant cumulative lag effect at lag02–lag05 and the greatest effect at lag05.

Figure 4 shows the effect of the six air pollutants on asthma admissions in children of different sexes. The impact of $PM_{2.5}$ on asthma admissions in girls was similar to that in the total study population. The single-day lag effect was significant at lag2 and lag3, and the cumulative lag effect was significant at lag02–lag05, with the largest effect observed at lag03. The risk of asthma admission increased by 3.64% (95% CI: 0.79–6.56%). However, there was no statistically significant impact on hospital admissions in boys. The effects of PM_{10} were similar to those of $PM_{2.5}$, with the largest cumulative lag effect at lag04, where the risk of asthma admission increased by 2.37% (95% CI: 0.35–4.43%). The

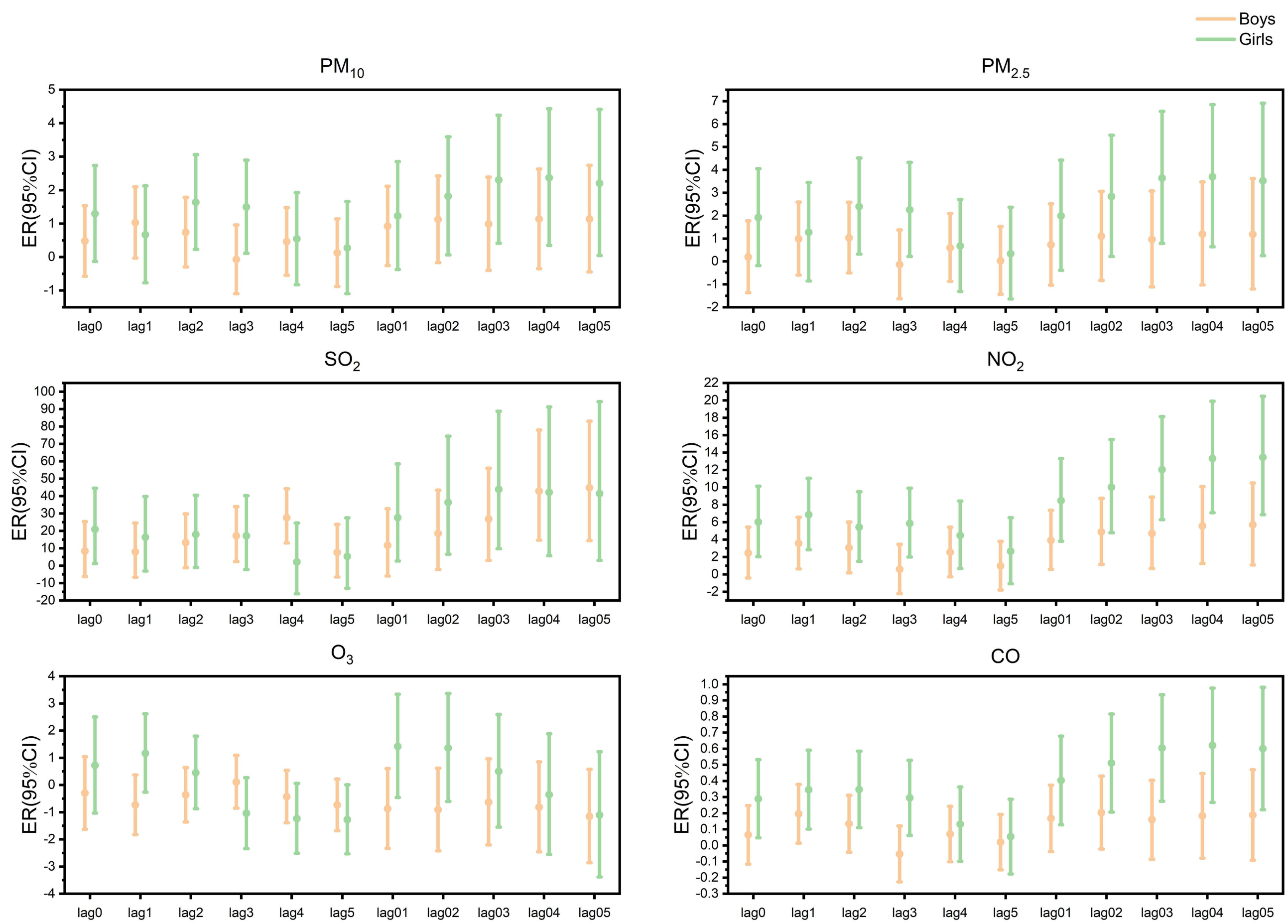

Figure 4 In single-lag models (lag 0, 1, 2, 3, 4, and 5) and cumulative lag models (lag 01, 02, 03, 04, and 05) stratified by sex group, a 10 μg/m^3 increase in air pollutants corresponds to a percentage increase in daily asthma hospitalizations (with 95% CI).
Abbreviations: PM, particulate matter; CO, carbon monoxide; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; O_3, ozone; ER, excess risk.

