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The impacts of air pollution on maternal stress during pregnancy

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To investigate the association of air pollution with maternal stress during pregnancy, we enrolled 1,931 women during mid-to-late pregnancy in Shanghai in 2010. The “Life-Event Scale for Pregnant Women” and “Symptom-Checklist-90-Revised Scale” (SCL-90-R) were used to evaluate life event stress and emotional stress, respectively. Air pollution data were collected for each district where pregnant women lived during pregnancy. We associated ambient air pollution with stress scores using multivariable logistic regression models. After adjusting for relevant covariates, an interquartile-range (IQR) increase in sulphur-dioxide (SO₂) (OR = 1.30, 95% CI: 1.11–1.52) and particulate-matter with an aerodynamic-diameter <10 μm (PM₁₀) (OR = 1.16, 95% CI: 1.02–1.34) concentrations on the recruitment day, and in the 5-day moving average concentrations of nitrogen-dioxide (NO₂) (OR = 1.34, 95% CI: 1.05–1.70) were associated with high Global-Severity-Indices (P75-P100) of the SCL-90-R. These associations were stronger among women bearing high levels (P25-P100) of air pollutants than among women experiencing low levels (P1-P25) of pollutants. The stronger associations and higher levels of pollutants were observed in the cool season than in the warm season. SO₂ increases on the recruitment day were also associated with an increased risk of high depression scores (P75-P100). Our findings supported a dose-dependent association between air pollution and emotional stress during pregnancy.

As the largest developing country in the world, China has achieved rapid development in the past two decades. However, this economic development is accompanied by increased levels of air pollution, particularly in large cities. In Shanghai, one of the largest developed cities in China, officials have become aware of the issue of air pollution and have implemented various prevention measures. Nonetheless, air pollution may remain a threat to public health in Shanghai^{1,2}.

In addition to the effects of air pollution on somatic disorders that have been extensively investigated, such as increased risks of pulmonary diseases^{3–5}, cardiovascular diseases^{6,7}, or mortality^{8–10}, a few studies have focused on the association between ambient air pollution and human psychological health. Exposure to air pollution was found to be related to increased risks of suicide¹¹, and depressive symptoms¹². Air pollution was also reported to be linked with higher perceived stress levels in old men, particularly in cold months¹³. Studies also reported that short-term exposure to ambient air pollution was associated with increased emergency department visits because of depression or suicide attempts^{14–16}.

The developing foetus is vulnerable to many adverse factors, including maternal stress during pregnancy. Previous studies have shown that excessive maternal stress during pregnancy could induce preterm birth¹⁷, low birth weight¹⁸, and adverse neurodevelopment outcomes in infants, including cognitive deficits and changes in temperamental traits^{19,20}. However, until now, no evidence is available to show the association between air pollution and maternal stress during pregnancy. Previous studies also reported that the respiratory diseases or symptoms differed at different levels of air pollution^{21,22}. Higher levels of air pollution may be more likely to induce oxidative stress, which played an important role in the development of depression²³; therefore, we wondered whether the magnitude of the association between air pollution and maternal stress during pregnancy varied at different levels of air pollution. Additionally, the complications of pregnancy were related to maternal stress during pregnancy^{24,25}, and air pollution was associated with the development of complications of pregnancy²⁶.

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However, the modifying effects of complications of pregnancy on the association between air pollution and maternal stress during pregnancy remain unclear^{27,28}.

Therefore, the present study was to evaluate the association between major air pollutants, including sulphur dioxide (SO₂), nitrogen dioxide (NO₂), and particulate-matter with an aerodynamic-diameter <10 μm (PM₁₀) and maternal stress levels during pregnancy in Shanghai, China.

Methods

Study design. This study evaluated data from 1,931 pregnant women who regularly visited 4 prenatal-care clinics for antenatal examination from February to October, 2010 in Shanghai. These women were recruited using stratified-cluster sampling. According to the 2010 Census, there were a total of 19 districts in Shanghai. The study districts were sampled among all districts in Shanghai. We randomly selected 2 districts (Minhang and Chongming) from the 10 suburban districts and 2 districts (Yangpu and Xuhui) from the 9 urban districts (the map of the sampling locations was shown in Fig. 1). Within each selected district, the largest maternity hospital was chosen. Therefore, 2 suburban hospitals (Xinhua Hospital Chongming branch and Minhang Maternal and Child Health Hospital) and 2 urban hospitals (International Peace Maternity and Child Health Hospital and Xinhua Hospital) were finally included, covering the north, south and central areas of Shanghai. These 4 hospitals were among the largest maternity hospitals in Shanghai, serving pregnant women from not only the districts where the hospitals were located but also from other districts. The study women were finally from all the districts of Shanghai (Fig. 1)²⁹.

We conducted an in-person interview to collect information on the women's socio-demographic characteristics and on their diseases and pregnancy histories. Women with "mental disabilities" were excluded according to their maternity medical record kept in prenatal care clinics²⁹. Special stress scales were used to assess the women's life event stress levels and emotional stress levels during pregnancy. Daily air quality data were collected for individual women.

We obtained written informed consent from all participants, and the study protocol was approved by the Medical Ethics Committee of Xinhua Hospital affiliated with the Shanghai Jiao Tong University School of Medicine. All the methods applied in the study were carried out in accordance with the approved guidelines.

Measures of maternal stress. Trained staff conducted face-to-face interviews to evaluate maternal stress during pregnancy using the Life Event Scale for Pregnant Women (LESPW) and the Symptom Checklist-90-Revised Scale (SCL-90-R).

