



Exploring the association between pulmonary function and air pollution exposure in healthy children in Jinan, Shandong Province: based on a cross-sectional study

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Background: Previous studies have focused on the effects of air pollution on lung function in children with respiratory diseases, and there is insufficient evidence on healthy children. This cross-sectional study therefore aimed to investigate the relationship between air pollutants and lung function in healthy children.

Methods: We collected lung function measurements between December 2016 and December 2020 from a total of 780 healthy children aged 7–11 years old in an elementary school in Jinan City. Air pollutant data, including particulate matter with an aerodynamic diameter ≤ 2.5 μm ($\text{PM}_{2.5}$) and ≤ 10 μm (PM_{10}), sulphur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO) and ozone (O_3), were collected from the nearest monitoring stations to the school. Multiple linear regression models were developed to assess the relationship between pollutants and children's lung function indices.

Results: Increasing pollutant concentrations were associated with decreases in forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), peak expiratory flow (PEF), forced expiratory flow at 25% (FEF_{25}) and forced expiratory flow at 75% (FEF_{75}). In addition, this effect had a lag effect and a cumulative lag effect, especially at lag 3 d, with significant decreases in FEV_1 and PEF. Specifically, for every 10 $\mu\text{g}/\text{m}^3$ increase in the concentrations of $\text{PM}_{2.5}$, PM_{10} , SO_2 , NO_2 , and CO , the FEV_1 decreased by 1.05 mL [95% confidence interval (CI): -2.02, -0.08], 1.18 mL (95% CI: -1.94, -0.42), 4.96 mL (95% CI: -8.08, -1.84), 4.94 mL (95% CI: -7.59, -2.28), and 0.11 mL (95% CI: -0.20, -0.01), respectively. For every 10 $\mu\text{g}/\text{m}^3$ increase in PM_{10} , SO_2 , NO_2 , and CO , PEF decreased by 3.80 mL (95% CI: -6.51, -1.08), 16.73 mL (95% CI: -27.83, -5.63), 17 mL (95% CI: -26.44, -7.55), and 0.39 mL (95% CI: -0.72, -0.05), respectively. Boys' lung function was more sensitive to pollutants than girls'.

Conclusions: Short-term exposure to air pollutants is harmful to children's health and appropriate protective measures should be taken to minimize the adverse effects of air pollution on children's health.

Keywords: Air pollution; children; pulmonary function; cross-sectional study

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Introduction

Air pollutants pose a serious threat to human health. Among them, particulate matter with an aerodynamic diameter $\leq 2.5 \mu\text{m}$ ($\text{PM}_{2.5}$) is of particular concern because it can penetrate deeper into the human respiratory tract and alveoli, and even further into the bloodstream, seriously damaging the respiratory system (1). Particulate matter with an aerodynamic diameter $\leq 10 \mu\text{m}$ (PM_{10}) can also enter the respiratory tract below the larynx, posing a potential hazard to human health (2). Long-term exposure to these air pollutants, especially PM_{10} , has been shown to be strongly associated with decreased lung function in non-asthmatic schoolchildren (3,4). Notably, even short-term exposure to high concentrations of nitrogen dioxide (NO_2) is directly associated with acute decrease in lung function and is strongly linked to a significantly elevated risk of pneumonia in children (5,6).

Children are more sensitive to air pollutants as their immune and respiratory systems are not fully developed; they are also likely to inhale more air pollutants than adults during physical exercise (7-9). Due to the lower height of children, they are closer to the ground and are therefore more likely to inhale air containing higher concentrations

of pollutants (10). Lung function is an important objective indicator of the health of the human respiratory system. Some studies have shown (11-13) that short-term exposure to air pollutants is associated with decreased lung function in children. Therefore, an in-depth investigation of the relationship between pollutants and children's lung function may help to improve our understanding of the threats of air pollution to children's respiratory health, which may provide a basis for the development of effective measures to protect children's respiratory health.

Although prior studies have demonstrated an association between elevated pollutant concentrations over short periods of time and decreased lung function in children, these studies focused on children with medical conditions (14-16), which limits the applicability of the findings to the healthy children. And these studies also focused on a single indicator or a limited number of indicators of lung function, such as forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1) and peak expiratory flow (PEF) (17-19), whereas in reality lung function tests cover a much wider range of indicators, for example, also including forced expiratory flow at 25% (FEF_{25}) and forced expiratory flow at 75% (FEF_{75}). In addition, most studies have focused primarily on the effects of a single pollutant (20-22), with only a few studies focusing on the joint effects of multiple pollutants (23).

In view of this, we sought to explore the short-term and lagged effects of air pollutants on healthy children using five key lung function indices (FVC, PEF, FEV_1 , FEF_{25} and FEF_{75}), and in addition to constructing a multi-pollutant model to investigate the joint effects of pollutants in order to gain a more comprehensive understanding of their potential impact on children's health. We hope that this study will provide practical significance and scientific basis for the formulation of more effective policies to protect children's respiratory health. We present this article in accordance with the STROBE reporting checklist (available at <https://tp.amegroups.com/article/view/10.21037/tp-24-438/rc>).

