Association between air pollution and lung development in schoolchildren in China

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ABSTRACT

Background China has been facing nationwide air pollution at unprecedented high levels primarily from fossil-fuel combustion in the past decade. However, few studies have been conducted on the adverse effect of severe air pollution on lung development in school-age children.

Methods Using wellness check and air pollution data from 2014 to 2017, we conducted a retrospective analysis of lung development in 21,616 school-age children from Shijiazhuang and Qingdao from North China with severe vs mild air pollution. Linear mixed effects model was performed to assess the effect of air pollution on forced vital capacity (FVC) growth.

Results Exposure to severe air pollution was associated with a dramatic reduction in annual FVC growth rate (−71.3 mL, p < 0.001). In addition, every 10 μg/m³ increase in annual PM2.5 level was associated with a reduction of annual FVC growth by 12.2 mL (p < 0.001). Sex discrepancy (boys vs girls) in FVC growth was greater in Qingdao (35.4 mL/year, 95% CI: 26.0 to 44.7) than in Shijiazhuang (19.8 mL/year, 95% CI: 9.3 to 30.3) (p for interaction=0.063). Exposure to indoor coal- or wood-burning stove heating (−79.4 mL, p < 0.001) and secondhand smoke at home (−59.3 mL, p= 0.003) were inversely associated with FVC growth.

Conclusion Our study raised serious alarm over the threat of severe air pollution to lung development in school-age children. Sex discrepancy in lung development was reduced dramatically in heavily polluted area.

INTRODUCTION

Ambient and indoor air pollution are the world’s most detrimental threat to children’s health and are also major causes for global inequality and environmental injustice.1 In China, residents have been exposed to nationwide air pollution at unprecedented high levels primarily from fossil-fuel combustion due to rapid urbanisation and industrialisation in the past two decades.2–4 In 2016, 81% of Chinese were living in places where the concentrations of particulate matter with aerodynamic diameters <2.5 μm (PM2.5) were higher than the Interim Target-1 limit (35 μg/m³) set by the WHO.5 6 Although humans of all ages could be affected by air pollution exposure, children are disproportionately affected because their lungs and immune systems are developing, and they are more active in environments with high levels of pollutants relative to adults.1 7

Forced vital capacity (FVC) reflects the total compliance from both the lung and the chest wall and serves as a common indicator of lung development in children.8 Compromised lung development in early life due to air pollution will not only affect the overall lung health at childhood but also be a predisposition factor for acquisition of chronic obstructive pulmonary disease and its associated diseases such as lung cancer and cardiovascular diseases at a later time.9 10 Studies conducted in East Europe and North America with low levels of air pollution had identified evidence supporting adverse effects of long-term air pollution exposure on children’s FVC level.11–15 However, question remains whether severe air pollution as seen in most cities in China affects the lung development in school-age children and if yes to what extent.

In this study, we assessed the association between long-term effect of ambient air pollution and lung development in 21,616 children aged 6–12 years from two big cities located in North China using data extracted from the Program of Physical Wellness Examination in School-age Children from 2014 to 2017. The effect of air pollution on sex discrepancy in lung development was analysed. Finally, the indoor air pollution sources were also explored with regard to their association with lung development in less polluted areas for identification of modifiable risk factors.

METHODS

Selection of study cities

The study protocol was approved by the Institutional Review Board of Qingdao University. Two big cities located in North China Plain with similar latitude and comparable Human Development Index (0.757–0.822) were selected.16 City A (Shijiazhuang City) from Hebei Province was one of the most polluted cities in North China, with seasonal PM2.5 levels ranging from 45 to 220 mg/m³ between 2014 and 2017. City B (Qingdao City) from Jiaodong Peninsula was one of the least polluted cities in North China, with seasonal PM2.5 levels ranging from 22 to 92 mg/m³ between 2014 and 2017 (figure 1 and online supplementary table S1).

Acquisition of physical wellness data

This cross-sectional survey was conducted from May to December 2018 in five and seven primary schools in urban areas of City A and City B and included 10,635 and 10,961 primary school students, respectively. The deidentified data including date of examination, age, sex, height, weight, FVC and grade for 21,616 children aged 6–12 years between 2014 and 2017 were extracted from the Program of Physical Wellness Examination in School-age Children upon
approval by municipal Centers for Disease Control and Prevention of each participating city. The board determined that consenting was not necessary.