impact of SO_2 exposure in boys was similar to that in the total study population; however, the single-day effect on hospital admission in girls was significant only at lag0. The impact of NO_2 on asthma admissions in children of different sexes was similar to that observed in the total study population, with the single-day lag effect reaching a maximum at lag1. The cumulative lag effect reached its maximum at lag 05, with the risk of admission for asthma increasing by 13.46% (95% CI: 6.86–20.48%) in girls and by 5.70% (95% CI: 1.09–10.51%) in boys. The impact of CO on girls was similar to that on the total study population. However, the single-day lag effect on hospital admission for boys with asthma was significant only at lag1.

Figure 5 shows the effects of the seasonality on asthma admissions in children. CO, SO_2, and NO_2 had significant effects on the admission of children with asthma in the winter but had no significant relationship with the concentration of pollutants in other season. However, the effects of PM_{10} and $PM_{2.5}$ on admission were not significantly modified by season.

In the two-pollutant model, two atmospheric pollutants (SO_2, CO, O_3, NO_2, PM_{10}, and $PM_{2.5}$) were included to study their impact on the percentage change in daily hospitalization for children with asthma. Since $PM_{2.5}$ and PM_{10} were highly correlated (R = 0.959), they were not included in the same model to avoid multicollinearity affecting the model stability. O_3 had no statistically significant effect on the hospitalization of children with asthma over the entire cumulative lag interval, and no separate two-pollutant model was established. As shown in Table 4, when $PM_{2.5}$ was included in the SO_2, NO_2, CO, and O_3 models, only O_3 was statistically significant. When PM_{10} was included in the SO_2, NO_2, CO, and O_3 models, the statistical significance was lost after NO_2 was included, whereas the other two pollution models remained significant, with O_3 having the greatest effect. SO_2 showed statistical significance after including NO_2, CO, O_3, PM_{10},

