Association between Ambient Air Pollutants and Pneumonia in Wuhan, China, 2014–2017

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Abstract: Objectives: To assess associations between short-time air pollution exposure and outpatient visits for pneumonia by the distributed lag nonlinear model (DLNM). Methods: Daily outpatient visits for pneumonia and air pollutant data were collected from Wuhan Basic Medical Insurance Database in China and 10 national air quality monitoring stations in Wuhan from 2014 to 2017, respectively. Taking the first percentile of the concentration as the reference, DLNM was used to estimate the impact of moderate (50th) and high levels (99th) of pollutants on pneumonia. Results: A total of 133,882 outpatient visits were identified during the period of the study. Moderate-level (P50) fine particulate matter (PM2.5) or sulfur dioxide (SO2) and high-level nitrogen dioxide (NO2) (P99) can increase the risk of pneumonia. The maximum RR was 1.198 (95% CI: 1.094–1.311) at lag0-11, 1.304 (95% CI: 1.166–1.458) at lag0-13, and 1.286 (95% CI: 1.060–1.561) at lag0-14, respectively. Females and children had greater risks. Conclusions: Short-time PM2.5, SO2, and NO2 exposure were associated with outpatient visits for pneumonia in Wuhan, China.

Keywords: air pollutants; pneumonia; outpatient visits; distributed lag nonlinear model; time series research

1. Introduction

Pneumonia is a common acute lower respiratory tract infection (LRTI) caused by altered alveolar and distal airway microbiota and immune responses [1,2]. The most common symptoms of pneumonia are cough, dyspnea, chest pain, sputum production, and multiple complications, which can lead to death in severe cases [3,4]. In 2016, the incidence of LRTI was 45.5 per 1000 people, causing nearly 2.38 million deaths worldwide, and it was one of the five main causes of global life loss [5]. In China, LRTIs were the 12th leading cause of years of life lost (YLLs). YLL per 100,000 population was 302 (95% uncertainty interval: 282 to 356), and deaths per 100,000 population was 13 (95% UI: 12 to 16) in 2017 [6].

Pollution is one of the main risk factors for lower respiratory tract infections [7,8]. Nonlinear relationships between pollution and respiratory system diseases have already been reported, and pollution not only affects human health on the day of exposure, but also continues to cause harm for a period of time in the future [9–11]. Even though extreme weather is relatively rare, the lagged hazards it creates are evident [12,13]. A lot of studies have demonstrated that increased concentrations of pollution were associated with an increased risk of pneumonia [14–16]. There were significant positive associations between fine particulate matter (PM2.5) and emergency room visit for pneumonia, hospitalization for
severe pneumonia, mortality, and health care costs for the elderly in Utah [17]. A 10 μg/m³ increase in PM$_{2.5}$ concentrations increased the number of pneumonia hospitalizations by 0.79% at lag 0–2 days in Beijing [18]. Interquartile increases in PM$_{2.5}$, sulfur dioxide (SO$_2$), and nitrogen dioxide (NO$_2$) were associated with an increase of 14.0%, 4.5%, and 14.1% odds of pediatric pneumonia for children in Taiwan [19]. However, most of these focused on more sensitive populations such as the elderly, children, and hospitalized patients with more severe clinical manifestations. In addition, hospitalization, emergency room, etc., as outcomes were used in previous studies, which may lead to underestimation of the short-term hazards of pollutants due to the time required for the disease to develop from the initial stage to a more severe stage. Furthermore, regarding differences in pollutant levels, pollutant sources, geographical conditions, and population composition, the extrapolation of research results is limited. In terms of statistical models, most of the studies use generalized linear models (GLM), generalized additive models (GAM), etc. Compared with them, the distributed lag nonlinear model (DLNM) [20] applies the idea of cross-base to fit the two dimensions of pollutant exposure response and lag response, which is more suitable for the complex interdependent relationship of environmental factors.

The distributed lag nonlinear model was used to analyze the association between air pollution and pneumonia outpatient visits in the whole population. We not only discussed the impact of medium-level pollutants on pneumonia, but also focused on the harm of extremely high concentrations of pollutants on pneumonia.