Methods

Study area

The present study was based in Jinan City, one of the most heavily air-polluted cities in China. Jinan is an inland city in northern China and the capital of Shandong Province; it covers a total of $8,177.21 \text{ km}^2$ and is divided into ten districts. It is located at 36.40°N latitude and 110.00°E longitude. As a northern inland city, the low temperatures

Highlight box

Key findings

- On the third day of exposure to air pollutants (lag 3 d), healthy children showed a decrease in lung function indices [forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), peak expiratory flow (PEF), forced expiratory flow at 25% (FEF_{25}) and forced expiratory flow at 75% (FEF_{75})], which was also shown by the results of the multi-pollutant modeling.

What is known and what is new?

- Previous studies have linked air pollutant exposure to decreased lung function in children, but there has been limited research on this relationship among healthy children. These studies typically focused on a narrow range of lung function indicators, such as FVC, FEV_1 , and PEF, and primarily utilized single pollutant models.
- This study lies in its demonstration that short-term exposure to air pollutants not only affects FVC, FEV_1 , and PEF but also impacts FEF_{75} and FEF_{25} in healthy children. Additionally, a joint effect of multiple pollutants on lung function was observed.

What is the implication, and what should change now?

- This study raises alarm bells about the threat of air pollution to lung development in healthy schoolchildren. It could inform the development of preventive measures.

in winter make it difficult for pollutants to disperse, and the burning of coal and other fossil fuels may also add to the air pollution (23). This city is also one of the important transportation hubs in east China, with its primary energy source dominated by coal. The climate there is a mid-latitude monsoon climate.

Study design and participants

This study was a longitudinal cross-sectional study. In this study, stratified random sampling was used to stratify the school's students in grades 3 through 5 by grade level, with each grade level serving as a separate stratum. In December of each year between 2016 and 2020, one class from each grade level stratum was randomly selected for testing. This random sampling strategy ensured that each class in each grade level had the same probability of being selected, effectively reducing the impact of selection bias on the study results. Before performing the lung function tests, we first interviewed the parents of the students to rule out any children with underlying respiratory conditions. Second, we measured the body indices, including height (cm) and weight (kg), of all study participants who participated in the test, and recorded their sex and date of birth in detail. Finally, a professional technician verifies basic information about each subject and performs brief health screenings on all participating children to ensure that they do not have respiratory illnesses or symptoms on the day of the test. These screenings include asking children if they have symptoms such as fever, cough or shortness of breath, and if they have recently sought medical attention.

To ensure the reliability of the findings and the quality of the survey, the main content and precautions of the survey were explained to students, their guardians and school leaders before the survey was conducted, and parents were assured that the information they provided would be kept strictly confidential and would not be used for any other purposes. The survey was entirely voluntary and informed consent was obtained from all participants and their primary guardians. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Shandong Second Medical University (No. 2021SDL188) and informed consent was taken from all the participants' guardians.

Measurement of pulmonary function

All pulmonary function tests are performed by trained

technicians in accordance with the 2005 Pulmonary Function Test Standards published by the American Thoracic Society (ATS) and the European Respiratory Society (ERS) (24). The spirometer was calibrated before the test. During the test, the child stood, wore a nose clip, and blew at least three times into a portable spirometer (Pony FX, Italy) with a disposable mouthpiece. If the difference between the two highest FVC and FEV₁ values was less than 150 mL (or within 5%) and the difference between the maximum and minimum PEF values was less than 0.67 L/s, the reproducibility of the test result was acceptable. For those children whose pulmonary function results did not meet this criterion, up to eight breath tests were required. Pulmonary function indices include FVC, FEV₁, PEF, FEF₇₅, FEF₂₅.

Air pollution exposure

Air quality data for Jinan during the study period were obtained from the National Urban Air Quality Real-time Distribution Platform operated by the China Environmental Monitoring Centre (<https://www.cnemc.cn>). The platform ensured that the data were updated daily and the nearest national control station to the study site was selected to obtain 24-hour air pollutant averages. Air pollutants include PM_{2.5}, PM₁₀, SO₂, NO₂, CO and O₃-8h. Concurrent weather data, including average temperature (Temp, °C) and relative humidity (RH, %), were sourced from the Jinan Meteorological Bureau's official website (<http://jnqx.jinan.gov.cn>).

Statistical analysis

Descriptive analysis was conducted for air quality indicators, weather conditions, subject characteristics, and pulmonary function indicators. Chi-squared tests were used for sex and age distributions. Spearman's correlation analysis assessed the relationships between pollutant concentrations, lung function indicators, and meteorological factors (temperature and humidity). Body mass index (BMI) was calculated as weight divided by height squared. Multiple linear regression models were established to evaluate the impact of elevated air pollutant concentrations on lung function, adjusting for age, sex, height, weight, temperature, and humidity. Separate subgroup analyses were also performed for male and female students. Stepwise regression was used to select the optimal model based on the lowest Akaike Information Criterion (AIC) value. The results were presented as

Table 1 Gender distribution of children who underwent pulmonary function tests

Variable	Male	Female	Total	χ^2	P value
Year				5.449	>0.05
2016	85 (48.30)	91 (51.70)	176		
2017	82 (51.25)	78 (48.75)	160		
2018	90 (56.60)	69 (43.40)	159		
2019	83 (59.29)	57 (40.71)	140		
2020	72 (49.66)	73 (50.34)	145		
Age (years)				0.580	>0.05
7–9	222 (53.75)	191 (46.25)	413		
10–11	190 (51.77)	177 (48.23)	367		

Data are presented as n (%).

changes in pulmonary function indicators per 10 $\mu\text{g}/\text{m}^3$ increase in the concentration of different air pollutants and the corresponding 95% confidence interval (95% CI).