The LESPW is a self-rating scale used to assess perceived stress levels during pregnancy³⁰. This scale consists of 53 items on family, work, learning, and social relationship-related problems, and the events are weighted to calculate the LESPW total score. The LESPW is a valid and reliable tool that has been widely used to assess life event stress levels during pregnancy in China³¹. A higher LESPW score indicates a higher level of life event stress during pregnancy.

The SCL-90-R is a self-reported inventory used to assess emotional stress or psychosocial distress³². Each individual symptom is rated as 1 (no distress), 2 (slightly distressed), 3 (moderately distressed), 4 (quite a bit of distress), and 5 (extremely distressed). The scale consists of 90 distress items to assess symptoms in 9 subscales, including somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism. The SCL-90-R is a scale with good reliability and validity, and has been widely used in China³³. We used the mean score of all items (90 items), namely the Global Severity Index (GSI) (GSI score = SCL-90-R total score/90), to represent the overall level of emotional stress, and we used the mean score of the items belonging to each subscale (total score of the subscale/the number of the items of the subscale) to represent the degree of the psychiatric symptom associated with the subscale. The GSI is a good indicator of the severity of general psychiatric symptoms. A higher GSI score indicates a higher level of emotional stress, and a higher subscale score suggests a higher level of the specific psychiatric symptom³².

Air pollution variables. We obtained daily air pollution data (including daily average SO₂, NO₂, and PM₁₀ concentrations) from the Shanghai Environmental Monitoring Centre based on the districts where the participating pregnant women lived during pregnancy. A 3-day moving average concentration (the recruitment day and the previous 2 days), a 6-day moving average concentration (the recruitment day and the previous 5 days), an 8-day moving average concentration (the recruitment day and the previous 7 days), and a 15-day moving average concentration (the recruitment day and the previous 14 days) of air pollution levels (including SO₂, NO₂, and PM₁₀) were calculated for each woman according to the daily average concentration of each pollutant. Acute and delayed effects of air pollutants on maternal stress were estimated using the following moving average lag structure: 0 day (air pollution levels on the recruitment day), 0–2 days (3-day moving average concentration), 0–5 days (6-day moving average concentration), 0–7 days (8-day moving average concentration), and 0–14 days (15-day moving average concentration).

Confounders. To control for the potential confounding effects of weather conditions, weather data during the study period, including daily average temperature, relative humidity, and wind speed were obtained from the Shanghai Meteorological Bureau. Other covariates, including maternal age, education, occupation, family monthly income, type of family structure, complications of pregnancy, and abortion history were collected through questionnaires and in-person interviews. Confounders were selected based on the following commonly used criteria: the variable was associated with the main predictor (air pollution) or the dependent variable (maternal stress level), and it was not in the causal pathway between the outcome and the main predictor.

Statistical analysis. We first examined the socio-demographic characteristics of the 1,931 participants and the overall characteristics of the air quality and weather. Spearman correlation was used to examine the