2. Materials and Methods

2.1. Study Area

Wuhan (29°58′–31°22′ N, 113°41′–115°05′ E), Hubei Province, is an important transportation hub in China. The permanent resident population of Wuhan was 10.77 million at the end of 2017, with a population density of 1256 person/sq.km. The city belongs to the northern subtropical monsoon (humid) climate, with abundant rainfall throughout the year, cold in winter and hot in summer, and four distinct seasons.

2.2. Outpatient Visits for Pneumonia Cases

The data of outpatient visits for pneumonia cases were obtained from Wuhan Basic Medical Insurance Database in Hubei Province. The database includes urban-staff-insured persons and urban-resident-insured persons. According to the agreed sampling strategy, we randomly sampled 1% based on the ID number. Then, we sampled according to the Chinese diagnosis and the corresponding International Classification of Diseases 10th version (ICD-10) codes (the classification includes 18 diseases such as “lower respiratory tract infection”, “pneumonia”, “bronchitis”, “pulmonary tuberculosis”, “asthma”, etc.), with a total of 3,892,270 outpatient visits to form a disease database. Finally, based on the principal diagnosis (J12–J18), we excluded nonpneumonia cases to form the final sample database from 1 January 2014 to 31 December 2017, including a total of 133,882 patient cases. The information included basic demographic characteristics, disease diagnosis, date of diagnosis, hospital, etc.

2.3. Air Pollution and Meteorological Data

Air pollution data were collected from 10 national air quality monitoring stations in Wuhan. We averaged the measurements from all valid monitoring sites. The air pollution data included the daily (24 h) mean concentrations of PM$_{2.5}$, SO$_2$, and NO$_2$ in Wuhan from January 2014 to December 2017. The daily (24 h) mean meteorological data included temperature (°C), relative humidity (%), wind speed (m/s), and precipitation (mm/h), all of which were obtained from the Hubei Meteorological Bureau.

2.4. Statistical Analysis

The daily outpatient visits for pneumonia cases were subjected to Poisson distribution, and air pollution had a nonlinear and lagged effect on pneumonia according to previous
reports. Therefore, we applied the distributed lag nonlinear model (DLNM) with Poisson regression to explore the exposure–lag-response relationship between outpatient visits for pneumonia cases and ambient air pollution. The model was built as follows:

$$\log[E(Y_t)] = \alpha + cb(P, df_1, lag, df_2) + \sum ns(X_i, df_3) + ns(Time, df_4) + factor(DOW)$$  

where $E(Y_t)$ was the expected number of outpatient visits for pneumonia cases on day $t$; $\alpha$ was the intercept; $cb$ referred to the cross-basis function, combining functions for both exposure and lag dimensions, which included natural cubic spline for air pollutants and a polynomial function for lag; $P$ was a pollutant ($PM_{2.5}$, $SO_2$, and $NO_2$), and $df_1$ of the pollutant was 4 and $df_2$ of the lag dimension was 3. Because the incubation period of pneumonia [21] and the fact that the most commonly selected lag times in the related research of pneumonia are 6, 7, and 14 days, the maximum lag time was 14 days in this study [22,23]. $\sum ns(X_i, df_3)$ represented the natural cubic spline function of meteorological factors, including temperature, relative humidity, wind speed, and precipitation, and $df_3$ were all three. $Time$ and $DOW$ (day of the week) were indicator variables that represented adjustments to seasonal and long-term trends and the influence of the day of the week, respectively. According to the results of Akaike Information Criterion (AIC), $df_4$ was 11.

In our study, all daily average concentrations ($N = 1461$) were arranged in ascending order from the minimum to the maximum. $P_1$ represented the first percentile concentration, $P_{50}$ represented the 50th percentile concentration, and $P_{99}$ represented the 99th percentile concentration. After confirming the parameters in the model, the first percentile’s concentration of air pollutants with the lowest risk of pneumonia was obtained as the reference value through model prediction. We calculated the relative risks (RR) and 95% confidence intervals (CI) of pneumonia cases at moderate levels ($P_{50}$, 50th percentile of concentration) and high levels ($P_{99}$, 99th percentile of concentration). We calculated single-day lag effects (such as lag0, lag1, lag2, and lag3) and cumulative lag effects (such as lag01, lag02, and lag03) to effectively characterize the association between air pollutants and outpatient visits for pneumonia cases. Furthermore, effects across age groups (0–14 years, 15–64 years, and >64 years) and genders were examined to identify a susceptible subpopulation. The divisions of age groups were similar to previous studies [24,25]. Additionally, a sensitivity analysis was applied to test the robustness of the models. We tested the reliability of the results by altering the df of the long-term trend.