To explore whether there was a lagged effect of different air pollutants on the pulmonary function of children, we analyzed the lagged effect of each pollutant independently in the model at a single lag (lag0–lag5) and cumulative lags (lag05), with lag0 referring to the pollutant concentration on the day of the pulmonary function test, Lag1 referring to the pollutant concentration on the day before the pulmonary function test and so on; Lag05 referring to the cumulative mean on the day of the pulmonary function test and the previous 5 days.

We constructed a multi-pollutant model to analyze the joint effects of multiple pollutants on lung function by selecting the pollutant with statistically significant differences (NO_2) as the main model in the single-pollutant model, and then adding the other pollutants ($\text{PM}_{2.5}$, SO_2 , and O_3 -8 h) to NO_2 , respectively. Since the correlation coefficients between NO_2 and PM_{10} and between NO_2 and CO were very high, which may indicate a multicollinearity problem. Therefore, we only included $\text{PM}_{2.5}$, SO_2 and O_3 in the multi-pollutant model for data analysis.

Data analysis was performed using the R software (version 4.2.3). We used the “dplyr” data processing package in R to calculate the lagged effects of pollutant exposure and further derived the cumulative lagged effects by accumulating multiple lagged values. All the tests were two-tailed, and a P value of less than 0.05 was indicative of statistical significance.

Results

General information

In this study, a total of 791 children participated in the initial survey. After screening, children with respiratory diseases such as asthma, pneumonia, bronchitis or colds, and those who were unable to attend school for the test due to leave of absence, totaling 11, were excluded. Eventually, a total of 780 children were included in the study and underwent pulmonary function tests, including 412 boys and 368 girls. There were no significant differences in gender ($\chi^2=5.449$, $P>0.05$) and age ($\chi^2=0.580$, $P>0.05$) across test years (Table 1).

The general characteristics and pulmonary function indicators of the subjects and meteorological factors are shown in Table 2. The mean height of the 780 children was 141.52 cm, the mean height was 38.94 kg, and the mean BMI was 19.13 kg/m^2 . The mean FVC was 2.03 L [standard deviation (SD) =0.44], the mean FEV_1 was 1.73 L (SD =0.38), and the mean PEF was 2.95 L/s (SD =0.93). According to the Ambient Air Quality Standards GB 3095-2012, the $\text{PM}_{2.5}$ concentration exceeded the secondary standard limits during the survey, with a mean $\text{PM}_{2.5}$ concentration of 88.83 $\mu\text{g}/\text{m}^3$ (SD =51.08) (Table 2).

Correlation analysis

All the pollutants were found to be positively correlated with Temp, with NO_2 showing the greatest correlation with Temp ($\rho=0.444$, $P<0.01$) and O_3 showing the minimum correlation with Temp ($\rho=0.250$, $P<0.01$) (Table 3). All pollutants except O_3 were positively correlated with RH, with $\text{PM}_{2.5}$ having the greatest correlation with RH ($\rho=0.642$, $P<0.01$).

The associations between air pollution exposure and pulmonary function parameters are presented in Table S1. Correlation analyses showed that air pollutants were negatively correlated with lung function indices on the day of exposure (lag0), on the third day of lag (lag3), and cumulative lag exposure up to 5 days (lag05).

Association between pollutant exposure and lung function

Single-pollutant model

The single-pollutant model showed varying degrees of lagged and cumulative lagged effects of air pollutants on children's lung function, with significant decreases in lung function FEV_1 and PEF (Figure 1, Table S2). At lag3, FEV_1

Table 2 General characteristics and pulmonary function parameters of the children and the meteorological factors

Variable	Mean \pm SD	Percentile				
		Min	Max	25th	50th	75th
Characteristics						
Height (cm)	141.52 \pm 8.79	120	177	135	140	147
Weight (kg)	38.94 \pm 11.79	18.40	85.20	30	36.60	45.58
BMI (kg/m ²)	19.13 \pm 4.15	12.16	33.59	15.90	18.27	21.88
Lung function parameters						
FVC (L)	2.03 \pm 0.44	1.00	4.02	1.73	1.98	2.27
FEV ₁ (L)	1.73 \pm 0.38	0.63	3.36	1.47	1.69	1.97
PEF (L/s)	2.95 \pm 0.93	0.67	5.78	2.28	2.89	3.54
FEF ₇₅ (L/s)	1.19 \pm 0.36	0.27	2.80	0.92	1.16	1.40
FEF ₂₅ (L/s)	2.78 \pm 0.90	0.65	5.75	2.17	2.73	3.38
Air pollutants						
PM _{2.5} (μg/m ³)	88.83 \pm 51.08	18.87	256.17	48.98	81.45	119.33
PM ₁₀ (μg/m ³)	147.58 \pm 63.23	49.30	335.74	100.58	138.69	184.13
SO ₂ (μg/m ³)	28.11 \pm 15.72	7.09	78.48	16.65	23.13	36.89
NO ₂ (μg/m ³)	59.98 \pm 18.31	13.33	112.52	47.16	60.67	70.60
CO (mg /m ³)	1.40 \pm 0.52	0.47	2.99	1.03	1.32	1.78
O ₃ (μg/m ³)	27.50 \pm 17.37	4.46	95.05	16.93	22.63	35.77
Weather conditions						
Temp/°C	3.03 \pm 4.06	−6.8	18	−0.6	4.3	5.85
RH/%	47.35 \pm 22.55	11.1	91	27	42.50	69

