Acute Effects of Exposure to Ambient Air Pollutants on Preterm Birth in Xiamen City (2015–2018), China

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ABSTRACT: Backgrounds: Urban energy consumption is one of the important causes of air pollution. The epidemiological risk assessment guided by air pollution is of great significance to the promotion of urban environmental protection.

Objectives: The work researched the acute impact of exposure to air pollution on preterm birth (PTB) in Xiamen city from 2015 to 2018. Furthermore, the economic losses were assessed as well.

Methods: Association of air pollution and PTB with economic losses were assessed using the generalized additive model.

Results: A total of 1991 PTB visits, who are inhabitant in Xiamen, have been investigated. An interquartile range (IQR) (10 μg/m³) increase of PM₁₀, NO₂, and SO₂ in the current day corresponded to the increase of 0.64% [95% CI: −1.22, 2.54%], 0.52% [95% CI: −5.21, 6.61%], and 2.33% [95% CI: −6.41, 11.58%] in daily PTB visits. Especially, PTB visits were significantly related with PM₁₀ and NO₂ in Lag 1 and NO₂ and SO₂ in Lag 2. Furthermore, for multipollutants, an IQR increase in PM₂.₅, O₃, and CO, after adjustment with SO₂, was related with 5.04% [95% CI: −5.90, 17.24], 2.49% [95% CI: −6.07, 11.81], and 7.10% [95% CI: −2.79, 18.00] increase of PTB morbidity, respectively. The estimates of the number of excess PTBs attributed to typical pollutants PM₁₀ and SO₂ were ∼2400 and 1200 people, respectively, every year. The highest excess PTBs was estimated to occur as a result of PM₁₀ and SO₂ effects.

Conclusions: Although Xiamen has a relatively low level of air pollution, short-term exposure to NO₂, SO₂, and PM₁₀ was linked to the increase of PTB visits.

1. INTRODUCTION

Ambient air pollutants have been causing public health problems, especially for children and vulnerable and elderly people, and have been a cause of concern.⁹¹⁰ Many epidemiologic studies have demonstrated that ambient air pollutants are related with an increased risk of adverse preterm birth (PTB) end point.³⁴⁵ PTB is an important factor closely related to perinatal outcomes. In China, premature delivery is defined as the termination of pregnancy from 28 weeks of gestation to less than 37 weeks of gestation from the first day of the last menstruation.⁶ Previous studies found that 75% of neonatal complications and 70% of neonatal deaths are related to PTBs.⁸ Recently, it has been found that PTB is not only a significant cause of neonatal death but also is closely related to adult diseases such as type II diabetes mellitus, coronary heart disease, and hypertension.⁹ Therefore, it is of great importance to find the cause of PTBs. Furthermore, experts and scholars at home and abroad began to pay attention to the relationship between ambient air pollutants and PTBs.⁹¹⁰ In overseas countries, such as the United States, Canada, Australia, and Lithuania, studies have been conducted on this topic.¹¹⁻¹³ Most of the results show that exposure of to NO₂, PM₁₀, SO₂, and other pollutants in the atmosphere may be related to premature delivery in pregnant women.¹⁵ Beijing and Shanghai in China have also carried out studies in this field,¹⁴ which have found that elevated concentrations of NO₂, PM₁₀, and SO₂ in the atmosphere were risk factors for premature delivery. Xiamen city is a special economic zone, which is located in the southeast coast of China, facing the Taiwan Strait.¹⁵ Recently, intensified industrialization and economic development might have increased the ambient air pollutant (such as SO₂ and NO₂) concentration in the Xiamen region.¹⁶ However, few studies have been done on the ambient air pollutants and human health, especially on the vulnerable group. It is crucial to research the influence of rapid urbanization on air pollution to promote ecological environmental protection of Xiamen city. Therefore, there is an urgent need to develop a methodology and construct a comprehensive evaluation framework suitable for air pollution risk assessment for PTBs in Xiamen, China.
Table 1. Summary Statistics of Daily Premature Birth Counts and Air Pollutants in Xiamen between 2015 and 2018*  

| Variable                  | mean ± SD | Min     | P (25%) | median  | P (75%) | Max  |
|---------------------------|-----------|---------|---------|---------|---------|------|
| premature birth counts    | 2 ± 1     | 0       | 0       | 1       | 2       | 6    |
| ambient air pollutants concentration (µg/m³) |           |         |         |         |         |      |
| PM_{2.5}                  | 27 ± 14   | 3       | 17      | 24      | 33      | 134  |
| PM_{10}                   | 49 ± 23   | 8       | 32      | 47      | 62      | 160  |
| NO₂                       | 16 ± 11   | 1       | 9       | 13      | 20      | 116  |
| SO₂                       | 11 ± 5    | 1       | 7       | 10      | 14      | 50   |
| CO                        | 567 ± 182 | 200     | 400     | 600     | 700     | 1700 |
| O₃                        | 74 ± 28   | 3       | 52      | 71      | 92      | 166  |

*PM_{2.5}, PM_{10}, NO₂, SO₂, CO—24 h; O₃—8 h.