In order to assess the effects of outdoor and indoor air pollution on FVC growth and respiratory symptoms, a questionnaire adapted from the Children’s Questionnaire recommended by the American Thoracic Society (ATS-DLD-78-C) was used to obtain relevant information in nine schools from City A and City B. The questionnaire was completed by children’s parents or legal guardians, and the overall participation rate was 98% among the nine schools. A total of 9118 students completed the questionnaire. There were 2019 participants from City A and the mean age was 9.3 years and 7099 participants from City B and the mean age was 8.8 years. The annual wellness check results between 2014 and 2017 from students who returned the questionnaire were acquired by retrieving the original medical records archived at the school nurse offices. Written consent was provided by a parent or legal guardian for all study participants who returned the questionnaires. Detailed information was available in online supplemental methods.

FVC measurement
The spirometry was conducted at schools by registered nurses according to the Technical Standard for Physical Examination for Students (GB/T 26343-2010) that adopted a similar procedure from the European Respiratory Society/American Thoracic Society guideline for spirometry. FVC was mandatorily measured every year for all children, and the participation rate was more than 98%. A detailed description of the procedure is available in supplemental methods.

Outdoor air pollution data
The real-time hourly concentrations of PM$_{2.5}$, particulate matter with aerodynamic diameters <10 μm (PM$_{10}$), carbon monoxide (CO), nitrogen dioxide (NO$_2$), sulfur dioxide (SO$_2$) and ozone (O$_3$) in the study areas between 2014 and 2017 were acquired from China National Environmental Monitoring Center and were used to compute the annual average concentrations in each city. Detailed information was available in online supplemental methods.

Indoor air pollution data
The indoor air pollution data were assessed by our questionnaire with several items, for example, exposure to secondhand smoking, method of indoor heating during winter and other exposures.

Statistical analysis
An analytical plan was developed during the study design stage to assess the project hypotheses. First, the linear mixed effects (LME) model with a subject-specific random intercept was used to assess the effect of outdoor air pollution on FVC growth by including an interaction term between time and air pollution (eg, City A vs City B, number of non-attainment days, or PM levels). Variable ‘time’ is time since enrollment (TSE). Fixed effects of baseline age, sex, height and body mass index (BMI) were included in each model. Second, a three-way interaction term among air pollution, sex and TSE was included in the LME model to assess whether the sex discrepancy in FVC growth differed or not between the two cities. Third, LME models were used to examine the effect of indoor air pollution on FVC growth by including an interaction term between individual indoor environmental factors and TSE in students from City B who completed the questionnaire. This analysis was only conducted in City B with a much cleaner background in terms of outdoor air pollution because we were concerned that the weaker effect of indoor air pollution might be disguised in an area with high background of outdoor air pollution. Finally, logistic regression was used to assess the difference of respiratory symptoms and illnesses between these two cities. All statistical analyses were conducted in SAS 9.4 (site 70 239 492).
RESULTS
Air pollution level in City A versus City B between 2014 and 2017
A clear seasonal fluctuation was observed for all pollutants (figure 1 and online supplementary table S1). City A always had higher levels of air pollutants except O3 compared with City B. The number of non-attainment days for air pollutants was also much higher in City A than that in City B during the entire study window, with PM2.5 and PM10 as the major air pollutants beyond Ambient Air Quality Standards of China in both cities (online supplementary table S2). Spearman correlation and principal component analyses were used to characterise the coexisting pattern of major air pollutants. PM2.5 correlated highly with PM10, CO, SO2 and NO2, with correlation coefficients ranging from 0.59 to 0.90, reflecting the common origin of these species (online supplementary table S3). Similar correlation pattern among air pollutants was also identified between the two cities, suggesting that the difference in air pollution between these two cities may be more of quantity rather than type (not shown).

Characteristics of the study subjects
This study included 10 655 and 10 961 primary school students with available information on the longitudinal spirometry measurements from two studied cities (online supplementary table S4). The demographic data of 9118 children whose parents completed the questionnaires are also summarised in online supplementary table S4. The absolute difference in studied demographic variables was trivial.

Association between outdoor air pollution and FVC growth
Compared with those from City B, children from City A had a reduced level of FVC at baseline (−158.4 mL, 95% CI: −169.1 to −147.6, p < 0.001) and a reduced FVC growth rate over time (−71.3 mL/year, 95% CI: −78.4 to −64.2, p < 0.001, table 1 and figure 2A). In addition, average annual PM2.5 and PM10 levels were regressed with FVC growth to further quantify the effect of PM exposure. Each 10 µg/m³ increase in PM2.5 and PM10 levels was associated with a reduction of 12.2 mL/year (95% CI: 11.0 to 13.4, p < 0.001) and 8.1 mL/year (95% CI: 7.4 to 8.9, p < 0.001) in FVC growth rate, respectively (table 1). Moreover, every 10 non-attainment days in PM2.5 was associated with a lower FVC growth rate by 6.4 mL/year (95% CI: 5.8 to 7.0, p < 0.001, online supplementary table S5).