2.5. Statistical Software

Microsoft Excel software was used for data collation, and the DLNM package in R software (version 3.6.1) was used for statistical analysis of the nonlinear exposure–lag effects.

3. Results

There was a total of 133,882 cases of outpatient visits for pneumonia in Wuhan, with an average of 92 people per day from 1 January 2014 to 31 December 2017 (shown in Table 1). The daily outpatient visits of people aged 0–14, 15–64, and over 64 years accounted for 57.70%, 25.10%, and 17.20%, respectively. Of the patients, 51.80% were male. The 50th percentile of concentration values for $PM_{2.5}$, $NO_2$, and $SO_2$ were 54.00 $\mu g/m^3$, 44.00 $\mu g/m^3$, and 14.00 $\mu g/m^3$, and the 99th percentile of concentration values for $PM_{2.5}$, $NO_2$, and $SO_2$ were 229.40 $\mu g/m^3$, 102.40 $\mu g/m^3$, and 69.00 $\mu g/m^3$, respectively. The daily temperature, relative humidity, precipitation, and wind speed were 17.24 °C, 78.81%, 0.16 mm/h, and 1.64 m/s.
Contour plots of the exposure–lag-response effects comprehensively illustrated that air pollutants (PM$_{2.5}$, SO$_2$, and NO$_2$) and outpatient visits for pneumonia were nonlinear associations with lag effects (Figure 1). Lag patterns varied at different concentration levels. The two peaks of risk for pneumonia visits appeared when the PM$_{2.5}$ concentration was around 30 µg/m$^3$ and 190 µg/m$^3$, the lag time duration was 0–12 d, and when the RR value was the highest (at 4–6 days). When the SO$_2$ concentration was within a range of 10–50 µg/m$^3$, the lag effects on pneumonia were observed. High concentration of NO$_2$ was a risk factor for pneumonia outpatient visits, and the lag time lasted from the day of exposure to about 12 days.

The single-day lag effects and cumulative lag effects of moderate- and high-level air pollutants on pneumonia under various lag days are shown in Table 2. The cumulative lag effects of air pollutants showed higher estimates than single-day effects. At the moderate-level PM$_{2.5}$, single lag effects appeared at lag2–lag9, and RR reached the maximum at lag4 (RR: 1.022, 95% CI: 1.009–1.036). Compared with 9 µg/m$^3$ (P$_1$), the moderate levels

Table 1. Description of outpatient visits for pneumonia cases, air pollutants, and meteorological factors in Wuhan from 1 January 2014 to 31 December 2017.