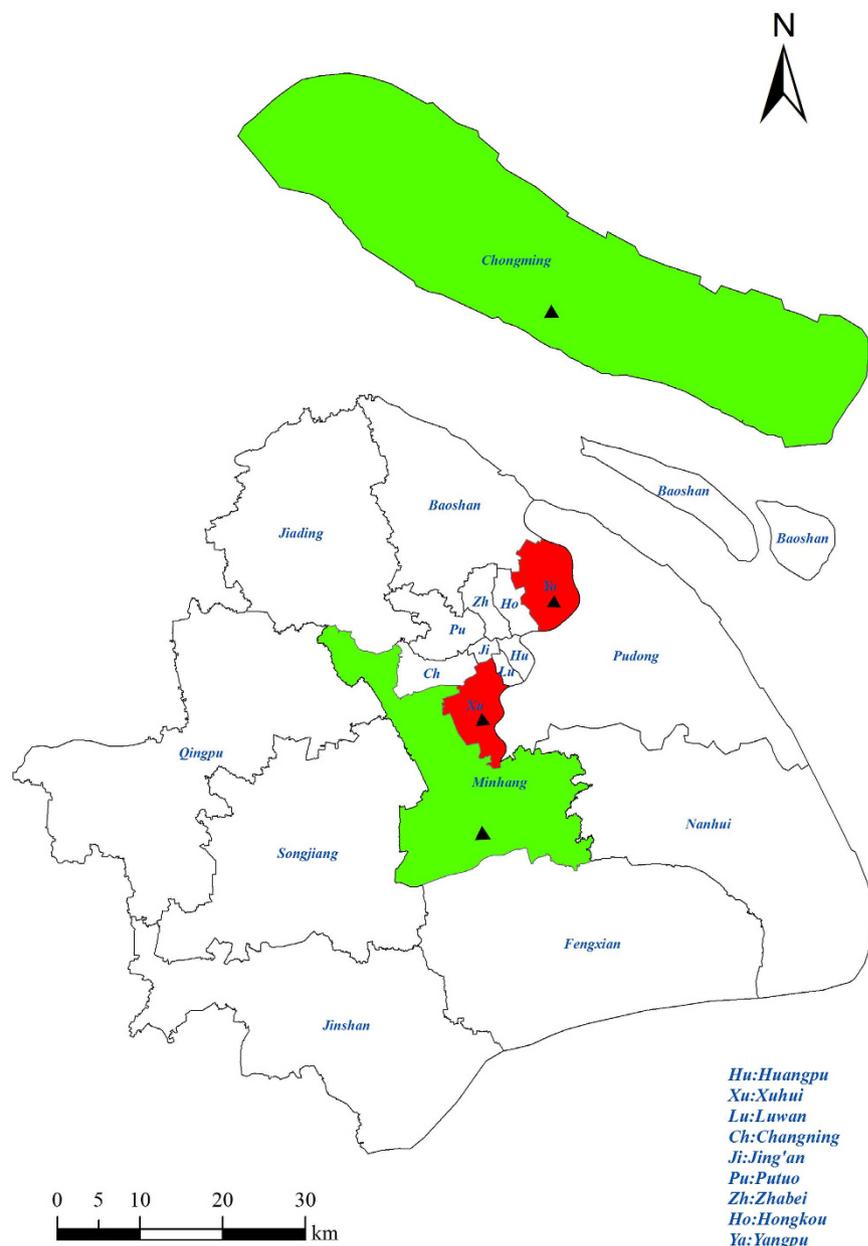


Figure 1. The map of Shanghai with the sampling locations marked. (The map was made by ArcGIS 10.0, URL link: <http://www.esri.com/>). A total of 1931 pregnant women living in the 19 districts of Shanghai were enrolled in 2010 in this study. The selected districts and hospitals were marked as above (hospitals were marked with triangle, the selected 2 urban districts were filled with red, and the selected 2 suburban districts were filled with green). The 9 urban districts: Huangpu, Luwan, Xuhui, Changning, Jingan, Putuo, Zhabei, Hongkou, Yangpu; The 10 suburban districts: Baoshan, Minhang, Jiading, Songjiang, Qingpu, Fengxian, Jinshan, Pudong, Nanhui, Chongming.

interrelationship between air pollutants and weather variables. Multivariate binary logistic regression analyses were used to evaluate the relationships between each air pollutant and maternal stress levels during pregnancy. Because the GSI, depression, and anxiety scores of the SCL-90-R and LESPW data showed non-normal distributions and there were no accepted reference ranges for these scores among pregnant women, we performed sensitivity analyses to determine the cut-off values for the definitions of high levels of maternal GSI/depression/anxiety/LESPW. We found that, for the GSI or depression scores, every 5 percent increase in the cut-off values of GSI or depression scores from the 75th percentile to the 95th percentile didn't significantly change the direction and strength of the associations between air pollution and maternal stress levels, however, every 5 percent decrease in the cut-off values of GSI or depression scores from the 75th percentile to the 50th percentile changed the strength of the associations (from significant positive associations to non-significant associations). In addition, the 75th percentile was frequently used as the cut-off value in previous studies. Therefore, high levels of GSI/depression/anxiety/LESPW were defined as GSI/depression/anxiety/LESPW scores ranging from P75-P100. The

estimated effect of an interquartile range (IQR) increase in the concentration of each air pollutant (including SO₂, NO₂, and PM₁₀) was expressed as the increased risk of maternal emotional stress/life event stress¹². $P < 0.05$ (2-tailed) was considered statistically significant.

To investigate whether the magnitude of the association between each air pollutant and maternal stress during pregnancy differed according to the levels of air pollutants, air pollution was categorized to simplify the interpretation. We estimated the relationship between each air pollutant and maternal stress separately within each quartile of air pollutant levels. We observed that for the highest 3 quartiles of air pollutant concentrations, the increase in each air pollutant level was significantly associated with an increased risk of high emotional stress (P75-P100), however in the lowest quartile, the increase in each air pollutant level was non-significantly associated with the risk of high emotional stress. Therefore, the high level of air pollution was defined as “the average concentrations of the air pollutants (including SO₂, NO₂ and PM₁₀) among P25-P100”, and the low level of air pollution was defined as “the air pollutant concentrations (including SO₂, NO₂ and PM₁₀) among P1-P25”.

Based on the lag structure that provided the best fit to the data, we further analysed the effects of air pollution separately for the warm season (from May to October, when the daily average temperatures ranged from 15.3 to 34.1 °C and the mean temperature was 24.7 °C) and the cool season (from November to the next April, when the daily average temperatures ranged from -0.6 to 17.9 °C and the mean temperature was 12.1 °C)³⁴.

To investigate whether complications of pregnancy modified the association between air pollution and maternal stress levels, the participants were classified into two categories (yes or no) based on whether they had complications of pregnancy or not, including gestational hypertension, gestational diabetes mellitus, anemia, polyhydramnios, oligohydramnios, intrahepatic cholestasis of pregnancy, hypohepatia and heart diseases, and the modifying effects were examined in the association between air pollution and maternal stress. We combined women with different kinds of complications mentioned above as the “complication” (yes) group, and women without any kind of complications as the “control” (no) group. In addition, because of the limited sample size for each type of complication except for anemia [the sample size of women with anemia was 129, and the sample sizes of women with other kinds of complications of pregnancy were all ≤ 65 ($\leq 3.4\%$ of our study population)], we only additionally estimated the modifying effect of anemia on the association between air pollution and maternal stress.

In order to examine the independent association of a certain pollutant after adjusting for the potential confounding effects caused by other pollutants, two- and three-pollutant models were used in our analyses.

The association of levels of air pollutants with depression and anxiety symptoms was estimated using a multivariate binary logistic regression model. We expressed the estimated effects of an IQR increase in the concentration of each pollutant (including SO₂, NO₂, and PM₁₀) as the increased risks of depression and anxiety symptoms.

All analyses were performed using Empower (R) (www.empowerstats.com, X&Y Solutions, Inc., Boston, MA, USA) and R (http://www.R-project.org).

Results

The average age of these 1,931 pregnant women was 28.0 years old, and most of the women were well-educated (58.6% of the women finished their college/university or postgraduate education). The proportion of the women who had various types of complications of pregnancy was 14.3% (275 participants), among which anemia occurred most commonly during pregnancy (Table 1).