Effect of outdoor air pollution on the sex discrepancy of FVC growth
As given in online supplementary table S6 and figures 2B and 2C, sex discrepancy (boys vs girls) in FVC growth was greater in City B (35.4 mL/year, 95% CI: 26.0 to 44.7) than in City A (19.8 mL/year, 95% CI: 9.3 to 30.3), suggesting boys might be particularly vulnerable to pulmonary effects of air pollution.

Effect of indoor air pollution factors on FVC growth
In children who were frequently exposed to secondhand tobacco smoke at home, FVC growth was significantly reduced by 59.7 mL/year (95% CI: 19.0 to 100.4, p = 0.004) compared with those who were never exposed (table 2). Compared with community-based central boiler heating, gas/electric heating (−44.5 mL/year, 95% CI: −72.7 to −16.3, p = 0.002) and coal/wood-burning stove heating (−80.1 mL/year, 95% CI: −111.2 to −49.1, p < 0.001) were significantly associated with a reduced FVC growth rate (table 2). We did not find any evidence to support shorter distance to main roads or no use of air purifier indoor as being associated with reduced FVC growth.

Joint effects of outdoor and indoor air pollution on FVC growth
We stratified our subjects into four groups: lower outdoor (City B) and lower indoor (never smoking/smoking less than once a week and central boiler heating) air pollution, lower outdoor (City B) and higher indoor (smoking at least once a week or no central boiler heating) air pollution, higher outdoor (City A) and lower indoor (never smoking/smoking less than once a week and central boiler heating) air pollution, higher outdoor (City A) and higher indoor (smoking at least once a week or no central boiler heating) air pollution. Compared with lower outdoor and lower indoor air pollution, lower outdoor and higher indoor air pollution (−21.4 mL/year, 95% CI: −33.0 to −9.9, p < 0.001), higher outdoor and lower indoor air pollution (−85.2 mL/year, 95% CI: −99.4 to −71.0, p < 0.001), and higher outdoor and higher indoor air pollution (−101.1 mL/year, 95% CI: −134.5 to −67.7, p < 0.001) were significantly associated with a reduced FVC growth rate (figure 3). However, there was no evidence of interaction of outdoor and indoor air pollution on FVC growth (p = 0.765).

Table 1 Estimation of district-specific FVC growth by linear mixed effects model

<table>
<thead>
<tr>
<th>Parameter</th>
<th>City A vs City B</th>
<th>PM2.5</th>
<th>PM10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>−2051.1 (−2112.1, −1990.1)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time</td>
<td>146.4 (140.4, 152.3)</td>
<td>&lt;0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Air pollution</td>
<td>−158.4 (−169.1, −147.6)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time×air pollution</td>
<td>−71.3 (−78.4, −64.2)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline age</td>
<td>87.9 (83.5, 92.2)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Boys</td>
<td>132.7 (123.5, 141.9)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI</td>
<td>12.3 (11.0, 13.6)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Height</td>
<td>18.4 (17.8, 19.1)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

BMI, body mass index; FVC, forced vital capacity.

The effect of air pollution on FVC growth was assessed by including an interaction term between air pollutant (City A vs City B or PM concentrations) and time since enrollment in the linear mixed effects model in 21 616 primary school students. Estimates for PM2.5 and PM10 were calculated based on every 10-mg/m³ increase.
Prevalence of respiratory diseases and symptoms between the two cities

Respiratory diseases and symptoms were surveyed in children to assess whether the effect of air pollution on FVC growth was due to higher prevalence of respiratory diseases in City A vs City B (online supplementary table S7). Chronic rhinitis had the highest prevalence (13.6% and 18.3% in City A and City B) followed by asthma (6.4% and 7.0% in City A and City B), seasonal cough (5.9% and 8.1% in City A and City B), chronic cough (5.8% and 5.6% in City A and City B) and pneumonia (6.0% and 5.5% in City A and City B). Interestingly, students in City A had significantly reduced prevalent for seasonal cough (especially in spring and summer) and chronic rhinitis than students in City B (online supplementary table S7). Thus, results did not support that the effect of air pollution on FVC growth is due to a higher prevalence of respiratory diseases or symptoms.

DISCUSSION

Based on archived children wellness data and national air quality monitoring data with high integrity from years 2014 to 2017, a retrospective analysis was conducted by comparing FVC growth in a large sample of elementary students from urban areas of two vice provincial cities located in North China with mild versus severe air pollution. We found that outdoor and indoor air pollution independently affected lung development in school-age children.