<table>
<thead>
<tr>
<th>Variables</th>
<th>N</th>
<th>Mean ± SD</th>
<th>Centiles</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpatient visits for pneumonia cases</td>
<td>All</td>
<td>133,882 (100%)</td>
<td>92.00 ± 47.00</td>
</tr>
<tr>
<td>Age 0–14 Years</td>
<td>77,247 (57.70%)</td>
<td>53.00 ± 32.00</td>
<td>4.00 10.00 29.00 40.00 61.00 142.00 247.00</td>
</tr>
<tr>
<td>Age 15–64 Years</td>
<td>33,601 (25.10%)</td>
<td>23.00 ± 11.00</td>
<td>4.00 7.00 16.00 38.00 56.00 60.00 106.00</td>
</tr>
<tr>
<td>Age &gt; 64 Years</td>
<td>23,034 (17.20%)</td>
<td>16.00 ± 10.00</td>
<td>1.00 3.00 10.00 44.00 70.00 48.00 113.00</td>
</tr>
<tr>
<td>Male</td>
<td>69,345 (51.80%)</td>
<td>47.00 ± 25.00</td>
<td>10.00 14.00 30.00 21.00 27.00 123.00 238.00</td>
</tr>
<tr>
<td>Female</td>
<td>64,537 (48.20%)</td>
<td>44.00 ± 23.00</td>
<td>9.00 13.00 28.00 14.00 19.00 112.00 214.00</td>
</tr>
<tr>
<td>Ambient Pollutants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{2.5}$ (µg/m$^3$)</td>
<td>1461</td>
<td>63.87 ± 43.03</td>
<td>5.00 9.00 33.00 54.00 82.00 229.40 287.00</td>
</tr>
<tr>
<td>NO$_2$ (µg/m$^3$)</td>
<td>1461</td>
<td>47.50 ± 20.02</td>
<td>11.00 17.00 32.00 44.00 60.00 102.40 119.00</td>
</tr>
<tr>
<td>SO$_2$ (µg/m$^3$)</td>
<td>1461</td>
<td>17.66 ± 13.84</td>
<td>2.00 3.00 8.00 14.00 23.00 69.00 105.00</td>
</tr>
<tr>
<td>Meteorological Factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temperature (°C)</td>
<td>1461</td>
<td>17.24 ± 8.83</td>
<td>−4.32 0.41 9.55 18.33 24.79 32.50 33.98</td>
</tr>
<tr>
<td>Relative Humidity (%)</td>
<td>1461</td>
<td>78.81 ± 11.03</td>
<td>40.67 49.28 71.50 79.33 87.04 98.53 100.00</td>
</tr>
<tr>
<td>Precipitation (mm/h)</td>
<td>1461</td>
<td>0.16 ± 0.55</td>
<td>0.00 0.00 0.00 0.00 0.05 2.25 8.00</td>
</tr>
<tr>
<td>Wind Velocity (m/s)</td>
<td>1461</td>
<td>1.64 ± 0.89</td>
<td>0.30 0.43 1.00 1.43 2.10 4.42 6.52</td>
</tr>
</tbody>
</table>

Figure 1. Contour plots of the exposure–lag-response effects between ambient pollutants and outpatient visits for pneumonia. Note: After adjusting for long-term trends, day-of-the-week effects, and meteorological factors, the distributed lag nonlinear model (DLNM) was used to obtain contour plots, with the first percentile concentration of air pollutants as the reference. (a): PM$_{2.5}$; (b): SO$_2$; (c): NO$_2$. 

The single-day lag effects and cumulative lag effects of moderate- and high-level air pollutants on pneumonia under various lag days are shown in Table 2. The cumulative lag effects of air pollutants showed higher estimates than single-day effects. At the moderate-level PM$_{2.5}$, single lag effects appeared at lag2–lag9, and RR reached the maximum at lag4 (RR: 1.022, 95% CI: 1.009–1.036). Compared with 9 µg/m$^3$ (P$_1$), the moderate levels
(54 µg/m³) of PM$_{2.5}$ increased the maximum cumulative risk of pneumonia by 19.8% at lag0–11. The single lag effects for moderate-level SO$_2$ were detected at lag1–lag11, manifesting as acute effects. Compared with 5 µg/m³ (P$_1$), the moderate level (14 µg/m³) of SO$_2$ increased the maximum cumulative risk of pneumonia by 30.4% at lag0–13. Under high-levels of NO$_2$ exposure, the single lag effect was the highest at lag2 (RR: 1.022, 95% CI: 1.001–1.044), and the lag effect continued to decrease, lasting for 7 days. Compared with 17 µg/m³ (P$_1$), the high level (102.4 µg/m³) of NO$_2$ increased the maximum cumulative risk of pneumonia by 28.6% at lag0–14.