Table 2 showed the characteristics of the air pollutants and weather variables in Shanghai during the study period. The mean values of the daily average concentrations of SO₂, NO₂, and PM₁₀ (23.7, 23.1, and 73.9 µg/m³, respectively) were lower than the limit values of China's current air quality standards (limit values for Chinese urban areas: 150 µg/m³ for SO₂, 80 µg/m³ for NO₂ and 150 µg/m³ for PM₁₀, respectively). The mean values of the daily average temperature, relative humidity, and wind speed were 21.5 °C, 70.6%, and 3.1 m/s, respectively. The ambient air pollutants were moderately correlated with one another (correlation coefficients range from 0.60 to 0.68) (Supplementary Table 1). The concentrations of air pollutants in the cool season were significantly higher than those in the warm season (P value < 0.05), and the PM₁₀ concentrations increased much more compared with the changes of NO₂ and SO₂ at lag 0 day (Table 3).

Figure 2A–C displayed the estimated risks of high maternal emotional stress (GSI among P75-P100) during pregnancy per IQR increase in air pollutant levels for different lag days. For high emotional stress, the best fitting lag structure for SO₂, NO₂, and PM₁₀ was lag 0, lag 0–5, and lag 0, respectively. The per IQR increase in SO₂ [OR = 1.30; 95% confidence intervals (CI): 1.11, 1.52; $P = 0.001$] (Fig. 2A, Supplementary Table 2) and PM₁₀ (OR = 1.16; 95% CI: 1.02, 1.34; $P = 0.029$) (Fig. 2C, Supplementary Table 2) at lag 0 days and the per IQR increase in NO₂ (Fig. 2B, Supplementary Table 2) at lag 0–5 days (OR = 1.34; 95% CI: 1.05, 1.70; $P = 0.018$) were significantly associated with high maternal GSI during pregnancy. However, a null association between these three air pollutants and high GSI was found for the other lag day lengths.

After stratified by levels of air pollutants, we observed that the association of air pollution with the risk of maternal emotional stress was more evident among the high air pollution groups (P25-P100) than among the low pollution groups (P1-P25) (Table 4). We found that, among the high pollution groups (P25-P100), an IQR increase in SO₂ concentrations at lag 0 day (OR = 1.36, 95%CI: 1.12–1.66), in PM₁₀ concentrations at lag 0 day (OR = 1.19, 95%CI: 1.02–1.40) and lag 0–5 days (OR = 1.30, 95%CI: 1.04–1.62), and an IQR increase in NO₂ concentrations at lag 0–5 days (OR = 1.60, 95%CI: 1.12–2.27) and lag 0–7 days (OR = 1.71, 95%CI: 1.13–2.59) were associated with increased risks of high maternal emotion stress (GSI among P75-P100) (all P value < 0.05). However, no significant association was found among the low pollution groups (P1-P25) ($P > 0.05$) (Table 4).

The association of air pollution with maternal stress changed with the season (Table 5). The association was much stronger in the cool season than in the warm season. The odds ratio of the association of PM₁₀ with high maternal stress was higher and more significant in the cool season than in the warm season. However, we did not find any significant seasonal difference in the associations of SO₂ and NO₂ with high maternal GSI.

Variable names	No (%), mean \pm SD, or Median (P25, P75)
Age (years); missing n = 9	28.0 (4.0)
Maternal education; missing n = 8	
Junior high school or lower	442 (23.0%)
Senior high school	353 (18.4%)
College or University level	985 (51.2%)
Postgraduate level	143 (7.4%)
Family monthly income (RMB/month); missing n = 37	
<2,000	311 (16.4%)
2,000–5,000	699 (36.9%)
5,000–10,000	565 (29.8%)
>10,000	319 (16.8%)
Type of family structure; missing n = 17	
Living with husband	997 (52.2%)
Living with husband and parents-in-law	605 (31.7%)
Living with parents	222 (11.6%)
Living alone	87 (4.6%)
Complications of pregnancy; missing n = 3	
No	1653 (85.7%)
Yes	275 (14.3%)
Abortion history; missing n = 15	
Never	1199 (62.6%)
1–2 times	654 (34.1%)
3 or more times	63 (3.3%)
Maternal GSI score	1.2 (1.1, 1.3)
Total score of LESPW; missing n = 3	230.7 (84.0, 332.0)

Table 1. Socio-demographic characteristics of the 1,931 participants

	Mean \pm SD	Median	Range	IQR
Mean temperature ($^{\circ}$ C)	21.5 \pm 6.7	22.5	–0.6–34.1	17.2–26.8
Relative humidity (%)	70.6 \pm 12.3	71.0	38.0–93.0	64.0–80.0
Wind speed (m/s)	3.1 \pm 1.1	3.0	1.2–6.6	2.4–3.8
Mean SO ₂ (μ g/m ³)	23.7 \pm 10.3	22.0	6.0–80.0	16.0–30.0
Mean NO ₂ (μ g/m ³)	23.1 \pm 8.6	23.2	4.8–79.2	16.8–29.6
Mean PM ₁₀ (μ g/m ³)	73.9 \pm 46.8	62.0	14.0–310.0	39.0–96.0

Table 2. Weather and air pollution levels in Shanghai during the study period.

Figure 2D–F showed that the association between air pollution and maternal emotional stress was modified by complications of pregnancy. The association was stronger among the participants without complications of pregnancy than among the women with complications (Fig. 2D–F, Supplementary Table 2). Figure 2G–I showed that participants without anemia were more susceptible to air pollution exposures than those with anemia (Fig. 2G–I, Supplementary Table 2).