In this study, the generalized additive model (GAM) was used to quantitatively evaluate the acute effects of air pollution including PM_{2.5}, PM_{10}, CO, O₃, NO₂, and SO₂ on the incidence of PTBs in Xiamen of Fujian Province by calculating the time series data of ambient air pollutants, meteorology, and PTBs between 2015 and 2018.

2. MATERIALS AND METHODS

2.1. Research Area. Xiamen is one of the coastal open cities, which is located in southeastern China, which has a moderate subtropical climate. Xiamen city consists of six districts, including Siming, Huli, Haicang, Jimei, Tong'an, and Xiang'an.

2.2. PTB Visits. Data were extracted from the First Affiliated Hospital of Xiamen University (PTBs counts of 1991) from 2015 to 2018. Data were representation and behaving random episodes. PTB means the termination of pregnancy from 28 weeks of gestation to less than 37 weeks of gestation from the first day of the last menstruation. The respondent information, including date of admission, data of birth, pregnancy time, and address, was documented in this investigation.

2.3. Environmental Data. The concentrations of O₃, CO, NO₂, PM_{2.5}, SO₂, and PM_{10} were obtained from Xiamen Environmental Monitoring Center (XEMC) from 1 January 2015 to 31 December 2018. Daily concentrations of these ambient air pollutants were available. The authenticity and representativeness of the data can be guaranteed.

2.4. Statistical Analysis. From 1 January 2015 to 31 December 2018, a total of 1991 PTBs were recorded. A time series is applied to research the association between pollutants and the health end point. The relationship between ambient air pollutants and PTBs was explored using the GAM in this investigation. We used multiple linear regression to investigate the association between PTBs and pollutants’ concentration, such as NO₂, CO, SO₂, O₃, PM_{10}, and PM_{2.5}. The consideration of impact modifiers and underlying confounders, including temperature, relative humidity, and the testing period parameter, was controlled. To consider the relationship of nonlinear exposure–response, we also use GAMs to evaluate the relation of air pollution and PTBs through testing the freedom degrees of the smooth connection per variable as a part of the procedure. The controlled variables are in agreement with the linear regression variables. The potential modifying and confounding effect was calculated when the final models were selected for target air pollution. Double pollutants models were calculated to test codependency in order to avoid the multicollinearity effect of target pollution. The Spearman correlation coefficient was applied to investigate the association between PTBs and pollutants. Then, the GAM was used to assess the relationship of air pollution and PTBs because of the meteorological conditions covariant in this work. The models were set up and then selecting the pollutant’s variables in order to analyze the acute effect on PTBs. We studied the effect of air pollution with vary lag structures on PTBs, including current-day (refer to Lag 0) and single lag day (refer to Lag 1). In detail, Lag 0 refers to the ambient air pollutant effect on current-day, and Lag 1 refers to the effect on previous day. We also investigated the effects of multi- and single pollutant on PTBs. The 95% confidence interval (CI) and relative risk (RR) were estimated as follows.

$$RR = e^{Q\times IQR - 1}$$

$$95\% \text{ upper} = e^{\beta_1\times IQR - 1}$$

$$95\% \text{ lower} = e^{\beta_2\times IQR - 1}$$

$$\beta = Q \pm 1.96 \times SE$$

where, Q is the estimated value and SE is the standard error. IQR means the interquartile range (the value is 10 µg/m³ in this study).

The investigation was calculated in R 2.11.1 (R Development Core Team, 2011). An IQR increase was selected for air pollution concentration and the percentage change in PTBs to compare with the previous investigation.