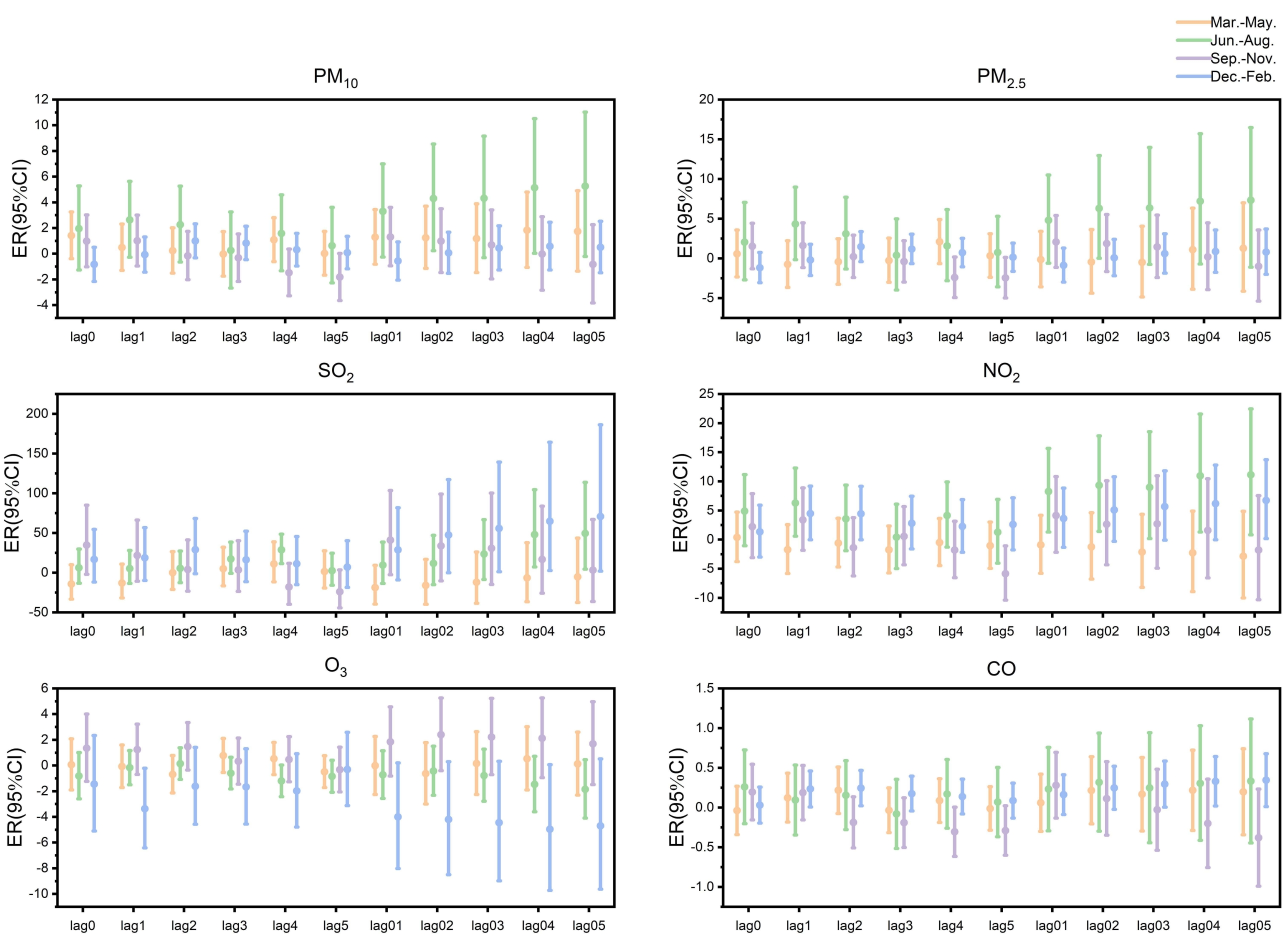

Figure 5 In single-lag models (lag 0, 1, 2, 3, 4, and 5) and cumulative lag models (lag 01, 02, 03, 04, and 05) stratified by season group, a 10 μg/m^3 increase in air pollutants corresponds to a percentage increase in daily asthma hospitalizations (with 95% CI).

Abbreviations: PM, particulate matter; CO, carbon monoxide; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; O_3, ozone; ER, excess risk.

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Table 4 In a Two-Pollutant Model, a 10μg/m^3 Increase in Pollutant Concentrations Corresponds to a Percentage Increase in Asthma Hospitalizations (Mean and 95% CI)

Pollutants		RR	Estimate
$PM_{2.5}$	NULL	1.002(1.0002–1.004)*(lag04)	2.067 (0.208–3.960)*
	$+SO_2$	1.002(0.999–1.004)	1.836 (−0.034–3.742)
	$+NO_2$	1.002(0.999–1.003)	1.553 (−0.334–3.475)
	+CO	1.002(0.999–1.004)	1.664 (−0.268–3.632)
	$+O_3$	1.002(1.000–1.004)*	2.072 (0.211–3.968)*
PM_{10}	NULL	1.002(1.000–1.003)*(lag04)	1.558 (0.332–2.800)*
	$+SO_2$	1.001(1.000–1.003)*	1.403 (0.167–2.656)*
	$+NO_2$	1.001(0.999–1.002)	1.174 (−0.083–2.446)
	+CO	1.001(1.000–1.003)*	1.326 (0.059–2.609)*
	$+O_3$	1.002(1.000–1.003)*	1.562 (0.333–2.805)*
SO_2	NULL	1.039(1.019–1.059)*(lag05)	45.689 (20.172–76.623)*
	$+PM_{10}$	1.035(1.016–1.055)*	42.879 (17.430–73.843)*
	$+NO_2$	1.033(1.014–1.052)*	39.972 (15.078–70.252)*
	+CO	1.036(1.017–1.055)*	43.408 (18.150–74.066)*
	$+O_3$	1.038(1.019–1.057)*	46.170 (20.487–77.326)*
	$+PM_{2.5}$	1.037(1.018–1.056)*	44.525 (18.772–75.864)*
NO_2	NULL	1.008(1.004–1.012)*(lag05)	8.157 (4.264–12.196)*
	$+PM_{10}$	1.008(1.004–1.012)*	8.289 (3.973–12.784)*
	$+SO_2$	1.007(1.004–1.011)*	7.585 (3.626–11.695)*
	+CO	1.008(1.004–1.011)*	7.769 (3.665–12.036)*
	$+O_3$	1.008(1.004–1.012)*	8.283 (4.360–12.354)*
	$+PM_{2.5}$	1.009(1.004–1.013)*	8.631 (4.538–13.367)*
CO	NULL	1.0003(1.0001–1.0005)*(lag04)	0.334 (0.118–0.550)*
	$+PM_{10}$	1.0003(1.0001–1.0005)*	0.300 (0.074–0.527)*
	$+SO_2$	1.0003(1.0001–1.0005)*	0.208 (0.090–0.525)*
	$+NO_2$	1.0003(1.0001–1.0005)*	0.278 (0.059–0.498)*
	$+O_3$	1.0003(1.0001–1.0005)*	0.334 (0.118–0.551)*
	$+PM_{2.5}$	1.0003(1.0001–1.0006)*	0.324 (0.095–0.553)*

Notes: *$P < 0.05$; Null: pollution effect corresponding to single pollution model.
Abbreviations: CI, confidence interval; PM, particulate matter; CO, carbon monoxide; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; O_3, ozone; RR, relative risk.

and $PM_{2.5}$, with O_3 having the greatest effect. NO_2 remained statistically significant after including SO_2, CO, O_3, $PM_{10,}$ and $PM_{2.5}$, with the inclusion of $PM_{2.5}$ having the greatest effect. CO was statistically significant when NO_2, SO_2, O_3, $PM_{10,}$ and $PM_{2.5}$ models were included, with O_3 having the greatest effect.