In two- and three-pollutant models, the inclusion of NO₂ and PM₁₀ into the models did not significantly influence the estimates for SO₂ association with high GSI. However, the association of NO₂ with maternal high GSI became non-significant when SO₂ was added into the models. The association of PM₁₀ with maternal high GSI became non-significant, and the estimates for the association decreased dramatically when SO₂ was added into the model (Table 6).

Table 7 depicted the associations of maternal depression symptoms with SO₂, NO₂, and PM₁₀. We observed that per IQR increase in SO₂ at lag 0 day was significantly associated with high maternal depression symptom scores (OR = 1.22; 95% CI: 1.05, 1.42; P = 0.010). However, we found no significant associations of NO₂ and PM₁₀ with the high depression symptom scores.

In addition, the results revealed no significant association of each air pollutant with anxiety symptom scores and with the LESPW total scores (all P values > 0.05).

Air pollutants	Lag days	Cool season (n = 476)	Warm season (n = 1455)	P-value ^a
SO ₂	Lag 0	22.19 (21.29, 23.14)	21.34 (20.87, 21.82)	0.141
	Lag 0–2	24.23 (23.55, 24.93)	21.40 (21.01, 21.79)	0.081
	Lag 0–5	25.41 (24.66, 26.19)	20.97 (20.63, 21.31)	0.002
	Lag 0–7	25.32 (24.64, 26.02)	21.24 (20.91, 21.57)	<0.001
	Lag 0–14	25.62 (25.02, 26.23)	21.83 (21.54, 22.12)	<0.001
NO ₂	Lag 0	22.15 (21.32, 23.01)	21.20 (20.79, 21.62)	<0.001
	Lag 0–2	24.57 (23.90, 25.27)	21.40 (21.05, 21.76)	<0.001
	Lag 0–5	24.67 (24.08, 25.28)	20.96 (20.66, 21.28)	<0.001
	Lag 0–7	24.06 (23.56, 24.57)	21.07 (20.76, 21.39)	<0.001
	Lag 0–14	23.77 (23.36, 24.19)	21.14 (20.87, 21.41)	<0.001
PM ₁₀	Lag 0	67.29 (63.37, 71.46)	60.30 (58.55, 62.10)	<0.001
	Lag 0–2	70.45 (66.62, 74.51)	61.61 (60.34, 62.91)	<0.001
	Lag 0–5	67.04 (64.16, 70.05)	59.73 (58.63, 60.85)	<0.001
	Lag 0–7	69.22 (66.41, 72.15)	61.38 (60.33, 62.44)	<0.001
	Lag 0–14	71.97 (69.18, 74.87)	63.72 (62.79, 64.67)	<0.001

Table 3. Geometric means (95%CI) of air pollutant concentrations in different seasons. ^aANOVA was used to examine the difference of the means (log transformation) of air pollution concentrations between the cool season and the warm season.

Discussion

The present study is the first population-based study that focused on the association between air pollution and psychological health among pregnant women. Our results showed that increasing concentrations of SO₂, NO₂, and PM₁₀ were all significantly associated with high emotional stress during pregnancy. The magnitude of the association may vary depending on the levels of air pollution, and may be modified by season and complications of pregnancy. Acute stress may be induced by exposure to SO₂ and PM₁₀, whereas a lagged stress may be a result of exposure to NO₂.

Although the association between air pollution and stress has not been reported among pregnant women, previous studies that examined the adverse effects of air pollution on psychological wellbeing among old people were consistent with our study³⁵. Bullinger found that increasing SO₂ concentrations had adverse effects on mood and stress among females³⁶. Szyszkowicz reported that SO₂ and NO₂ were associated with increased emergency department visits because of depression symptoms¹⁴. Air pollution, such as gases from the combustion of fossil fuels in motor vehicles, was reported to be associated with affective disorders and suicide attempts¹⁶. Animal research also indicated that air pollution could provoke depressive-like behaviours in mice³⁷.

Currently, as far as we know, only one study has investigated the lag effect of air pollution on human psychological health¹². Inconsistent with our study, the previous study found that the symptom of depression in the elderly were associated with a 3-day moving average concentration of PM₁₀ and an 8-day moving average concentration of NO₂, and a null association was found between SO₂ and the symptom of depression¹². We speculate that the difference between that study and ours may be due to the difference in air pollution levels. Additionally, the susceptibility to air pollutants may be different among different populations³⁸.

The biological mechanisms underlying the effects of air pollution on maternal stress during pregnancy remain unknown. There were several possible explanations. First, air pollution during pregnancy may induce oxidative stress³⁹. Oxidative stress has been implicated as the molecular mechanism in the pathogenesis of depression⁴⁰. Pregnant women were reported to be much more vulnerable to oxidative stress than the general population because of their altered physiology and increased energy requirement^{41,42}. Second, animal studies in mice have demonstrated that exposure to air pollution could induce the activation of the hypothalamic-pituitary-adrenal axis⁴³, which was associated with stress⁴⁴, and stress-related disorders⁴⁵. Third, exposure to particulates was demonstrated to be associated with hippocampal pro-inflammatory cytokine expression and changes in hippocampal neuron morphology³⁷, by which the neurotoxic effects of environmental pollutants on maternal stress may be mediated^{13,46}.

We found that the association between air pollution and maternal stress during pregnancy differed under different levels of air pollution, which may suggest that if the pollution level was low, and the population did not realize that it was a “polluted” day, they may not worry about the impacts of air quality on their health. The possible explanations for the positive dose-dependent association between air pollution and maternal stress may be as follows. First, the effect of air pollution on oxidative stress, a potential molecular mechanism underlying the effect of air pollution on human psychological health, was dose-dependent. One previous study proved that high levels of air pollution were associated with oxidative stress, whereas no significant association was found between lower levels of air pollution and oxidative stress²³. Second, higher levels of air pollution may induce a greater effect on inflammatory cytokine expression and neuron morphology in the hippocampus, which were related with the development of maternal stress³⁷.