3. RESULTS

3.1. Impact of Air Pollution on PTB Visits. Table 1 sums up the daily premature birth counts and air pollutant concentration. Daily air pollution mean concentrations were 27 ± 14 µg/m³ of PM_{2.5}, 49 ± 23 µg/m³ of PM_{10}, 74 ± 28 µg/m³ of O₃, 11 ± 5 µg/m³ of SO₂, 16 ± 11 µg/m³ of NO₂, and 567 ± 182 µg/m³ of CO. In general, the correlation coefficients among PM_{10}, SO₂, CO, and PM_{2.5} are all relatively high between air pollutants except CO with NO₂, CO with PM_{10} (Table 2).

Table 2. Correlation Coefficients between Daily Air Pollutant Concentration in Xiamen between 2015 and 2018*

| Variable | PM_{2.5} | PM_{10} | NO₂ | SO₂ | CO | O₃ |
|----------|----------|---------|-----|-----|----|----|
| PM_{2.5} | 1.00     | 0.85    | 0.49 | 0.57 | 0.67 | 0.19 |
| PM_{10}  | 0.85     | 1.00    | 0.36 | 0.57 | 0.52 | 0.33 |
| NO₂      | 0.49     | 0.36   | 1.00 | 0.56 | 0.43 | −0.10 |
| SO₂      | 0.57     | 0.57   | 0.66 | 1.00 | 0.36 | 0.12 |
| CO       | 0.67     | 0.52   | 0.43 | 0.36 | 1.00 | −0.10 |
| O₃       | 0.19     | 0.33   | −0.10| 0.12 | −0.10| 1.00 |

*Significant Spearman correlation coefficients (r > 0.5) are marked bold.
Table 3 shows the single-pollutant impact using exposure at current day (Lag 0). Results show that an IQR increase in PM2.5, NO2, and SO2 with 0.64%, 0.52, and 2.33% increase for PTB morbidity, respectively. However, the link of PM10, O3, and CO with PTBs decreases and statistically insignificant. Furthermore, in multipollutant models (Table 4), an IQR increase of 10 μg/m3 in Air Pollutants (PM2.5, PM10, NO2, SO2, NO2, and CO) in Xiamen, in Multipollutant Models Adjusted for Pollutants.

| air pollutants | premature birth (increase % [95% CI]) |
|----------------|----------------------------------------|
| PM2.5          | −0.41 [−3.42, 2.71]                    |
| PM10           | 0.64* [−1.22, 2.54]                    |
| NO2            | 0.52 [−5.21, 6.61]                     |
| SO2            | 2.33 [−6.14, 11.58]                    |
| CO             | −0.19 [−0.44, 0.07]                    |
| O3             | −0.21 [−1.88, 1.51]                    |

*p < 0.5.

Table 4. Increase in Premature Birth Associated with an Increase of 10 μg/m3 in Air Pollutants (PM2.5, PM10, NO2, SO2, NO2, and CO) in Xiamen, in Multipollutant Models Adjusted for Copollutants.

| air pollutants | premature birth (increase % [95% CI]) |
|----------------|----------------------------------------|
| PM2.5 with PM10| 2.98 [−0.53, 6.63]                     |
| PM2.5 with SO2 | 5.04 [−5.90, 17.24]                    |
| PM2.5 with NO2 | 1.10 [−5.32, 7.98]                     |
| PM2.5 with O3  | −0.17 [−1.88, 1.58]                    |
| PM2.5 with CO  | 2.10* [−2.04, 6.42]                    |
| PM10 with SO2  | 0.68 [−10.06, 12.69]                   |
| PM10 with NO2  | 0.74 [−1.40, 2.93]                     |
| PM10 with O3   | 0.78 [−1.18, 2.18]                     |
| PM10 with CO   | 2.04 [−0.23, 4.36]                     |
| SO2 with NO2   | 3.60 [−8.34, 17.10]                    |
| SO2 with O3    | 2.49 [−6.07, 11.81]                    |
| SO2 with CO    | 7.10* [−2.79, 18.00]                   |
| NO2 with O3    | 0.58 [−5.18, 6.69]                     |
| CO with O3     | 2.42 [−3.77, 9.00]                     |
| O3 with CO     | −0.19 [−0.44, 0.96]                    |

*p < 0.05.

increase in PM2.5, O3 and CO, after adjusting for SO2, were related to a 5.04% [95% CI: −5.90, 17.24], 2.49% [95% CI: −6.07, 11.81] and 7.10% [95% CI: −2.79, 18.00] increase of PTBs morbidity, although PM2.5, O3, and CO with PTBs decrease in the single pollutant model. We also research the relationship of SO2 with NO2 (3.60%), PM10 with SO2 (0.68%), and PM10 with NO2 (0.74%) in multipollutant models.