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Discussion

Our study showed that environmental levels of SO_2, NO_2, CO, $PM_{10,}$ and $PM_{2.5}$ were associated with hospitalization in children with asthma, with SO_2 having the strongest association. A stratified analysis by sex showed that CO, $PM_{10,}$ and $PM_{2.5}$ had greater impacts on asthma admissions in girls, and SO_2 had a greater impact on asthma admissions in boys. A stratified analysis by age showed that $PM_{2.5}$ and PM_{10} had greater impacts on asthma admissions in children aged 5–6 years old; SO2 mainly affected children aged 0–4 years and 7–18 years, whereas NO_2 and CO mainly affected children aged under 7 years old. Stratified analysis by season showed that SO_2, $NO_{2,}$ and CO significantly influenced asthma admission during the winter.

Many previous studies have shown a relationship between air pollutants and asthma. Nonetheless, most of these studies have focused on developed countries in Europe and the United States or on adults.[25–28] However, due to factors such as longer outdoor stays, more active outdoor activities, higher respiratory rates, limited metabolic capacity owing to incomplete lung development, and more air pollutants inhaled and retained per unit weight, children are often more vulnerable to the adverse effects of air pollution than adults.[29] Recently, an increasing number of Chinese researchers have focused on the harmful effects of atmospheric pollution on children's respiratory health.[20,30]

This is the first study in Chengdu on the relationship between air pollutants and asthma admissions in children. Our findings may provide a reference for improving environmental air quality, thereby preventing asthma attacks, and reducing the burden of asthma.

In the Air Quality Guideline (AQG) recommended by the World Health Organization in 2021, the AQG values of $PM_{2.5}$, PM_{10}, SO_2, NO_2, CO and O_3 were 15μg/m^3, 45μg/m^3, 40μg/m^3, 25μg/m^3, 4 mg/m^3 and 100 μg/m, respectively.[3,31] Except for CO, all other pollutant concentrations exceeded the AQG values, particularly PM_{10}, which exceeded 90.92% of the days during the study period. For children aged < 5 years, airway hyper-responsiveness and asthma symptoms are more common in boys than in girls, with a ratio of approximately 2:1. High sensitivity to asthma in males persists until adolescence, making them vulnerable to ambient air pollution.[32] Children aged 0–4 years accounted for 81.56% of the study participants, and most (67.06%) were boys. Other scholars have found similar research results.[33–37]

Particulate matter (PM) originates from a wide range of sources and consists of a mixture of liquid and solid particles suspended in air. It is the main carrier of pollutants released by human activity. PM_{10} and $PM_{2.5}$ refer to particles with a diameter < 10 μm and < 2.5 μm, respectively.[20] The respiratory system is the direct target organ of $PM_{2.5}$ and PM_{10}, and the mechanism of PM-induced asthma attacks may be related to oxidative stress, immune inflammation damage, and airway hyperresponsiveness.[12] Our study found that levels of $PM_{2.5}$ and PM_{10} were significantly related to hospitalization for asthma in children, with a more significant cumulative lag effect, which is consistent with other studies conducted in Turkey, Denmark, and China.[35–40] A study in Hong Kong on the impact of air pollution on asthma hospital admission rates found that $PM_{2.5}$ concentration led to the greatest increase in the risk of asthma admission at lag04 (2.4%) and PM_{10} at lag05 (2.3%) in the 0–14 year age group.[14] This was consistent with our findings that $PM_{2.5}$ had the greatest increase in asthma admission risk at lag04 and PM_{10} at lag05. A Greek study of factors influencing acute hospitalizations for asthma in children aged 0–14 years found that for every 10 μg/m^3 increase in PM_{10}, the number of children hospitalized for asthma increased by 2.54% (95% CI: 0.06–5.08%),[33] which is consistent with our study findings. However, a study in New York found no association between pollutants and urban asthma among children with higher asthma prevalence.[13] This may be related to the differences in age structure, sex ratio, lifestyle, behavioral activities, and air pollutant concentration of different populations. A clear explanation for this difference in the impact of PM_{10} and $PM_{2.5}$ on asthma-related hospitalizations remains elusive.