Consistent with studies reporting the seasonal difference in the effects of air pollution on mortality³⁴, we found a stronger association between air pollution and maternal emotional stress in the cool season than in the warm season. This finding may be explained in part by the following reasons. First, the difference may be due to the different air pollution levels between the cool season and the warm season (the air pollution levels in the cool season

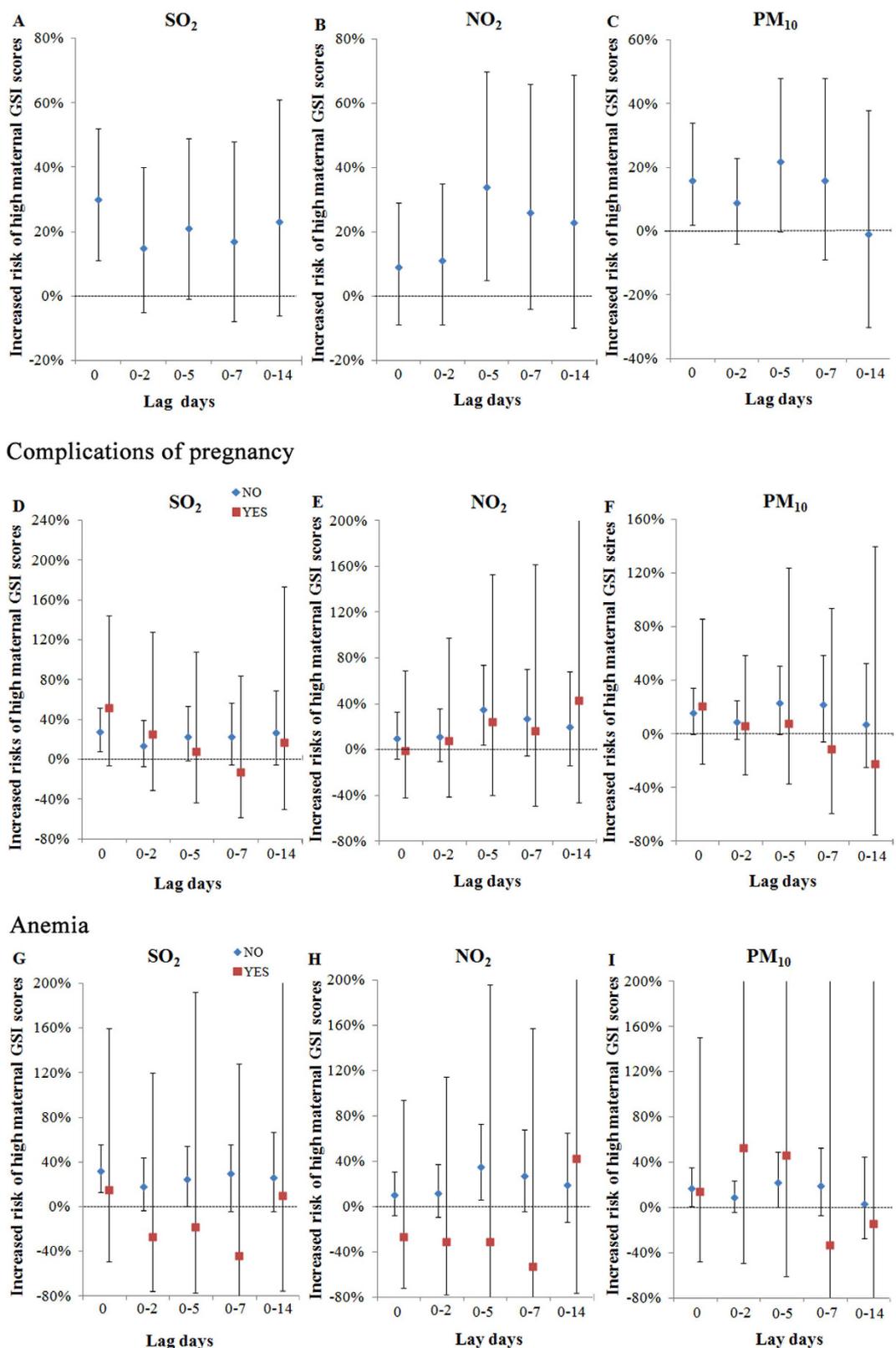


Figure 2. Increased risks of high maternal emotional stress (GSI scores: P75-P100) for an IQR increase in SO₂ (A, IQR = 14.0 μg/m³), NO₂ (B, IQR = 12.8 μg/m³), and PM₁₀ (C, IQR = 57.0 μg/m³) at different lag days, and the modifying effects of complications of pregnancy (D–F) and anemia (G–I). The best fitting lag structures for SO₂, NO₂, and PM₁₀ were lag 0 (A), lag 0–5 (B), and lag 0 (C), respectively. In D–I, blue square: women without complications of pregnancy/anemia; red square: women with complications of pregnancy/anemia. The association was stronger among participants without complications of pregnancy/anemia than among women with complications of pregnancy/anemia.