BMI, body mass index; CO, carbon monoxide; FEF₂₅, forced expiratory flow at 25%; FEF₇₅, forced expiratory flow at 75%; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; NO₂, nitrogen dioxide; O₃, ozone; PEF, peak expiratory flow; PM_{2.5}, particulate matter with an aerodynamic diameter \leq 2.5 μ m; PM₁₀, particulate matter with an aerodynamic diameter \leq 10 μ m; RH, relative humidity; SD, standard deviation; SO₂, sulphur dioxide; Temp, temperature.

decreased by 1.05 mL (95% CI: -2.02, -0.08), 1.18 mL (95% CI: -1.94, -0.42), 4.96 mL (95% CI: -8.08, -1.84), 4.94 mL (95% CI: -7.59, -2.28) and 0.11 mL (95% CI: -0.20, -0.01) for every 10 μ g/m³ increase for PM_{2.5}, PM₁₀, SO₂, NO₂, and CO, respectively; for every 10 μ g/m³ increase in PM₁₀, SO₂, NO₂, and CO, PEF decreased by 3.80 mL (95% CI: -6.51, -1.08), 16.73 mL (95% CI: -27.83, -5.63), 17 mL (95% CI: -26.44, -7.55), and 0.39 mL (95% CI: -0.72, -0.05), respectively. Furthermore, all five lung function indices were significantly decreased in children when exposed to SO₂ and NO₂ ($P < 0.05$).

Multi-pollutant model

Table 4 shows the results of the multi-pollutant models.

According to the principle of statistical significance in the single-pollutant model, the optimal effect day of lung function indices FVC, FEV₁, PEF, FEF₇₅, and FEF₂₅ was determined to be lag3.

The dual-pollutant model showed a significant ($P < 0.05$) decrease in FEV₁ and PEF when NO₂ was jointed with PM_{2.5}, SO₂ and O₃. The multi-pollutant model showed a significant ($P < 0.05$) decrease in PEF when particulate matter was combined with gaseous pollutants (Table 4).

After correction of the P value by the Bonferroni test (Table S3), both the two-pollutant model and the multi-pollutant model showed that the children's lung function indices still showed significant decreases of varying magnitude ($P < 0.05$) when irritant gases were jointed with

Table 3 Correlation between pollutants and meteorological factors

Variable	PM _{2.5}	PM ₁₀	SO ₂	NO ₂	CO	O ₃	Temp	RH
PM _{2.5}	1.000							
PM ₁₀	0.907**	1.000						
SO ₂	0.438**	0.561**	1.000					
NO ₂	0.684**	0.802**	0.697**	1.000				
CO	0.888**	0.845*	0.498**	0.773*	1.000			
O ₃	-0.231*	-0.265**	-0.063	-0.429**	-0.350**	1.000		
Temp	0.402**	0.435*	0.341**	0.444*	0.400**	0.250**	1.000	
RH	0.642**	0.521*	0.123	0.326**	0.550**	-0.331**	0.159	1.000

*, significant correlation at the level of $\alpha=0.05$; **, significant correlation at the level of $\alpha=0.01$. CO, carbon monoxide; NO₂, nitrogen dioxide; O₃, ozone; PM_{2.5}, particulate matter with an aerodynamic diameter ≤ 2.5 μm ; PM₁₀, particulate matter with an aerodynamic diameter ≤ 10 μm ; RH, relative humidity; SO₂, sulphur dioxide; Temp, temperature.

particulate matter.

Gender analysis

The results showed (Table 5) that pollutants had inconsistent effects on lung function in boys and girls, with boys showing a significant decrease in the lung function index FVC compared to girls ($P<0.05$). For every 10 $\mu\text{g}/\text{m}^3$ increase in SO₂ and NO₂, the boys' FVC decreased by 8.05 and 5.63 mL, respectively.