Figure 1 shows the relationship of exposure–response of PM2.5, PM10, NO2, and SO2 with PTBs. In terms of PM2.5 and PTBs risk, the curve presents as rapid growth when pollutant concentration is high (>75 μg/m³). Even if lower than the current air quality standard (PM2.5, daily average concentration: 75 μg/m³), we can observe obvious increase for PTBs morbidity. For NO2, the relationship of the exposure–response curve is similar to that of PM2.5, which presents as a J-shaped curve between NO2 and PTBs. Moreover, the linear exposure–response relationship was found between SO2 and PTBs. The curve presents slight increase with concentration increase of air pollution. PM10 was similar to those of SO2 in exposure–response relationships. The exposure–response curves were not presented between O3 and CO because of insignificant relationship.

Table 5 lists the single-lag (from Lag 1 to Lag 3) impact for the percentage increase in PTBs per IQR. An IQR increase in Lag 1 concentration of PM10 and NO2 corresponded to 0.32% [95% CI: −2.17, 2.88] and 0.42% [95% CI: −6.57, 7.94] increase of PTBs. PTBs were significantly associated with the Lag 2 effect for SO2 but air pollution did not show any statistically significant association for PTBs morbidity in Lag 2.

### 3.2. Calculation of the Economic Losses in Terms of the Impact of Ambient Air Pollutants on PTBs.

The parameters of the lag effect of PM10 and SO2 on the excess number of PTBs were estimated using the GAM model. The method of estimating the number of the excess PTB number was explained by the sum of the estimated parameters of PM10 and SO2 at the current day and the effects of 1–2 lags. The parameter of $f_i$ was calculated as follows:

$$f_i = \frac{\exp(\beta \times (C - C_0))}{E}$$

where, $E$ means the excess number of PTBs; $f_i$ means the PTB ratio in current air pollutants; $P_i$ is the number of PTB persons; $\beta$ is the estimate value.

In this study, we select $f_i$ of 7% and $P_i$ of 1.20 million according to the medsci website. The estimates of the number of excess PTBs attributed to typical pollutants PM10 and SO2 were ~2400 and 1200 people, respectively (Table 6). The highest excess PTB was observed between PM10 and SO2 effect.

### 4. DISCUSSION

This time series study (2015–2018) explored the acute effect of exposure to ambient air pollutants on PTBs in Xiamen city, China. This work systematically investigates the potential detrimental influences of air pollution on PTBs, although Xiamen has a less-polluted city label.

Many epidemiological investigations have assessed significant association between air pollution and increased PTBs risk. A study in Ontario, Canada, reported that an IQR (2 μg/m³) increase in PM2.5, O3 and CO, after adjusting for SO2, were related to a 5.04% [95% CI: −5.90, 17.24], 2.49% [95% CI: −6.07, 11.81] and 7.10% [95% CI: −2.79, 18.00] increase of PTBs morbidity, although PM2.5, O3, and CO with PTBs decrease in the single pollutant model. We also research the relationship of SO2 with NO2 (3.60%), PM10 with SO2 (0.68%), and PM10 with NO2 (0.74%) in multipollutant models.

In Wang’s analysis, the strongest associations were observed for PM10 and NO2, which present 1.05% [95% CI: 1.03, 1.062] increase risk for PTB per IQR (IQR = 37.0 μg/m³). Our study presented that an IQR increase of PM10, NO2, and SO2 corresponded to increase of 0.64% [95% CI: −1.22%, 2.54%], 0.52% [95% CI: −5.21%, 6.61%], and 2.33% [95% CI: −6.41%, 11.58%] in daily PTBs in Lag 0, respectively. Several research studies have also suggested the significant impact of air pollution on PTBs. Similarly, Ji et al. found that a 10 μg/m³ increase in NO2 concentrations was related with 1.03 (95% CI: 0.96, 1.10) PTB risk.