Air pollutants	The odds ratios (95%CI) of high maternal stress (GSI: P75-P100)				
	Lag 0	Lag 0-2	Lag 0-5	Lag 0-7	Lag 0-14
SO ₂ (µg/m ³)					
<25 th	0.33 (0.06, 1.96)	0.46 (0.10, 2.07)	1.36 (0.24, 7.76)	2.16 (0.53, 8.85)	1.07 (0.28, 4.11)
≥25 th	1.36 (1.12, 1.66)*	1.12 (0.88, 1.44)	1.22 (0.92, 1.61)	1.22 (0.87, 1.71)	1.05 (0.71, 1.57)
NO ₂ (µg/m ³)					
<25 th	1.13 (0.28, 4.50)	1.01 (0.32, 3.19)	0.54 (0.8, 1.59)	0.51 (0.19, 1.40)	1.34 (0.45, 3.95)
≥25 th	1.04 (0.82, 1.32)	1.00 (0.76, 1.32)	1.60 (1.12, 2.27)*	1.71 (1.13, 2.59)*	1.35 (0.83, 2.19)
PM ₁₀ (µg/m ³)					
<25 th	3.93 (0.40, 38.18)	0.17 (0.02, 1.29)	3.77 (0.31, 45.77)	0.94 (0.06, 13.92)	2.02 (0.10, 42.59)
≥25 th	1.19 (1.02, 1.40)*	1.09 (0.95, 1.26)	1.30 (1.04, 1.62)*	1.23 (0.93, 1.63)	1.14 (0.76, 1.70)

Table 4. The dose-dependent association between levels of air pollutants (per IQR increase) and the risks of high maternal emotional stress^a. * $P < 0.05$. ^aAdjusted for maternal age, education, occupation, complications of pregnancy, abortion history, family monthly income, structures of family type, average temperature, relative humidity, and wind speed.

Air pollutants	Lag days	Cool season ^b	Warm season ^c
SO ₂	Lag 0	1.31 (1.00, 1.73)	1.21 (0.98, 1.49)
	Lag 0-2	1.21 (0.84, 1.75)	0.99 (0.78, 1.27)
	Lag 0-5	1.19 (0.82, 1.73)	1.11 (0.84, 1.45)
	Lag 0-7	0.93 (0.56, 1.55)	1.06 (0.79, 1.44)
	Lag 0-14	1.06 (0.58, 1.94)	1.12 (0.79, 1.58)
NO ₂	Lag 0	1.05 (0.78, 1.42)	1.11 (0.89, 1.39)
	Lag 0-2	1.14 (0.79, 1.63)	1.04 (0.81, 1.34)
	Lag 0-5	1.58 (0.98, 2.54)	1.29 (0.94, 1.78)
	Lag 0-7	1.37 (0.77, 2.43)	1.17 (0.82, 1.66)
	Lag 0-14	1.30 (0.67, 2.54)	1.20 (0.80, 1.79)
PM ₁₀	Lag 0	1.28 (1.04, 1.57)*	1.04 (0.86, 1.27)
	Lag 0-2	1.09 (0.93, 1.27)	1.00 (0.75, 1.33)
	Lag 0-5	1.25 (0.91, 1.72)	1.19 (0.89, 1.61)
	Lag 0-7	1.06 (0.62, 1.82)	1.08 (0.76, 1.55)
	Lag 0-14	0.68 (0.34, 1.37)	1.14 (0.56, 2.31)

Table 5. Increased risks [OR (95%CI)] of high maternal emotional stress (GSI: P75-P100) for an IQR increase in SO₂, NO₂, and PM₁₀ concentrations by season^a. ^aAdjusted for maternal age, education, occupation, complications of pregnancy, abortion history, family monthly income, types of family structure, average temperature, relative humidity, and wind speed. ^bCool season: from November to the next April. ^cWarm season: from May to October. *The risks were significantly different between the warm season and the cool season ($P < 0.05$).

were significantly higher than that in the warm season in our study). Second, based on a previous investigation, Shanghai residents closed their windows and used air conditioners more frequently in the summer than they did in the winter³⁴, thus, the chance of exposure to outdoor air pollutants in the warm season or summer may be less than in the cool season or winter. Third, pregnant women may be more likely to go outdoors in the cool season or winter than in the warm season or summer because Shanghai is usually sunny with low humidity in the cool season and rainy with high humidity in the warm season³⁴. Therefore, the seasonal difference in the association may be a result of different patterns of exposure to air pollutants among different seasons. However, the seasonal difference may vary by location in different parts of the world because of different weather conditions and lifestyles⁴⁷.

This study reported that the complications of pregnancy appeared to modify the effects of air pollution on maternal emotional stress. Air pollution was closely associated with high maternal emotional stress among participants without complications of pregnancy, whereas the association was weaker among women with complications of pregnancy. Our results were consistent with those from a study performed among elderly people, which found that a history of cardiovascular disease may modify the association between air pollutants and the symptom of depression, and the association was weaker among elderly people with cardiovascular disease than those without cardiovascular disease¹². One possible explanation for this phenomenon may be that when women were suffering from complications of pregnancy, they might care less about air pollution. However, caution should be taken when interpreting the results because we did not examine the modifying effect of each type of complication during pregnancy.

Air pollutants cannot be selectively inhaled in real life, and all of the air pollutants may be the indicators of the same pollutant mixture according to the results of the correlation analysis⁴⁸. The associations of NO₂ and PM₁₀

Pollutants and models	Lag days	OR (95% CI)	P-value
SO ₂			
Single model ^a	Lag 0	1.30 (1.11, 1.52)*	0.001
+NO ₂	Lag 0	1.38 (1.14, 1.66)*	0.001
+PM ₁₀	Lag 0	1.27 (1.05, 1.53)*	0.013
+NO ₂ +PM ₁₀	Lag 0	1.33 (1.09, 1.63)*	0.006
NO ₂			
Single model ^a	Lag 0–5	1.34 (1.05, 1.70)*	0.018
+SO ₂	Lag 0–5	1.28 (0.94, 1.75)	0.116
+PM ₁₀	Lag 0–5	1.25 (0.95, 1.65)	0.111
+SO ₂ +PM ₁₀	Lag 0–5	1.24 (0.90, 1.71)	0.195
PM ₁₀			
Single model ^a	Lag 0	1.16 (1.02, 1.34)*	0.029
+SO ₂	Lag 0	1.04 (0.88, 1.23)	0.640
+NO ₂	Lag 0	1.18 (1.00, 1.38)	0.054
+SO ₂ +PM ₁₀	Lag 0	1.08 (0.91, 1.29)	0.382

Table 6. Air pollutant levels (an IQR increase) and increased risks of maternal high emotional stress (GSI: P75-P100) using single-, two-, and three pollutant models. * $P < 0.05$. ^aAdjusted for maternal age, education, occupation, complications of pregnancy, abortion history, family monthly income, types of family structure, average temperature, relative humidity, and wind speed.