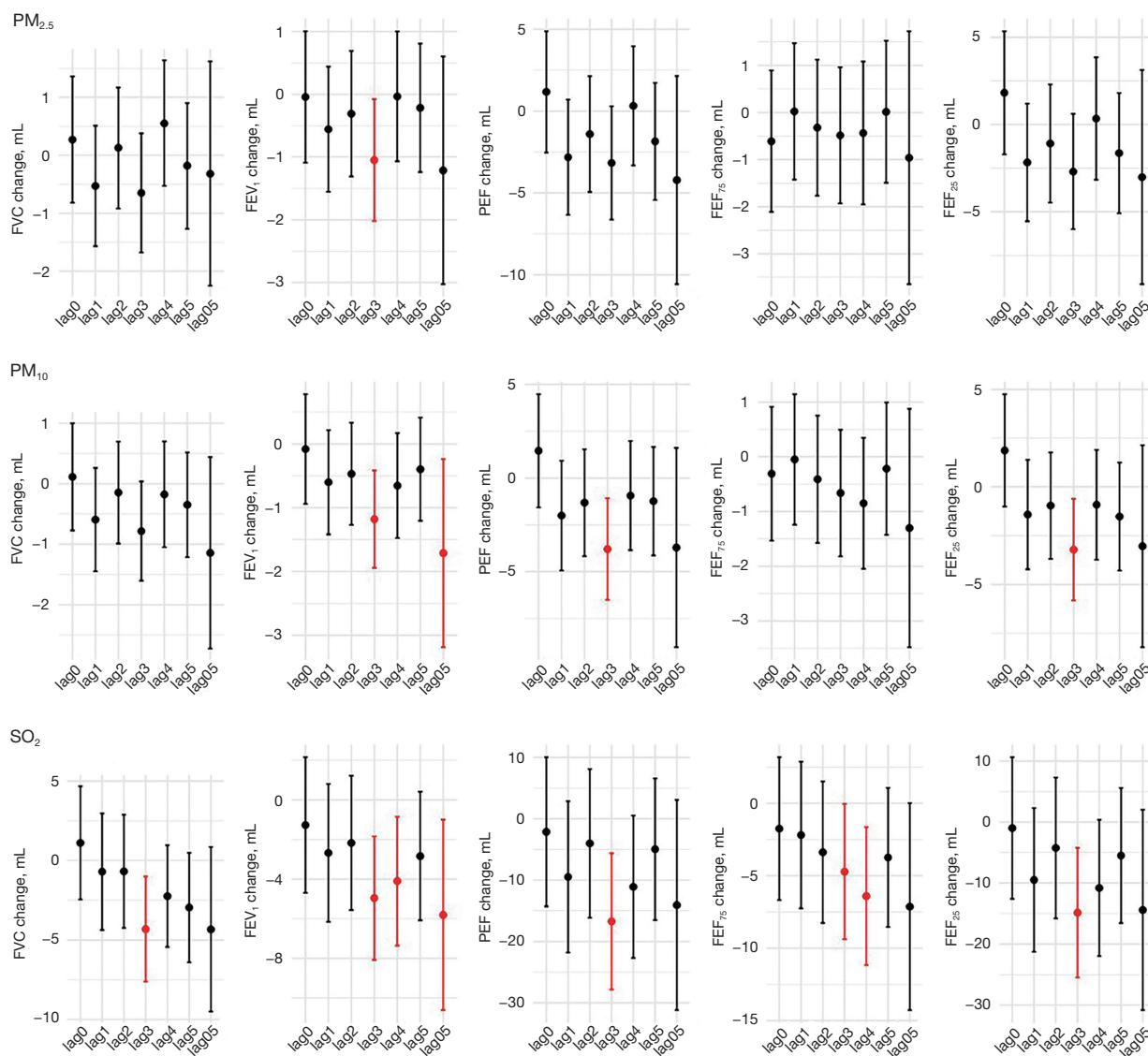
Discussion

This study explored the relationship between short-term exposure to air pollutants and children's lung function by measuring lung function in healthy children. The results of the study showed that children's lung function decreased after short-term exposure to pollutants. Further studies found that the effects were not limited to the moment of exposure, but that there was a significant lag effect and a cumulative lag effect. In particular, the pulmonary function index showed a significant decrease on the lag 3 d. In order to gain a more comprehensive understanding of the effects of different pollutants on children's lung function, we used a multi-pollutant model for our analysis. The results showed a significant decrease in FEV₁ and PEF when NO₂ was combined with PM_{2.5}, SO₂ and O₃. In addition, the study conducted a stratified analysis to explore changes in lung function in children of different genders in response to pollutant exposure. It was found that boys' lung function was more sensitive to pollutant exposure.

Our results showed a statistically significant association

between increasing pollutant concentrations and decreasing lung function indices in children, indicating that short-term exposure to air pollutants decreases lung function in healthy children. This finding is consistent with previous studies (25-27), all of which confirm the potential adverse effects of air pollutants on lung function in children. More importantly, we also observed a lagged and cumulative lagged effect of pollutants on lung function, a result supported by previous studies (7,14,28), confirming the persistence of the health risks posed by pollutants on children's lung function.