### Table 2. The RR and 95% confidence interval of ambient pollutants on outpatient visits for pneumonia cases.

<table>
<thead>
<tr>
<th>Lag</th>
<th>PM$_{2.5}$</th>
<th>Moderate Level (P$_{50}$)</th>
<th>High Level (P$_{90}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SO$_2$</td>
<td>NO$_2$</td>
<td>PM$_{2.5}$</td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1.006 (0.977–1.036)</td>
<td>1.020 (0.987–1.054)</td>
<td>0.972 (0.897–1.053)</td>
</tr>
<tr>
<td>1</td>
<td>1.013 (0.996–1.030)</td>
<td>1.020 (1.001–1.039)</td>
<td>1.021 (0.988–1.055)</td>
</tr>
<tr>
<td>2</td>
<td>1.018 (1.006–1.031)</td>
<td>1.020 (1.007–1.033)</td>
<td>1.019 (0.992–1.046)</td>
</tr>
<tr>
<td>3</td>
<td>1.021 (1.008–1.034)</td>
<td>1.021 (1.007–1.034)</td>
<td>1.021 (0.987–1.056)</td>
</tr>
<tr>
<td>4</td>
<td>1.022 (1.009–1.036)</td>
<td>1.022 (1.008–1.036)</td>
<td>1.021 (0.987–1.057)</td>
</tr>
<tr>
<td>5</td>
<td>1.022 (1.010–1.035)</td>
<td>1.023 (1.010–1.036)</td>
<td>1.019 (0.993–1.047)</td>
</tr>
<tr>
<td>6</td>
<td>1.021 (1.010–1.032)</td>
<td>1.024 (1.013–1.035)</td>
<td>1.021 (0.995–1.046)</td>
</tr>
<tr>
<td>7</td>
<td>1.019 (1.008–1.029)</td>
<td>1.024 (1.014–1.034)</td>
<td>1.022 (0.997–1.047)</td>
</tr>
<tr>
<td>8</td>
<td>1.016 (1.005–1.026)</td>
<td>1.024 (1.013–1.035)</td>
<td>1.001 (0.988–1.015)</td>
</tr>
<tr>
<td>9</td>
<td>1.012 (1.000–1.024)</td>
<td>1.022 (1.010–1.033)</td>
<td>1.003 (0.989–1.017)</td>
</tr>
<tr>
<td>10</td>
<td>1.008 (0.995–1.021)</td>
<td>1.020 (1.006–1.034)</td>
<td>1.005 (0.990–1.019)</td>
</tr>
<tr>
<td>11</td>
<td>1.004 (0.991–1.016)</td>
<td>1.016 (1.003–1.029)</td>
<td>1.007 (0.993–1.022)</td>
</tr>
<tr>
<td>12</td>
<td>1.000 (0.988–1.012)</td>
<td>1.010 (0.998–1.023)</td>
<td>1.010 (0.996–1.024)</td>
</tr>
<tr>
<td>13</td>
<td>0.996 (0.981–1.011)</td>
<td>1.003 (0.987–1.019)</td>
<td>1.013 (0.997–1.030)</td>
</tr>
<tr>
<td>14</td>
<td>0.992 (0.967–1.018)</td>
<td>0.993 (0.966–1.022)</td>
<td>0.997 (0.962–1.043)</td>
</tr>
</tbody>
</table>

Note: The first percentile of each air-pollutant concentration was selected as the reference. The RR was estimated by comparing the 50th percentile of each air-pollutant concentration and 99th percentile of each air-pollutant concentration, respectively. Statistically significant results are shown in bold (p < 0.05).

The cumulative lag effects of moderate and high levels of air pollutants on pneumonia for subgroups are presented in Figures 2 and 3. We found that females were more susceptible to moderate levels of PM$_{2.5}$, SO$_2$, and high levels of NO$_2$. Compared with the males, the cumulative lag effects were earlier and lasted longer for females. The influence of moderate and high levels of PM$_{2.5}$ and the moderate level of SO$_2$ were stronger in children than in adults and old men. When exposed to high levels of NO$_2$, the risk of pneumonia was slightly higher before lag0–12 in adults than in children.
The cumulative lag effects of moderate and high levels of air pollutants on pneumonia for subgroups are presented in Figures 2 and 3. We found that females were more susceptible to moderate levels of PM$_{2.5}$, SO$_2$, and high levels of NO$_2$. Compared with the males, the cumulative lag effects were earlier and lasted longer for females. The influence of moderate and high levels of PM$_{2.5}$ and the moderate level of SO$_2$ were stronger in children than in adults and old men. When exposed to high levels of NO$_2$, the risk of pneumonia was slightly higher before lag0–12 in adults than in children.