Item	Lag day	SO ₂ (IQR = 14.0 μg/m ³)	NO ₂ (IQR = 12.8 μg/m ³)	PM ₁₀ (IQR = 57.0 μg/m ³)
		OR (95% CI)	OR (95% CI)	OR (95% CI)
Depression scores	Lag 0	1.22 (1.05, 1.42)*	1.05 (0.89, 1.24)	1.08 (0.94, 1.23)
	Lag 0–2	1.11 (0.92, 1.33)	1.02 (0.84, 1.23)	1.04 (0.92, 1.18)
	Lag 0–5	1.12 (0.92, 1.37)	1.21 (0.96, 1.52)	1.13 (0.94, 1.37)
	Lag 0–7	1.10 (0.88, 1.38)	1.19 (0.92, 1.54)	1.09 (0.86, 1.38)
	Lag 0–14	1.15 (0.89, 1.49)	1.20 (0.89, 1.63)	1.05 (0.76, 1.45)

Table 7. Estimated effects of air pollutants (per IQR increase) on high maternal depression scores (P75-P100)^{a,b}. * $P < 0.05$. ^aLogistic regression models were used. ^bAdjusted for maternal age, education, occupation, complications of pregnancy, abortion history, family monthly income, types of family structure, average temperature, relative humidity, and wind speed.

became weaker after adjusting for SO₂, indicating that among these three pollutants, SO₂ may have a relatively stronger effect on maternal emotional stress than NO₂ and PM₁₀. Therefore, SO₂ may be an important component in the air pollution mixture in Shanghai, and has an independently adverse effect on human psychological health. However, until now, there is no consensus on the comparison of the relative effects of these three pollutants. Consistent with our results, some studies found that the impact of SO₂ was greater than that of NO₂ and PM₁₀⁴⁷, whereas other studies found that the effect of PM₁₀ was more significant than that of SO₂⁴⁹. This inconsistency may be a result of the difference in local meteorological conditions and the demographic characteristics of different populations⁴⁷.

This study examined the association of air pollution with maternal symptom of depression. Our results indicated that SO₂ may have a stronger effect on maternal symptom of depression during pregnancy than NO₂ or PM₁₀. Our study may provide an evidence for policy making regarding the control or reduction of total SO₂ emissions.

There are several limitations in this study. First, this study was conducted from February to October, 2010. In Shanghai, the cool season is usually from November to the next April; therefore, we missed the time from November to next January. Thus, the statistical power on the comparison of the seasonal difference in the association of air pollution with maternal stress may be limited (a total of 476 women were enrolled in cool season (from February to April), and 1455 women were enrolled in warm season (from May to October) in this study. Second, because SO₂, NO₂ and PM₁₀ were the only three criteria pollutants routinely monitored in Shanghai during our study period, we failed to investigate the association of other pollutants including ozone and carbon monoxide with maternal stress during pregnancy. Third, the noise data were not available in our study, and we were unable to control for the confounding effects of noise in our multivariable analyses. Fourth, the air pollution data were obtained from the monitoring stations of each district the women lived during pregnancy but were not based on each woman's home. The distance between each woman's home and the monitoring station, and the length of time each participant spent outdoors were not measured. Fifth, although we have tried our best to minimize the chance of selection bias in the sampling of study subjects, because we didn't include all the pregnant women in Shanghai in this study, and considering the small number of districts in Shanghai using our stratified-cluster sampling approach, the possibility of selection bias cannot be completely excluded. Sixth, although extensive information

on social-economic factors that may be potentially associated with maternal stress during pregnancy has been taken into consideration in our analyses, some factors that may explain the associations may not be included in this study.

There is no doubt that maternal stress is affected by more complex circumstances than simply air pollution. However, ambient air pollutants might be a triggering or exacerbating factor. Our findings may help elucidate the effects of air pollution on human psychological health. Because maternal stress during pregnancy is important in the development of offspring, further in-depth studies are required to bring these issues to the public's attention. Further control of air pollution, particularly SO₂, may result in health benefits.

Conclusions

In conclusion, our study suggested that increasing concentrations of SO₂, NO₂, and PM₁₀ were associated with increased risks of maternal emotional stress during pregnancy, and the associations between air pollution and maternal stress may be dose-dependent and may be modified by season and complications of pregnancy. Exposure to SO₂ and PM₁₀ may induce acute development of maternal emotional stress, whereas exposure to NO₂ may cause a lagged stress. Increasing concentrations of SO₂ may also be a risk factor for maternal depressive symptoms.

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Author Contributions

J.X. designed the study and supervised the data collection. Y.L. conducted the statistical analyses and drafted the manuscript. L.Z., J.X. and H.K. were responsible for the collection of the data. J.X., Z.L., H.K., J.Z., C.Y. and J.Z. assisted with the data interpretation and manuscript revision. All authors read and approved the final manuscript.

Additional Information

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