Compared with previous studies, we were more comprehensive in the selection of study indicators. While previous studies focused on the core indices of FVC, FEV₁, and PEF, our study included important indices such as FEF₂₅ and FEF₇₅ in addition to FVC, FEV₁, and PEF. For example, a study of 315 schoolchildren aged 9 to 16 years in Bangladesh revealed that PEF and FEV₁ showed a decrease of -4.19% and -2.05%, respectively, for every 20 $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} concentration (29). Another panel study of 86 children in China similarly showed that for every 10 $\mu\text{g}/\text{m}^3$ increase in the 1-day moving average concentration of PM_{2.5}, the values of FVC, FEV₁, and PEF decreased by 23.22 mL, 18.93 mL, and 29.38 mL/s, respectively (30). In addition, a Japanese study also found a significant -3.67 L/min decrease in PEF for every 13.6 ppb increase in O₃ exposure over the interquartile range (31). The comparison of these findings further highlights the comprehensiveness of our study in terms of indicator selection. And in clinical practice (32,33), FVC is often used to assess the function of the large airway, FEV₁ is used



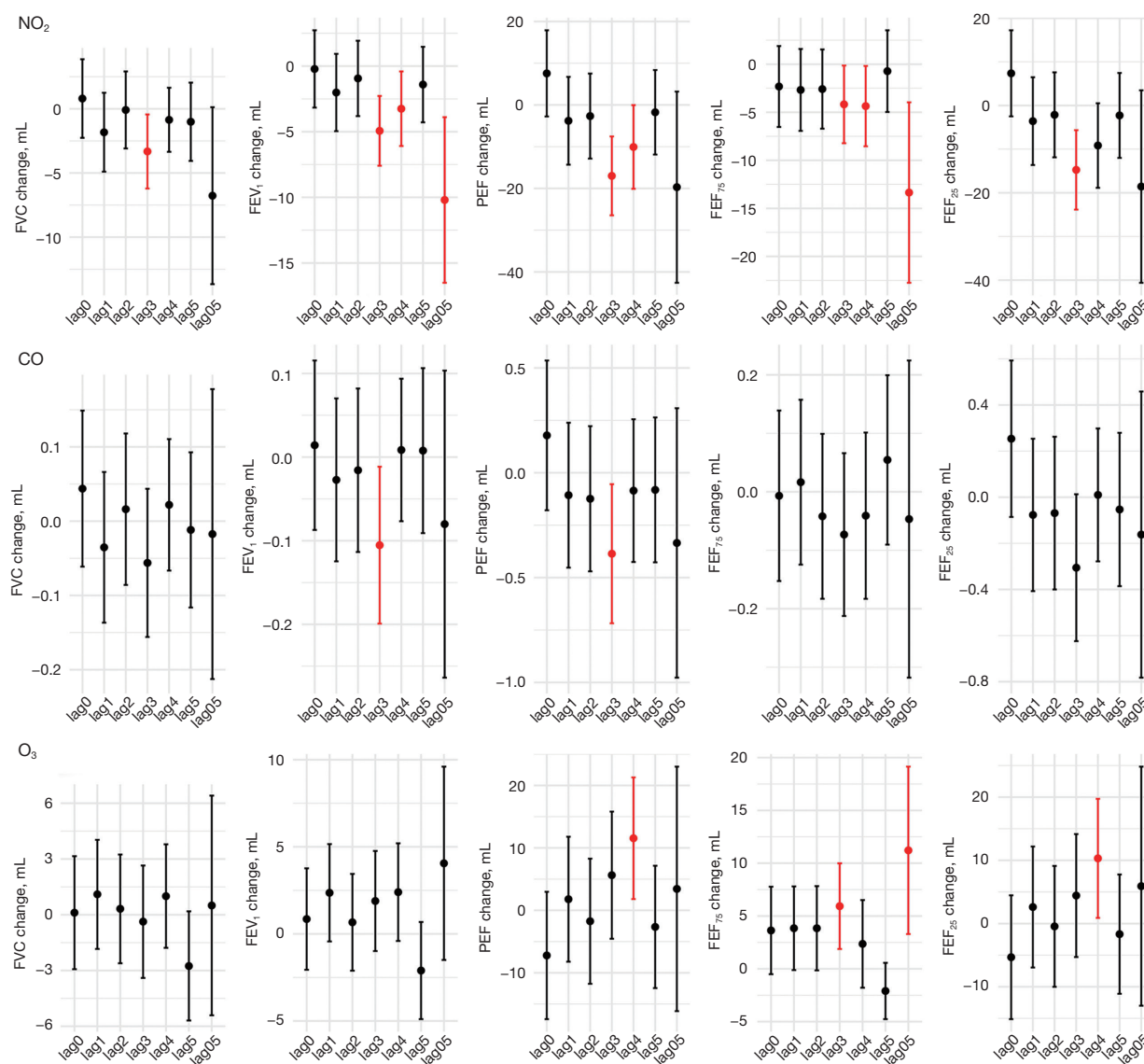


Figure 1 Association of short-term air pollution exposure with children's lung function. Estimates are presented as coefficients with 95% CI per $10 \mu\text{g}/\text{m}^3$ increase in each pollutant. Red line indicates $P < 0.05$, black line indicates $P > 0.05$. Results are shown for current day exposure (lag0) to 5 days before exposure (lag-5) and for cumulative lag exposure up to 5 days (lag05). The multiple linear regression models were adjusted for age, weight, height, sex, relative humidity, and average temperature. CI, confidence interval; CO, carbon monoxide; FEF_{25} , forced expiratory flow at 25%; FEF_{75} , forced expiratory flow at 75%; FEV_1 , forced expiratory volume in 1 second; FVC, forced vital capacity; NO_2 , nitrogen dioxide; O_3 , ozone; PEF, peak expiratory flow; $\text{PM}_{2.5}$, particulate matter with an aerodynamic diameter $\leq 2.5 \mu\text{m}$; PM_{10} , particulate matter with an aerodynamic diameter $\leq 10 \mu\text{m}$; SO_2 , sulphur dioxide.