The main sources of SO_2 in China are emissions during energy production and industrial processes, and their toxic effects on patients with asthma are biologically reasonable. Studies have found that SO_2 is associated with the onset and exacerbation of asthma caused by increased airway inflammation, eosinophilia, bronchospasm, and airway obstruction. The higher the concentration of SO_2, the more severe the airway contraction.[12] Our study found a significant correlation between SO_2 exposure and hospitalization for childhood asthma, consistent with the conclusions of other studies[33,35,37,38] and meta-analyses.[41,42] Our study also found that SO_2 had the greatest impact on hospital admissions for asthma, which is consistent with the research findings in Taiwan.[37] However, a study in Hong Kong found no significant association between increased SO_2 concentrations and the risk of hospitalization for asthma in children aged 0–14 years.[14] In China, burning coal fuel for home heating also produces SO_2. We speculate that the source and distribution concentration of SO_2 may be inconsistent in different countries or in different regions of the same country, and the different economic conditions and behavioral activities of the study population may also lead to different research results.

NO_2 is formed mainly by the O_3 reaction with the NO emitted during the burning of fossil fuels.[12] Although many epidemiological studies have shown that NO_2 exposure is significantly associated with an increase in asthma incidence,[35,37–39] relatively few toxicological studies exist. Some studies have shown that the toxic effect of NO_2 might be related to the lipid peroxidation of cell membranes caused by O_3 and the production of various free radicals, which altogether damage the structure and function of the asthmatic airway and enhance the airway response of asthmatic individuals to inhaled allergens.[43] A study in Hong Kong found that elevated NO_2 concentrations led to the greatest increase (3.9%) in the risk of asthma hospitalization in the 0–14 year age group at lag04 day,[14] which is similar to our findings.

Unfortunately, it remains uncertain whether a direct relationship exists between CO and asthma, and some studies on the relationship between CO and asthma have been conducted only in adults and outpatient visits. A study in Chongqing found that short-term exposure to CO might lead to hospitalization for childhood asthma.[35] A meta-analysis showed that the lag exposure was 1 d for CO,[44] which was consistent with our finding that the single-day lag effect of CO was the greatest at lag1.

O_3 is a strong oxidant that can cause respiratory symptoms by inducing increased airway reactivity, airway damage, inflammation, and systemic oxidative stress.[45] O_3 contributes to more severe asthma symptoms and an increase in hospital admissions.[46] Currently, research on the impact of O_3 exposure on asthma remains inconsistent. A study conducted in Seoul, South Korea, showed that an increase in O_3 levels (IQR) could lead to a 5% increase in daily hospital admissions for children with asthma.[47] A study in Hefei, China, found that O_3 concentration was positively associated with hospitalization rates in children with asthma.[36] A study in Hong Kong found that an increase in O_3 concentration increased asthma hospitalization risk by 3.9% in children in the 0–14 age group.[14] However, this study did not find a clear correlation between O_3 and asthma admissions in children, which is consistent with the results of a study in Chongqing.[35] This may be related to factors, such as the different sources of pollutants, population characteristics, and regional climate change in different countries. For example, according to the descriptive results of Hefei,[36] the O_3 concentration in Hefei was higher than that in Chengdu, which may have led to a stronger correlation. In summary, the relationship between O_3 levels and hospitalization due to asthma in children requires further investigation.

Subgroup analyses by age showed that $PM_{2.5}$ and PM_{10} had greater impacts on asthma admissions in children aged 5–6 years old; however, the effects on admission rates for children aged 0–4 years and 7–18 years were not statistically significant, which is consistent with the findings of a study in Lisbon that found no significant correlation with environmental variables in children aged 0–4 years.[15] A study in Mexico found that an increase in PM_{10} and $PM_{2.5}$ significantly reduced the relative risk of asthma admissions in children under 5 years old, suggesting no relationship between PM and asthma attacks in this group of young children.[16] A study in Shanghai found that the impact of $PM_{2.5}$ on children aged 5–14 years was higher than on children aged 0–4 years ($P < 0.05$).[34] These findings align with our results, possibly because school-aged children engage in more outdoor activities and have prolonged exposure to pollutants. In contrast, preschoolers might be well protected by their parents and may have less exposure to air pollutants. Our study also found that SO_2, NO2, and CO had a larger impact on asthma admissions in children under 5 years of age, possibly due to the frequent exposure of children under 5 years of age to indoor air pollutants produced by burning coal-fired fuel at home and exposure to second-hand smoke. However, a study in Turkey found that an increase in $PM_{2.5}$ and PM_{10} levels was more closely related to asthma hospitalization in children under 5 years old.[38] This close relation might be due to the varying levels of air pollution and age distribution of populations in different regions.

To date, it has not been confirmed whether sex influences the relationship between asthma admissions and air pollutants. Most studies have concluded that boys are more affected by outdoor air pollution than girls did,[33,37,39,44] which is inconsistent with our findings. Whether sex affects the relationship between asthma-related hospitalization and air pollutants remains to be confirmed.

