

The Association Between Air Pollution and Low Birth Weight and Preterm Labor in Ahvaz, Iran

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Reihaneh Sarizadeh¹
Maryam Dastoorpoor²
Gholamreza Goudarzi³
Masoumeh Simbar¹

¹Midwifery and Reproductive Health Research Center, School of Nursing and Midwifery, Shahid Beheshti University of Medical Science, Tehran, Iran;

²Department of Biostatistics and Epidemiology, Menopause Andropause Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran;

³Department of Environmental Health Engineering, Air Pollution and Respiratory Diseases Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Purpose: Pregnant women and fetuses are sensitive to air pollution due to physiological changes in pregnancy. The aim of this study was to determine the relationship between exposure to air pollution, low birth weight and preterm labor in Ahvaz.

Methods: This research was a time-series study. The research sample consisted of all data about low birth weight and preterm labor pregnant women from Imam Khomeini Hospital and Razi Hospital in Ahvaz city. Air pollutant data including O₃, NO, NO₂, SO₂, CO, PM₁₀ and PM_{2.5} and climate data were collected from the Environmental Protection Agency and the Khuzestan Province during a 10-year period from 2008 to 2018. The generalized additive models (GAMs) with different air pollutant lags up to 6 days were used.

Results: The results of multiple GAM model have shown that there is a direct and significant relationship between exposure to PM₁₀ at 0–6-day lag, SO₂ at 2- and 3-day lag and low birth weight. In addition, there was a direct and significant correlation between exposure to NO₂, NO, CO and PM_{2.5} at 0–6-day lag and preterm labor.

Conclusion: The results indicate the effect of air pollutants on low birth weight and preterm labor. Therefore, pregnant women should be informed about the negative consequences of air pollution and avoid exposure to polluted air during pregnancy.

Keywords: air pollution, low birth weight, preterm labor, Ahvaz, time series

Introduction

In many countries, the persistence or increase in air pollution is an environmental and public health problem.¹ Air pollution in 2012 caused 3.7 million deaths in the world, 88% of which occurs in low- and middle-income countries.² Air pollutants include ozone (O₃), sulfur dioxide (SO₂), nitrogen dioxide (NO₂), carbon monoxide (CO), hydrocarbons, particulate matters (PM), benzene and soot.³ Particulate matters are solid particles that are often larger than colloids and can suspend in the air or in combination with another gas temporarily.⁴ These particles can have a significant effect on human health.⁵ Ozone is a very strong oxidizing agent that is an index for photochemical oxidants and is produced by the effect of sunlight on nitrogen dioxide and the generation of radical atomic oxygen.^{6,7} Nitrogen dioxide is a potent corrosive and oxidant gas that physiologically stimulates the lower respiratory tract and is very toxic.^{8,9} At concentrations above the medium and high levels, carbon monoxide is a silent killer, which results in the formation of carboxyhemoglobin in the blood that prevents oxygen intake.^{4,10}

Sulfur dioxide is a colorless and non-explosive gas that more than 80% of it is produced by human beings during the combustion of fossil fuels.¹¹ Pregnant women

Correspondence: Masoumeh Simbar
Midwifery and Reproductive Health Research Center, Department of Midwifery and Reproductive Health, School of Nursing and Midwifery, Shahid Beheshti University of Medical Science, Tehran, Iran
Email msimbar@gmail.com

and their fetuses are sensitive to air pollution due to physiological changes that occur during pregnancy.¹² Exposure to particulate matters less than 2.5 microns is associated with the risk of chronic disorders in pregnancy, including low birth weight, preterm labor and adverse health outcomes of the child (cognitive impairment and asthma).^{13–17} Many pieces of evidence suggest that pregnant women's exposure to air pollution is associated with a number of pregnancy outcomes, including low birth weight, intrauterine growth restriction, preterm labor, fetal death and congenital anomalies.^{18–21} Among the complications due to SO₂ and NO₂ exposure are increased risk of low birth weight infant during 3rd to 5th months of gestation,²² reduction in the age of pregnancy and complications arising from it such as preterm labor,^{23,24} fetal cardiovascular and pulmonary abnormalities^{25,26} and increased risk of small for gestational age (SGA) newborn.²⁷

Preterm labor is one of the side effects of some pollutants.²³ About 130 million newborns are born annually 15 million of which are due to preterm labor. Prematurity is a major cause of mortality and illnesses that have long-term adverse effects on the health of babies.²⁸ Preterm labor is defined as birth before 37 weeks of pregnancy and the newborn is a preterm infant.²⁹ According to a meta-analysis conducted in 2015, the prevalence of preterm labor in Iran is reported as 9.2%.³⁰ Evidence suggests that maternal exposure to air pollution during pregnancy is associated with an increased risk of preterm labor, especially in the first trimester of pregnancy.^{31–34}