to reflect the obstruction of large and small airways, and PEF is used to reveal airway obstruction and respiratory muscle strength. FEF_{25} and FEF_{75} are often regarded as proxies for peripheral small airway function. In this study, we found that all lung function indices of children decreased

as the concentration of air pollutants increased; thus, it is evident that exposure to air pollutants not only affects children's large airway function, but also has a significant negative effect on their small airway function. This finding further emphasizes the importance of good air quality in

Table 4 Results of multi-pollutant modeling of air pollutant concentrations per 10 µg/m³ increase and lung function indicators in children

Pollutant model	FVC (mL)	FEV ₁ (mL)	PEF (mL)	FEF ₇₅ (mL)	FEF ₂₅ (mL)
Dual-pollutant model					
NO ₂	-3.32 (-6.21, -0.44)*	-4.94 (-7.59, -2.28)***	-17.00 (-26.44, -7.55)***	-4.18 (-8.22, -0.14)*	-14.75 (-23.84, -5.65)**
+PM _{2.5}	-3.95 (-7.99, 0.10)*	-5.55 (-9.27, -1.82)**	-20.85 (-34.06, -7.64)**	-6.27 (-11.91, -0.63)*	-18.27 (-30.99, -5.55)**
+SO ₂	-1.38 (-5.41, 2.64)	-3.78 (-7.51, -0.06)*	-13.45 (-26.72, -0.18)*	-2.59 (-8.26, 3.09)	-11.25 (-24.03, 1.52)
+O ₃	-4.48 (-7.73, -1.23)**	-5.21 (-8.24, -2.18)***	-18.35 (-29.08, -7.61)**	-1.89 (-6.39, 2.61)	-16.20 (-26.54, -5.85)**
Multi-pollutant model					
NO ₂ + PM _{2.5}	-3.95 (-7.99, 0.10)*	-5.55 (-9.27, -1.82)**	-20.85 (-34.06, -7.64)**	-6.27 (-11.91, -0.63)*	-18.27 (-30.99, -5.55)**
+SO ₂	-1.76 (-6.98, 3.46)	-4.30 (-9.13, 0.53)	-17.37 (-34.54, -0.21)*	-4.77 (-12.10, 2.55)	-14.79 (-31.32, 1.74)
+O ₃	-5.23 (-9.59, -0.87)*	-5.88 (-9.94, -1.82)**	-22.38 (-36.74, -8.03)**	-3.85 (-9.86, 2.17)	-19.91 (-33.75, -6.07)**

Data are presented as β (95% CI). *, significant correlation at the level of α=0.05; **, significant correlation at the level of α=0.01; ***, significant correlation at the level of α=0.001. These estimates are from dual and multi-pollutant regression models, with adjustments for age, sex, height, weight, average temperature and relative humidity. CI, confidence interval; FEF₂₅, forced expiratory flow at 25%; FEF₇₅, forced expiratory flow at 75%; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; NO₂, nitrogen dioxide; O₃, ozone; PEF, peak expiratory flow; PM_{2.5}, particulate matter with an aerodynamic diameter ≤2.5 µm; SO₂, sulphur dioxide.

Table 5 Changes in lung function indicators of children of different sexes per 10 µg/m³ increase in air pollutant concentration

Pulmonary function	Air pollutants	Male	Female
FVC (mL)	PM _{2.5}	1.15 (-1.04, 3.34)	0.03 (-1.11, 1.17)
	SO ₂	8.05 (1.33, 14.76)*	-0.51 (-4.50, 3.49)
	NO ₂	5.63 (0.18, 11.08)*	-0.65 (-4.09, 2.80)
FEV ₁ (mL)	PM _{2.5}	0.64 (-1.37, 2.64)	-0.21 (-1.40, 0.97)
	SO ₂	-0.06 (-6.51, 6.38)	-0.54 (-4.70, 3.61)
	NO ₂	1.87 (-3.26, 6.99)	-0.43 (-4.02, 3.15)
PEF (mL)	PM _{2.5}	4.40 (-2.77, 11.58)	-0.24 (-4.50, 4.02)
	SO ₂	-0.37 (-23.69, 22.94)	-3.43 (-18.31, 11.45)
	NO ₂	14.84 (-3.33, 33.01)	3.93 (-8.90, 16.75)
FEF ₇₅ (mL)	PM _{2.5}	-1.47 (-4.26, 1.31)	-0.13 (-1.98, 1.72)
	SO ₂	-7.76 (-16.49, 0.97)	1.91 (-4.54, 8.36)
	NO ₂	-6.08 (-13.07, 0.92)	0.17 (-5.42, 5.75)
FEF ₂₅ (mL)	PM _{2.5}	4.53 (-2.38, 11.44)	0.73 (-3.28, 4.75)
	SO ₂	-3.00 (-25.48, 19.47)	0.94 (-13.13, 15.02)
	NO ₂	11.63 (-6.06, 29.32)	6.05 (-5.98, 18.08)