We studied different lag effects using different lag structures (L1, L2, and L3) in Xiamen than previous works in other cities. For example, in Liang’s cohort analysis, an IQR increase for O3 and SO2 concentration in current day were corresponding to 1.18 (95% CI: 1.12, 1.23) and 1.48 (95% CI: 0.53, 6.63) increase of excess PTBs attributed to typical pollutants PM10 and SO2. However, the link of PM2.5, NO2, and CO with PTBs decreases and statistically insignificant. Furthermore, in multipollutant models (Table 4), an IQR increase of 10 μg/m3 in Air Pollutants (PM2.5, PM10, NO2, SO2, NO2, and CO) in Xiamen, in Multipollutant Models Adjusted for Copollutants.
However, we found that an IQR increase for PM10 and NO2 concentration in L1 were corresponding to 0.32% [95% CI: −2.17, 2.88] increase and 0.42% [95% CI: −6.57, 7.94] increase of PTBs, respectively. In L2, an IQR increase for SO2, O3, and NO2 concentration was corresponding to 2.09% [95% CI: −8.00, 13.29] increase, 0.37% [95% CI: −1.77, 2.57] increase, and 0.46% [95% CI: −0.25, 1.23] increase of PTBs, respectively. We did not find any effects in the other lag day. Many potential factors are responsible for heterogeneity. First, Xiamen is a fastest growing open coastal city with a relatively complex energy structure. The annual average PM10 concentrations between 2015 and 2018 were 49 μg/m³ in Xiamen, which exceed the WHO standard (40 μg/m³). Second, ambient air pollutants in Xiamen show different characteristics (such as harbor air pollutants). Third, the social and demographic situation of local residents may be diverse, such as the disease pattern or structure.

Understanding the relationship of exposure–response is significant in the assessment of health end point. Second, ambient air pollutants in Xiamen show different characteristics (such as harbor air pollutants). Third, the social and demographic situation of local residents may be diverse, such as the disease pattern or structure.
a rationale for improving the normal birth rate. For instance, pregnant women can be asked to stay at home when air pollution is serious.

Considering the variation and multlinearity in exposure measurement errors of air pollutants, the influence of damages on PTBs could be inseparable. After the adjustment for other pollutants, associations of PTBs and air pollution are still significant, indicating that gaseous pollutants have different underlying mechanisms with particulate matter, such as NO2 and PM10.17,30,31 We found that PM2.5, CO, and O3 had no acute effect on pregnant women, but when mixed with other air pollutants (mixtures), PM2.5, CO, and O3 had a significant effect on premature delivery in pregnant women, which notably increased the probability of premature delivery in pregnant women. For example, a 10 μg/m3 increase of SO2 corresponding to 2.33% [95% CI: −6.14, 11.58] increase for PTBs. However, a 10 μg/m3 increase of PM10 with SO2 corresponding to 5.04% [95% CI: −5.90, 17.24] increase for PTBs.

The GAM model was used to estimate the number of excess PTBs attribute to typical pollutants. The estimates of the number of excess PTBs attribute to typical pollutants were about 3600 persons. Also, the highest excess PTBs were estimated to occur for the PM10 and SO2 effect. These results indicate that although Xiamen is a relatively less-polluted city, attention should also be paid to individual pollutants, such as SO2 and PM10. Furthermore, improvement of fertility quality through risk assessment between the environment and PTBs is necessary, especially for low pollution-level city.

This work has several strengths. First, previous works studied the relationships of air pollution and PTBs in one aspect. This investigation evaluated and confirmed the relation between air pollution and PTBs. This investigation also researched the lag impact, relationship with single- and multipollutant impact, RR assessment, and exposure–response analysis. Second, few studies based on PTBs, which might better reflect the impacts of air pollution on PTBs. Third, this work may serve as the theoretical basis to the National Open Second Birth Policy, as it is accessible by local policy makers.

Nevertheless, limitations of the study are also present. As in many previous relevant studies, there is a certain degree of the exposure measurement error in the calculation of air pollution exposure response, and thus, estimates are skewed downward. Also, the PTBs had by Xiamen First Affiliated Hospital may not be fully consistent with other hospitals of Xiamen. Future research is still necessary to explore the effect of air pollutants on PTBs.

5. CONCLUSIONS

The acute effect of SO2, NO2, and PM10 were associated with PTB increase. Especially, NO2 and PM10 have stronger effect on PTBs when the adjustment of SO2 was considered. For further works, we found the cause by which pollutants induce PTBs are necessary to deal with the combined effect or independent of PM10, SO2 and NO2 for PTBs. These results also provide some suggestions for adaption to the National Open Second Birth Policy in Xiamen.

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Q.C. and S.H. carried out the research, collected the data, and wrote the manuscript. Q.C. supervised the study and approved the version to be published. D.L. and Z.H. formally analyzed the data. L.Y. and X.D. drew all the figures and tables.

Notes
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