We found that $PM_{2.5}$ had a significant effect in the single-pollutant model; however, after SO_2, NO_2, CO, and O_3 were included, only O_3 remains statistically significant. This indicated that $PM_{2.5}$ might be affected by other air pollutants in the single-pollutant model, consistent with the findings of the Hefei study.[36]

This study has some limitations. First, the study was conducted in one city, and the data were obtained from one hospital, limiting the generalizability of our results. Second, the use of the average value of pollutants from fixed monitoring stations cannot reflect children's actual exposure. Pollutant concentrations in different locations within a city can vary greatly depending on traffic intensity, wind direction, speed, and building topography. Third, our study did not include individual factors, such as indoor pollution exposure, smoking, and activity patterns. Finally, although Chengdu is rich in flora and pollen, we did not have pollen data to be used in our models and did not consider the impact of the COVID-19 pandemic and winter flu outbreaks.

Conclusion

Our study found that air pollutants, including SO_2, NO_2, CO, $PM_{2.5}$, and $PM_{10,}$ were associated with the risk of hospitalization for childhood asthma, with SO_2 showing the strongest association. We believe that reducing air pollution in Chengdu could prevent hospitalization with asthma as the primary diagnosis. Air pollution indicators can serve as predictive factors for asthma, providing epidemiological evidence for developing prevention strategies to reduce childhood asthma hospitalization risks. Further studies are planned to explore the long-term effects of air pollution on childhood asthma, consider indoor pollution and other individual factors, and include diverse geographical locations for broader applicability.

Abbreviations

AQG, air quality guidelines; CI, confidence interval; CO, carbon monoxide; DOF, degree of freedom; DOW, day of the week; ER, excess risk; PACF, Partial Autocorrelation Function; GAM, generalized additive model; IQR, interquartile range; ISAAC, International Study of Asthma and Allergies in Childhood; NO_2, nitrogen dioxide; O_3, ozone; PM, particulate matter; R, correlation coefficient; RR, relative risk; SO_2, sulfur dioxide; WHO, World Health Organization.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Chengdu Women's and Children's Central Hospital [approval B2021(5)].The study was conducted according to the Declaration of Helsinki. Informed consent was obtained from all the parents or guardians of minors. All research activities were conducted in accordance with hospital's guidelines and requirements.

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Disclosure

The authors(s) report no conflicts of interest.

References

1. van Boven JFM, Alffenaar JC. The global asthma report. *Int J Tuberc Lung Dis*. 2022;26(1):1–3. doi:10.5588/ijtld.21.0613
2. Ferrante G, La Grutta S. The burden of pediatric asthma. *Front Pediatr*. 2018;6:1–7. doi:10.3389/fped.2018.00186
3. Global initiative for asthma. *Global Strategy for Asthma Management and Prevention*; 2023. Accessed 31, July, 2023. Available from: http://www.ginasthma.org.