Figure 2. The cumulative lag effects of ambient pollutants on outpatient visits for pneumonia cases by gender. Note: After adjusting for long-term trends, day-of-the-week effects, and meteorological factors, the distributed lag nonlinear model (DLNM) was used to obtain the cumulative lag effects, with the first percentile concentration of air pollutants as the reference. (a): The moderate levels. (b): The high levels.
Sensitivity Analysis.

We changed the df of the long-term trend (8 to 11 df) to test the stability of the model, and found that the estimated value was stable and the shape of the effect diagram does not change (Figure A1 in Appendix A).

Figure 3. The cumulative lag effects of ambient pollutants on outpatient visits for pneumonia cases by age (child: aged 0–14 years; adult: age 15–64 years; old: age >64 years). Note: After adjusting for long-term trends, day-of-the-week effects, and meteorological factors, the distributed lag nonlinear model (DLNM) was used to obtain the cumulative lag effects, with the first percentile concentration of air pollutants as the reference. Note: (a): The moderate levels. (b): The high levels.
4. Discussion

In this study, we found nonlinear lag effects between PM$_{2.5}$, SO$_2$, NO$_2$, and outpatient visits for pneumonia cases. Pollutants with different exposure levels presented different lag effects. Moderate levels of PM$_{2.5}$ and SO$_2$, and high levels of NO$_2$ could increase the risk of pneumonia. Females and children had a stronger risk for pneumonia. Furthermore, the lag effects of gaseous pollutants (SO$_2$ and NO$_2$) on pneumonia were greater than particulate matter (PM$_{2.5}$).

Due to the nonlinear relationship between pollutants and pneumonia, we analyzed the exposure risk of moderate- and high-concentration pollutants to pneumonia, respectively. The present study found moderate-level PM$_{2.5}$ and SO$_2$ were positive associations with the pneumonia of outpatient visits in the short term, with the first percentile concentration of air pollutants as the reference. However, we had not found a significant result in high-level PM$_{2.5}$ and SO$_2$. Previous studies are consistent with this finding [26,27]. A time-series analysis in 184 cities in China from 2014–2017 showed that compared to higher concentrations, the risk of pneumonia admission was greater at lower concentrations of PM$_{2.5}$ (below 75 µg/m$^3$) and PM$_{10}$ (below 100 µg/m$^3$) [28]. Another study about daily outpatient visits for respiratory diseases in Lanzhou [29] found that when the concentration of PM$_{2.5}$ was less than 50 µg/m$^3$, outpatient volume increased rapidly, but when concentration exceeded 100 µg/m$^3$, this effect gradually weakened. On the one hand, this phenomenon could be due to the “harvest effect”, because people may have been sick already and diagnosed before the air-pollutant concentration reached a high level. On the other hand, people could have taken some protective measures (such as wearing masks) under severely polluted weather conditions [28]. In terms of SO$_2$, we did not find significant effects at high levels, which may be due to relatively low emission in our area. However, it still had a clear impact on phenomena at moderate levels, other and studies showed similar conclusions [30,31]. On the contrary, NO$_2$ showed obvious nonlinear lag effects at high-level exposure, while it did not cause significant effects at moderate levels. In a study about adult pneumonia outpatient visits in Qingdao, the results of DLNM also showed that the 50th and 75th percentiles of NO$_2$ concentrations did not cause lag effects, while the 90th and 95th percentiles of NO$_2$ concentrations were significantly associated [22]. A meta-analysis dividing NO$_2$ into outdoor sources and higher-concentration traffic sources showed the latter had significantly stronger impacts on chronic obstructive pulmonary diseases (RR:1.017 vs. 1.178). The above studies all suggest that high concentrations of NO$_2$ have more considerable effects on health [32], which is a noteworthy problem. Lots of studies reported NO$_2$ may exacerbate underlying respiratory diseases [26,33,34]. It reduced CD62 expression, leading to inhibition of neutrophil-mediated inflammatory clearance mechanisms, thereby prolonging recovery time from diseases [35].