Outdoor air pollution

Children from City A with severe air pollution had a dramatic reduction in FVC growth rate (−71.3 mL/year, 95% CI: −78.4 to −64.2, p < 0.001) compared with children from City B, with the level of reduction equivalent to more than one-third of the annual gain in FVC growth (eg, 160–200 mL/year) seen in students from City B or national survey for reference values of FVC, forced vital capacity.

Table 2 The association between indoor air pollution factors and traffic-related air pollution index and FVC growth (in City B, n = 7099)

<table>
<thead>
<tr>
<th>Environmental factor</th>
<th>Prevalence</th>
<th>Time (mL)</th>
<th>Factor (mL)</th>
<th>Time×factor (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposed to secondhand smoke at home (vs never)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than once a week</td>
<td>42.0%</td>
<td>173.6 (154.0, 193.2)</td>
<td>15.4 (−21.2, 51.9)</td>
<td>0.410</td>
</tr>
<tr>
<td>At least once a week</td>
<td>9.1%</td>
<td>173.6 (154.0, 193.2)</td>
<td>49.4 (−16.1, 114.9)</td>
<td>0.140</td>
</tr>
<tr>
<td>Heating type (vs central boiler heating †)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gas/electric</td>
<td>16.2%</td>
<td>187.7 (169.8, 205.6)</td>
<td>84.4 (39.5, 129.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Coal- or wood-burning stove</td>
<td>18.9%</td>
<td>187.7 (169.8, 205.6)</td>
<td>72.6 (22.7, 122.5)</td>
<td>0.004</td>
</tr>
<tr>
<td>Air purifier use (vs never)</td>
<td>23.1%</td>
<td>167.6 (150.5, 184.6)</td>
<td>−16.9 (−60.4, 26.7)</td>
<td>0.448</td>
</tr>
<tr>
<td>Distance from main traffic &lt;500 m (vs ≥500 m)</td>
<td>41.6%</td>
<td>159.7 (141.0, 178.3)</td>
<td>−9.2 (−44.7, 26.3)</td>
<td>0.611</td>
</tr>
</tbody>
</table>

FVC, forced vital capacity.

Association between indoor air pollution factors and FVC growth was explored using linear mixed effects model with adjustment for baseline age, sex, height, body mass index, family income and mother’s education.

* p < 0.001.

† Community-based central boiler heating is a most common heating method in northern China cities that used circulated hot water inside radiators to heat rooms in winter. Hot water around 80°C at the entry of the houses is supplied through pipe network and heated by massive boilers that burn fossil fuel (eg, gas, natural oil or coal) and usually locate close to residential zone. Each massive boiler unit can provide hot water to meet winter heating need for hundreds of families. These massive boilers are of high efficiency and have excellent emission treatment system to minimise its effect on air quality in winter.
to a different dose–response curve and different sources of air pollution (heating in winter vs traffic-related yearlong) leading to different constituents carried by the PM and subsequently different pulmonary toxicity. However, it is important to note that a cohort study of 3273 children aged 6–12 years from four Chinese cities of Chongqing, Guangzhou, Lanzhou and Wuhan with annual average PM$_{2.5}$ level of 50–150 mg/m$^3$ between 1993 and 1996 identified that every 10-μg/m$^3$ increase in quarterly average of PM$_{2.5}$ was associated with a reduction of only 1.5 mL/year in FVC growth rate. Their results may be biased by the large variation in income and lifestyle between regions, mixing the South and North China cities with strikingly different winter heating patterns in one study and lack of daily air quality data.

We also found evidence that FVC growth in boys was much more vulnerable to the adverse effect of air pollution compared with girls. A similar pattern was identified in the Taiwan Children’s Health Study that the PM$_{2.5}$’s adverse effect on FVC growth in boys was 23% worse than that seen in girls. The exact mechanisms underlying this sex discrepancy are unclear; however, this may implicate boys spending more time outdoors and being more physically active, inherited differences in lung structure and airway development and differences in sex hormones regulating lung development. Thus, in future, delineation of the molecular mechanism underlying the observed sex discrepancy for adverse effect of air pollution on lung development may receive high priorities for research.