4. Pitchon RR, Alvim CG, de Andrade CR, Lasmar LMLBF, Cruz ÁA, Reis APD. Asthma mortality in children and adolescents of Brazil over a 20-year period. *J Pediatr*. 2020;96(4):432–438. doi:10.1016/j.jped.2019.02.006
5. Asher MI, García-Marcos L, Pearce NE, Strachan DP. Trends in worldwide asthma prevalence. *Eur Respir J*. 2020;56(6):2002094. doi:10.1183/13993003.02094-2020
6. National Cooperative Group on Childhood Asthma; Institute of Environmental Health and Related Product Safety. Chinese Center for Disease Control and Prevention; Chinese Center for Disease Control and Prevention. *Zhonghua Er Ke Za Zhi*. 2013;51(10):729–735. PMID:24406223.
7. Gehring U, Wijga AH, Hoek G, et al. Exposure to air pollution and development of asthma and rhinoconjunctivitis throughout childhood and adolescence: a population-based birth cohort study. *Lancet Respir Med*. 2015;3(12):933–942. doi:10.1016/S2213-2600(15)00426-9
8. Wu C, Zhang Y, Wei J, et al. Associations of Early-Life Exposure to Submicron Particulate Matter With Childhood Asthma and Wheeze in China. *JAMA Network Open*. 2022;5(10):e2236003. doi:10.1001/jamanetworkopen.2022.36003
9. Zhang Y, Yin Z, Zhou P, et al. Early-life exposure to PM(2.5) constituents and childhood asthma and wheezing: findings from China, Children, Homes. *Health Study Environ Int*. 2022;165:107297.
10. Kouis P, Galanakis E, Michaelidou E, et al. Improved childhood asthma control after exposure reduction interventions for desert dust and anthropogenic air pollution: the MEDEA randomised controlled trial. *Thorax*. 2024;79(6):495–507. doi:10.1136/thorax-2023-220877
11. Tian F, Zhong X, Ye Y, et al. Mutual Associations of Exposure to Ambient Air Pollutants in the First 1000 Days of Life With Asthma/Wheezing in Children: prospective Cohort Study in Guangzhou, China. *JMIR Public Health and Surveillance*. 2024;10:e52456. doi:10.2196/52456
12. Guarnieri M, Balmes JR. Outdoor air pollution and asthma. *Lancet*. 2014;383(9928):1581–1592. doi:10.1016/S0140-6736(14)60617-6
13. Lovinsky-Desir S, Acosta LM, Rundle AG, et al. Air pollution, urgent asthma medical visits and the modifying effect of neighborhood asthma prevalence. *Pediatr Res*. 2019;85(1):36–42. doi:10.1038/s41390-018-0189-3
14. Ko FW, Tam W, Wong TW, et al. Effects of air pollution on asthma hospitalization rates in different age groups in Hong Kong. *Clin Exp Allergy*. 2007;37(9):1312–1319. doi:10.1111/j.1365-2222.2007.02791.x
15. Rodrigues M, Natário I, Do Rosário De Oliveira Martins M. Estimate the effects of environmental determining factors on childhood asthma hospital admissions in Lisbon, Portugal: a time series modelling study. *Theor Appl Climatol*. 2021;143(1–2):809–821. doi:10.1007/s00704-020-03415-w
16. Hayes L, Mejia-Arangure JM, Errington A, et al. Relationship between air quality and asthma-related emergency hospital admissions in Mexico City 2017-2019. *Thorax*. 2023;79(1):43–49. doi:10.1136/thorax-2022-219262
17. Byers N, Ritchey M, Vaidyanathan A, Brandt AJ, Yip F. Short-term effects of ambient air pollutants on asthma-related emergency department visits in Indianapolis, Indiana, 2007-2011. *J Asthma*. 2016;53(3):245–252. doi:10.3109/02770903.2015.1091006
18. Pawankar R, Wang JY, Wang IJ, et al. Asia Pacific Association of Allergy Asthma and Clinical Immunology White Paper 2020 on climate change, air pollution, and biodiversity in Asia-Pacific and impact on allergic diseases. *Asia Pac Allergy*. 2020;10(1):e11. doi:10.5415/apallergy.2020.10.e11
19. Anenberg SC, Henze DK, Tinney V, et al. Estimates of the Global Burden of Ambient [Formula: see text], Ozone, and [Formula: see text] on Asthma Incidence and emergency room Visits. *Environ Health Perspect*. 2018;126(10):107004. doi:10.1289/EHP3766
20. Guan WJ, Zheng XY, Chung KF, Zhong NS. Impact of air pollution on the burden of chronic respiratory diseases in China: time for urgent action. *Lancet*. 2016;388(10054):1939–1951. doi:10.1016/S0140-6736(16)31597-5
21. Min LI, Zhang Q, Shi W-J, et al. Epidemiological survey and analysis of asthma in children aged 0-14 years old in urban and rural areas of Chengdu region. *Chin J Contemp Pediatr*. 2013;15(08):609–613.
22. The Editorial Board, Chinese Journal of Pediatrics; the Subspecialty Group of Respiratory Diseases, the Society of Pediatrics, Chinese Medical Association. Recommendations for diagnosis and management of bronchial asthma in children. *Chin J Pediatr*. 2020;58(9):708–717.
23. Schwartz J, Spix C, Touloumi G, et al. Methodological issues in studies of air pollution and daily counts of deaths or hospital admissions. *J Epidemiol Community Health*. 1996;50(suppl 1):S3–S11. doi:10.1136/jech.50.Suppl_1.S3
24. Peng RD, Dominici F, Louis TA. Model choice in time series studies of air pollution and mortality. *J R Stat Soc A*. 2006;169(2):179–203. doi:10.1111/j.1467-985X.2006.00410.x
25. Tian Y, Xiang X, Juan J, et al. Fine particulate air pollution and hospital visits for asthma in Beijing, China. *Environ Pollut*. 2017;230:227–233. doi:10.1016/j.envpol.2017.06.029
26. Cai J, Zhao A, Zhao J, et al. Acute effects of air pollution on asthma hospitalization in Shanghai, China. *Environ Pollut*. 2014;191:139–144. doi:10.1016/j.envpol.2014.04.028
27. Raji H, Riahi A, Borsi SH, et al. Acute effects of air pollution on hospital admissions for asthma, COPD, and bronchiectasis in Ahvaz, Iran. *Int J Chron Obstruct Pulmon Dis*. 2020;2020:501.
28. Chang HH, Pan A, Lary DJ, et al. Time-series analysis of satellite-derived fine particulate matter pollution and asthma morbidity in Jackson, MS. *Environ Monit Assess*. 2019;191(suppl 2):280. doi:10.1007/s10661-019-7421-4
29. World Health Organization. Air Pollution and Child Health: prescribing Clean Air. Summary. Geneva: World Health Organization. 2018. Accessed June 1, 2024. Available from: https://www.who.int/publications/i/item/WHO-CED-PHE-18-01.
30. Hong C, Zhang Q, Zhang Y, et al. Impacts of climate change on future air quality and human health in China. *Proc Natl Acad Sci U S A*. 2019;116(35):17193–17200. doi:10.1073/pnas.1812881116
31. World Heath Organization. *WHO Global Air Quality Guidelines. Particulate Matter (PM2.5 and PM10), Ozone, Nitrogen Dioxide, Sulfur Dioxide and Carbon Monoxide*. Geneva: World Health Organization; 2021.
32. Dharmage SC, Perret JL, Custovic A. Epidemiology of asthma in children and adults. *Front Pediatr*. 2019;7:246. doi:10.3389/fped.2019.00246
33. Samoli E, Nastos PT, Paliatsos AG, Katsouyanni K, Priftis KN. Acute effects of air pollution on pediatric asthma exacerbation: evidence of association and effect modification. *Environ Res*. 2011;111(3):418–424. doi:10.1016/j.envres.2011.01.014
34. Hua J, Yin Y, Peng L, Du L, Geng F, Zhu L. Acute effects of black carbon and $PM_{2.5}$ on children asthma admissions: a time-series study in a Chinese city. *Sci Total Environ*. 2014;481:433–438. doi:10.1016/j.scitotenv.2014.02.070
35. Ding L, Zhu D, Peng D, Zhao Y. Air pollution and asthma attacks in children: a case-crossover analysis in the city of Chongqing, China. *Environ Pollut*. 2017;220(A):348–353. doi:10.1016/j.envpol.2016.09.070
36. Zhang Y, Ni H, Bai L, et al. The short-term association between air pollution and childhood asthma hospital admissions in urban areas of Hefei City in China: a time-series study. *Environ Res*. 2019;169:510–516. doi:10.1016/j.envres.2018.11.043