Diverse lag patterns were presented for different pollutants [36–38]. The maximum single lag effects of PM$_{2.5}$ and SO$_2$ at moderate levels appeared at lag4 and lag7, and the highest cumulative lag effects appeared at lag0–11 and lag0–13, respectively. Under high levels of exposure, NO$_2$ reached the maximum single lag effect at lag2 and cumulative lag effect at lag0–14. A prospective cohort of 433,032 participants showed that the risk of pneumonia hospitalizations reached the maximum at lag4 weeks for SO$_2$ [23]. Furthermore, Yan Tao [39] found the maximum lag effect of hospital admissions for pneumonia due to NO$_2$ appeared at lag2 in Lanzhou, with a lag of 1–4 days. The reason for the different specific lag times may be due to research design, statistical models, air pollution components, population susceptibility, etc. [16,26]. Compared with hospital admissions in previous studies, outpatient data may be more timelier, and sensitively reflect the short-term effects of air pollution on pneumonia in our study. Furthermore, this study found that gaseous pollutants’ (SO$_2$ and NO$_2$) effects on pneumonia were greater than effects from particulate matter (PM$_{2.5}$). Previous studies had similar findings [24,26,40]. Pollutants often came from the same source and were exposed at the same time [41]. SO$_2$ and NO$_2$ could adhere to particulate matter [42], leading to the idea that the observed harmful effects of SO$_2$ and NO$_2$ may actually be due to fine particulate matter.
The results of subgroups showed that females and children were more susceptible to pneumonia, which was in line with other studies [43–45]. After excluding gynecological and reproductive diseases, females remained more alert and experienced physical symptoms more intensely than males due to biological differences and social roles [46]. In addition, air pollutants may cause greater impacts on nonsmokers than smokers [47,48]. Males made up the majority of smokers in China [49]. Due to the dominant harmful impacts of smoking for males, additional effects of air pollutants may not be fully captured, limited by physiological upper bounds [50]. We also found an interesting phenomenon that children had greater impacts under moderate-level NO\textsubscript{2}, while adults had greater impacts under high-level NO\textsubscript{2}. Medical measures may have been taken before exposure to high levels of NO\textsubscript{2} due to the undeveloped immune system and respiratory system in children. An experiment with pulmonary function testing in 163 school-aged children showed a clear, acute effect on children’s lung functions even when NO\textsubscript{2} levels were below European limits [51]. Compared with children, adults were more frequently exposed to high-level NO\textsubscript{2}. Because NO\textsubscript{2} mainly comes from traffic pollution in Wuhan [52,53], and its concentration was negatively correlated with the distance from the highway [54]. In addition, our results did not find a significant effect on the elderly. The elderly generally suffered from underlying diseases and multiple comorbidities. Compared with children and adults, pneumonia symptoms were mostly atypical [55], so it was easy to delay medical treatment, resulting in severer symptoms, higher hospitalization rates, and higher mortality [56,57].

The data of this study came from the Basic Medical Insurance Database, which was accurate and realistic, and the risk of pneumonia caused by air pollution could be timely and sensitively reflected by outpatient data. In addition, we also discussed the relationship between pollutants and pneumonia at different levels in order to understand the impact of pollutants on human health in detail. However, this study also had some limitations. First of all, exposure measurement bias in ecological studies was unavoidable, and air pollution concentrations from air quality monitoring stations may overestimate individual exposure levels. Secondly, we were unable to finely control for individual-level confounders due to data limitations. In future research, it is necessary to precisely measure individual exposure levels and adjust individual characteristics to reflect the impact of air pollution exposure on human health.

5. Conclusions

In summary, our study demonstrated significant associations between air pollutants and outpatient visits for pneumonia cases in a short time, especially under moderate-level PM\textsubscript{2.5}, SO\textsubscript{2}, and high-level NO\textsubscript{2}. In addition to females and children being susceptible groups, the effects of high concentrations of NO\textsubscript{2} on adults are also worthy of attention.

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Appendix A. Sensitivity Analysis

Figure A1. Cont.
Figure A1. Single-day lag of PM$_{2.5}$, SO$_2$, and NO$_2$, with time-trend degrees of freedom from 8 to 11.

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