Data are presented as β (95% CI). *, significant correlation at the level of α=0.05. The multiple linear regression models were adjusted for age, weight, height, sex, relative humidity, and average temperature. CI, confidence interval; FEF₂₅, forced expiratory flow at 25%; FEF₇₅, forced expiratory flow at 75%; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; NO₂, nitrogen dioxide; O₃, ozone; PEF, peak expiratory flow; PM_{2.5}, particulate matter with an aerodynamic diameter ≤2.5 µm; SO₂, sulphur dioxide.

maintaining respiratory health.

The association between exposure to pollutants and decreased lung function observed in this study may be due to multiple mechanisms. It has been suggested that oxidative stress and inflammatory responses are the core mechanisms by which air pollutants adversely affect human health (34,35). Specifically, $PM_{2.5}$, due to its extremely small particle size, easily penetrates the alveoli and activates an inflammatory response (36), and even low levels of $PM_{2.5}$ may trigger airway inflammation (15), which can ultimately lead to a decrease in lung function. On the other hand, SO_2 exposure should not be ignored. Studies have shown that SO_2 can increase the expression levels of certain genes involved in inflammatory pathways, which in turn triggers oxidative damage in the lungs (37). In addition, air pollutants such as NO_2 have been shown to induce the production of reactive oxygen species (ROS), which further contributes to tissue inflammation and cell death, resulting in potential damage to lung function (38).

It is worth mentioning that the present study also revealed the existence of a lagged effect of O_3 on lung function, in particular the persistent correlation with FEF_{75} . The low water solubility of O_3 , a pollutant with significant acute health effects, makes it more likely to be retained in the small airways (39); this is in line with our study, where O_3 was associated with a decrease in FEF_{75} , which represents the function of small airways. However, the effects of O_3 on children's pulmonary function are not significant compared to other pollutants, which might be related to the lower temperature in winter, at which the concentration of O_3 is usually lower. An analysis of air pollution control measures and their co-benefits in Jinan showed a significant increasing trend in ozone concentrations in the city since 2013 (40), which further highlights the importance of continuous monitoring and assessment of the public health impacts of air pollution. This reminds us of the need to comprehensively consider the characteristics of different pollutants and their health impacts when formulating air quality improvement measures.

In our multi-pollutant model, the correlation coefficients between NO_2 and PM_{10} and between NO_2 and CO are very high, suggesting the problem of multicollinearity. Therefore, we included only $PM_{2.5}$, SO_2 and O_3 in our multi-pollutant model. The modeling results showed that NO_2 was associated with a decrease in lung function indices ($P < 0.05$), especially PEF, which is consistent with the results of a national cohort study (41). These results strongly suggest that traffic-related air pollution, represented by

NO_2 , has a significant impact on children's respiratory health.

The specific mechanisms by which sex differences play a role in the response to air pollutants are currently unknown. Although existing studies have given increasing attention to this issue, the conclusions are not consistent. Notably, our study reveals that boys' lung function is more sensitive to air pollutants compared to girls', which is consistent with previous studies (42,43). However, there are also studies with opposite findings (9,44,45). These differences may stem from differences in methodology, measurement techniques, and age distribution of subjects across studies, while the types of air pollutants studied may also have an impact on the results. Therefore, to fully understand the role of gender in the response to air pollutants, future research needs to integrate these factors and use more standardized research methods.

Despite the insights of this study, there are some limitations. First, because air pollutant data are derived from existing and fixed monitoring stations, their measurements may deviate from the actual exposure of individuals, and this indirect assessment of exposure may lead to misclassification. Second, the study failed to adequately consider and adjust for some important confounding factors, such as home environment, parental smoking habits, and socioeconomic status, which may have an impact on children's lung function, and therefore future studies could incorporate home environment questionnaires to collect data on household pollutants (e.g., indoor smoking, cooking practices, heating equipment, etc.) to more comprehensively assess the actual exposure of children's levels. Third, since the pulmonary function tests in this study were performed specifically in December of each year, this temporal limitation makes the significance and generalizability of the findings somewhat limited. However, even with these limitations, the present study revealed a strong association between short-term exposure to different air pollutants and acute impairment of lung function in children and pointed out the lagged and cumulative lagged effects of air pollutants.

Conclusions

Overall, the present study reveals a significant negative association between some atmospheric pollutants and lung function in healthy children, especially those closely related to transportation, such as NO_2 and SO_2 . Therefore, to effectively safeguard the respiratory health of children and

adolescents, we need to adopt a series of targeted public health measures.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://tp.amegroups.com/article/view/10.21037/tp-24-438/rc>

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Shandong Second Medical University (No. 2021SDL188) and informed consent was taken from all the participants’ guardians.

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