Another side effect of the pollutants is an increased risk of low birth weight.²⁷ There are several markers for determining the health status of a community, one of the most important of which is birth weight, which is directly related to infant mortality rates.³⁵ Low birth weight refers to the weight below 2500 grams in newborns.³⁶ It has been shown in several studies in some Iranian cities, including Guilan and Khuzestan provinces, that the prevalence of low birth weight in Iran was 11.6%.³⁷ Another complication of exposure to air pollution is the increased risk of birth of a baby weighing less than 2500 grams.²⁷ As several studies have shown, the increase in air pollutants is associated with decreased average birth weight,^{38,39} low birth weight^{40–45} and small for gestational age (SGA) newborns.^{46,47}

In 2011, according to the annual average of PM₁₀ (372 micrograms per cubic meter), the World Health Organization declared Ahvaz as the most polluted city in Iran and the

world.⁴⁸ Several studies have been carried out on the effects of air pollutants on health outcomes in Iran. However, it seems that there has not been a time-series study in Ahvaz to examine the acute effects of pollution on hospital admissions due to low birth weight. Therefore, this time-series study is intended to investigate the acute effects of exposure to the daily average of air pollutants, PM_{2.5}, CO, NO₂, PM₁₀, SO₂ and O₃, on the daily number of hospitalized admissions due to low birth weight and preterm labor through the course of 10 years with a 6-day lag of exposure.

Materials and Methods

Study Design

This time-series study was conducted on pregnant women referred to referral Obstetrics and Gynecology Hospitals in Ahvaz city with low birth weight and preterm labor.

The Participants

The total number of pregnant women referred to the Obstetrics and Gynecology department during the 10-year period was 150,766. The total low birth weights and preterm labor during these 10 years were 863 and 5776.

Data Collection

The data included the number of hospital admissions due to low birth weight, preterm labor, air pollutants including PM_{2.5}, PM₁₀, NO₂, NO, O₃ and SO₂ and meteorological variables including air-temperature and relative humidity recorded since March 2008 to March 2018.

After obtaining permission from the Ethics Committee of Shahid Beheshti University of Medical Sciences, by referring to the referral Obstetrics and Gynecology Hospitals in Ahvaz city, daily information about low birth weight and preterm labor were collected from medical records of pregnant women aged 18 to 35 years during a 10-year period.

Hourly values for air pollutants and meteorological parameters were collected from the Environmental Protection Agency and the Meteorological Office of Khuzestan province, and the daily average amounts were added.

Statistical Analysis

In this study, descriptive statistics including mean, standard deviation, first, second, third, and minimum and maximum quartets were used. In the analytical section, a multi-pollutant generalized additive model (GAM) was used to estimate the risk ratio (RR) effects of air pollutants on response variables. This is a developed form of GAM

that has high flexibility. As it can be used for modeling nonlinear trends, this model is used in many studies.^{49,50} Six days are the number of lags for pollutants in the multi-model, and their relationship with the low birth weight and preterm labor was determined.

The optimal number of spline bases was used for each auxiliary variable in the model. The possibility of the presence of some confounding variables including temperature, relative humidity, time trends and days per week was also provided in the model. The effective degree of freedom (EDF) for smoothers was estimated using generalized cross-validation (GCV). All calculations were done with the mgcv package in the R software, which allows estimating the penalized generalized aggregate models based on regression fitted splines by calculating the smoothness.^{51,52}

Ethics

All patients signed a consent form while admitted and allowed their information to be used for research purposes. Meanwhile, researchers received de-identifiable data. Ethics License of the present study was acquired from the Ethics Committee of Shahid Beheshti University of Medical Sciences for Human Research based on the Declaration of Helsinki (Code of ethics: IR.SBMU.PHNM.1396. 906).

Results

Descriptive Statistic

The total number of pregnant women referred to the Obstetrics and Gynecology department during the 10-year period was 150,766. The total low birth weights and

preterm labor during these 10 years were 863 and 5776. During the study period, the average daily PM₁₀ and PM_{2.5} concentrations were 216.9 and 85.7 µg/m³, respectively, which were above the WHO-defined limit. The lowest and highest daily temperatures in Ahvaz were 1.4 and 47.8°C, respectively, with a mean daily average of 27°C. Other details of the descriptive indexes of consequences, pollutants and meteorological parameters in the city of Ahvaz have been presented in Table 1 in the years of the study.

Relationship Between Exposure to Air Pollutants and Low Birth Weight

The results of fitting the multiple GAM model on the relationship between air pollutants and low birth weight are shown in Table 2 and Figure 1. This table indicates the information of different fitted models in terms of low birth weight with air pollutants corresponding to 0–6-day lags.

The results of the multiple GAM model show that there is a direct and significant relationship between exposure to PM₁₀ at 0–6-day lags and SO₂ at 2- and 3-day lags and low birth weight.