37. Kuo CY, Chan CK, Wu CY, Phan DV, Chan CL. The short-term effects of ambient air pollutants on childhood asthma hospitalization in Taiwan: a national study. *Int J Environ Res Public Health*. 2019;16(2):203–216. doi:10.3390/ijerph16020203
38. Ünal E, Özdemir A, Khanjani N, Dastoorpoor M, Özkaya G. Air pollution and pediatric respiratory hospital admissions in Bursa, Turkey: a time series study. *Int J Environ Health Res*. 2022;32(12):2767–2780. doi:10.1080/09603123.2021.1991282
39. Iskandar A, Andersen ZJ, Bønnelykke K, Ellermann T, Andersen KK, Bisgaard H. Coarse and fine particles but not ultrafine particles in urban air trigger hospital admission for asthma in children. *Thorax*. 2012;67(3):252–257. doi:10.1136/thoraxjnl-2011-200324
40. Tecer LH, Alagha O, Karaca F, Tuncel G, Eldes N. Particulate matter (PM(2.5), PM(10−2.5), and PM(10)) and Children's Hospital admissions for asthma and respiratory diseases: a bidirectional case-crossover study. *J Toxicol Environ Health A*. 2008;71(8):512–520. doi:10.1080/15287390801907459
41. Orellano P, Quaranta N, Reynoso J, Balbi B, Vasquez J. Effect of outdoor air pollution on asthma exacerbations in children and adults: systematic review and multilevel meta-analysis. *PLoS One*. 2017;12(3):e0174050. doi:10.1371/journal.pone.0174050
42. Zheng XY, Orellano P, Lin HL, Jiang M, Guan WJ. Short-term exposure to ozone, nitrogen dioxide, and sulphur dioxide and emergency department visits and hospital admissions due to asthma: a systematic review and meta-analysis. *Environ Int*. 2021;150:106435. doi:10.1016/j.envint.2021.106435
43. Ezratty V, Guillossou G, Neukirch C, et al. Repeated nitrogen dioxide exposures and eosinophilic airway inflammation in asthmatics: a randomized crossover study. *Environ Health Perspect*. 2014;122(8):850–855. doi:10.1289/ehp.1307240
44. Zheng XY, Ding H, Jiang LN, et al. Association between air pollutants and asthma emergency room visits and hospital admissions in time series studies: a systematic review and meta-analysis. *PLoS One*. 2015;10(9):e0138146. doi:10.1371/journal.pone.0138146
45. D'Amato G, Holgate ST, Pawankar R, et al. Meteorological conditions, climate change, new emerging factors, and asthma and related allergic disorders. A statement of the World Allergy Organization. *World Allergy Organ J*. 2015;8(1):25. doi:10.1186/s40413-015-0073-0
46. D'Amato G, Pawankar R, Vitale C, et al. Climate change and air pollution: effects on respiratory allergy. *Allergy Asthma Immunol Res*. 2016;8(5):391–395. doi:10.4168/aair.2016.8.5.391
47. Lee J-T, Cho Y-S, Son J-Y. Relationship between ambient ozone concentrations and Daily Hospital admissions for childhood asthma/atopic dermatitis in two cities of Korea during 2004–2005. *Int J Environ Health Res*. 2010;20(1):1–11. doi:10.1080/09603120903254033