**Indoor air pollution**

Secondhand cigarette smoke and solid fuel for domestic heating in winter are two major sources of indoor air pollution and have been linked to many health problems. We found that frequent exposure to secondhand cigarette smoke at home and use of coal/wood-burning stove as major indoor heating source in winter season were associated with a reduction of 60–80 mL/year in FVC growth in children, a level of retardation in lung development comparable with that caused by exposure to severe outdoor air pollution. Researches have shown that households that allow indoor smoking or use of coal- or wood-burning stoves for cooking and winter heating have dramatically increased levels of PM that are comparable with or much worse than the air pollution scenario currently seen in Beijing’s winter.

Ambient PM$_{2.5}$ concentration has been used as a parameter quantifying the association between air pollution and lung health in many epidemiological studies. In our study, every 10-μg/m$^3$ increase in average PM$_{2.5}$ level was associated with a reduction of FVC growth by 12.2 mL/year (95% CI: 11.0 to 13.4, p < 0.001). The Taiwan Children’s Health Study conducted in areas with annual PM$_{2.5}$ level of 19.3–52.5 mg/m$^3$ found that every 10-μg/m$^3$ increase of PM$_{2.5}$ was associated with an annual deficit in FVC growth by 41.9 mL/year in boys and 34.0 mL/year in girls. The implementation of air quality-control policies in Southern California has gradually reduced the air pollution level, and the Children Health Study found that every 10-μg/m$^3$ decrease in PM$_{2.5}$ could accelerate FVC growth by 25.2 mL/year, with starting regional PM$_{2.5}$ level lingering around 18–34 mg/m$^3$. The smaller effect observed in our study might be caused by a higher level of air pollution leading through parenthood smoking cessation plan and improvement of winter heating appliance and ventilation at home.

**CONCLUSIONS**

In summary, the findings of our study raised serious alarm over the threat of severe air pollution to lung development in school-age children. Children living in the heavily polluted city lost one-third of the FVC growth compared with children from the city with mild air pollution, despite that the air pollution level in the reference city in this study was already twofold to ninefold over the WHO recommended ‘safe level’. Moreover, boy’s advantage in lung development was reduced dramatically in heavily polluted areas. Considering the large number of children living in many cities with moderate-to-severe air pollution in China, this young generation with compromised lung health before adulthood may pose a heavy burden on individual health and even national social security later due to increased predisposition for smoking/smoking less than once a week and central boiler heating) air pollution. Joint effects were explored using LME model with adjustment for baseline age, sex, height, BMI, family income and mother’s education. BMI, body mass index; FVC, forced vital capacity; LME, linear mixed effects.

**Figure 3** Joint effects of outdoor and indoor air pollution on FVC growth. We stratified our subjects into four groups: lower outdoor (City B) and lower indoor (never smoking/smoking less than once a week and central boiler heating) air pollution (reference), lower outdoor (City B) and higher indoor (smoking at least once a week or no central boiler heating) air pollution, higher outdoor (City A) and lower indoor (never smoking/smoking less than once a week and central boiler heating) air pollution, and higher outdoor (City A) and higher indoor (smoking at least once a week or no central boiler heating) air pollution. Joint effects were explored using LME model with adjustment for baseline age, sex, height, BMI, family income and mother’s education. BMI, body mass index; FVC, forced vital capacity; LME, linear mixed effects.
acquisition of ageing-related pulmonary and extrapulmonary diseases. Thus, the data urge Chinese government to take a more aggressive action on its air pollution mitigation policy and to protect children from adverse effects of outdoor and indoor air pollution.

What is already known on this subject

► Studies conducted in East Europe and North America with low levels of air pollution had identified evidence supporting adverse effects of long-term air pollution exposure on children’s FVC level.

► However, question remains whether severe air pollution as seen in most cities in China affects the lung development in school-age children and if yes to what extent.

What this study adds

► Exposure to severe air pollution caused a reduction in annual FVC growth rate equivalent to one-third of annual FVC growth seen in school-age children living in less polluted or clean areas in China.

► FVC growth in boys was much more vulnerable to the adverse effect of air pollution compared with girls.

► Exposure to indoor coal- or wood-burning stove heating and secondhand smoke at home was two modifiable risk factors for preservation of FVC growth in children.

► The data urge Chinese government to take a more aggressive action on its air pollution mitigation policy and to protect children (age 6–12 years) from adverse effects of outdoor and indoor air pollution.

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Correction notice This article has been corrected since it first published online. The contributor statement has been corrected.

Contributors TW: Formal analysis, methodology, visualisation, data curation, writing—original draft. HW: investigation. JC: investigation. JW: investigation.

DF: formal analysis. WH: investigation. HW: formal analysis. WH: formal analysis. SL: funding acquisition, supervision, writing—review & editing. RZ: investigation, writing—review & editing. YZ: funding acquisition, supervision, writing—review editing.

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