The results showed that there was a significant and direct correlation between exposure to PM₁₀ and low birth weight at zero (RR=1.003 (95% CI:1.001–1.004)), one (RR=1.002 (95% CI:1.000–1.004)), two (RR=1.003 (95% CI:1.002–1.005)), three (RR=1.004 (95% CI:1.002–1.005)), four (RR=1.002 (95% CI:1.001–1.004)), five (RR=1.002 (95% CI:1.001–1.004)) and six (RR=1.002 (95% CI:1.001–1.004)) day lags after exposure. In other words, the risk of admission due to low birth weight per 10 µg/m³ increase in PM₁₀ at 0-, 1-, 2-, 3-, 4-, 5- and 6-day lags increases by 0.3,

Table 1 Descriptive Indexes of Hospital Admissions Due to Low Birth Weight and Preterm Labor, Air Pollutant Concentrations and Meteorological Parameters in Ahvaz During 2008–2018

Variable (Mean per Day)	N	Mean	SD	Min	Max	Q1	Median	Q3
Low Birth Weight	863	0.2	0.6	0.0	5.0	0.0	0.0	0.0
Premature Birth	5776	1.6	1.9	0.0	12.0	0.0	1.0	2.0
O ₃ (µg/m ³)	–	70.5	188.6	0.04	6520.0	26.4	42.7	64.6
PM _{2.5} (µg/m ³)	–	85.7	150.4	0.57	3938	35.9	52.7	81.2
PM ₁₀ (µg/m ³)	–	216.9	278.3	1.8	4324.2	105.8	149.2	222.4
NO ₂ (µg/m ³)	–	46.4	43.1	1.5	443.8	17.8	35.6	60.7
NO (µg/m ³)	–	29.1	31.0	0.12	608.7	9.1	19.6	38.2
CO (µg/m ³)	–	1.5	2.1	0.1	70.4	0.6	1.13	2.0
SO ₂ (µg/m ³)	–	48.8	57.0	0.0	907.4	19.3	35.9	59.3
Temperature (° C)	–	27.0	9.4	1.4	47.8	18.4	27.7	36.0
Relative Humidity (%)	–	42.3	17.9	7.0	96.0	27.5	40.0	54.5

Abbreviations: O₃, ozone; SO₂, sulfur dioxide; NO, nitrogen monoxide; NO₂, nitrogen dioxide; CO, carbon monoxide; PM₁₀, particulate matter 10 micrometers or less in diameter; PM_{2.5}, particulate matter 2.5 micrometers or less in diameter.

Table 2 The Results of the Modified GAM of the Relationship Between Air Pollutants and Low Birth Weight of Ahvaz (Increasing the Cases of Daily Low Birth Weight per Increasing 10 Units in a Daily Average of the Pollutant)

Lag	Pollutant	edf	Risk Ratio	95% CI	P-value*
Lag 0	O ₃	8.578	0.988	0.978–0.997	0.014 [†]
	NO ₂	6.073	0.872	0.848–0.896	<0.001 [†]
	NO	5.790	0.869	0.839–0.900	<0.001 [†]
	SO ₂	8.399	1.010	0.999–1.020	0.067
	CO	6.152	0.616	0.369–1.028	0.064
	PM ₁₀	4.322	1.003	1.001–1.004	0.002 [†]
	PM _{2.5}	6.559	1.000	0.996–1.005	0.906
Lag 1	O ₃	8.286	0.983	0.973–0.994	0.002 [†]
	NO ₂	5.960	0.874	0.850–0.898	<0.001 [†]
	NO	5.880	0.883	0.853–0.914	<0.001 [†]
	SO ₂	6.076	1.008	0.997–1.018	0.143
	CO	4.605	0.597	0.358–0.996	0.048 [†]
	PM ₁₀	3.776	1.002	1.000–1.004	0.029 [†]
	PM _{2.5}	4.282	0.999	0.993–1.004	0.640
Lag 2	O ₃	7.344	0.983	0.972–0.993	0.002 [†]
	NO ₂	5.690	0.879	0.856–0.902	<0.001 [†]
	NO	7.683	0.897	0.868–0.927	<0.001 [†]
	SO ₂	6.952	1.014	1.004–1.023	0.005 [†]
	CO	5.568	0.884	0.602–1.296	0.526
	PM ₁₀	3.818	1.003	1.002–1.005	<0.001 [†]
	PM _{2.5}	4.257	1.001	0.997–1.006	0.589
Lag 3	O ₃	8.263	0.990	0.981–0.999	0.027 [†]
	NO ₂	5.304	0.865	0.841–0.890	<0.001 [†]
	NO	8.194	0.857	0.827–0.889	<0.001 [†]
	SO ₂	8.341	1.012	1.002–1.022	0.016 [†]
	CO	5.550	0.978	0.711–1.346	0.893
	PM ₁₀	3.657	1.004	1.002–1.005	<0.001 [†]
	PM _{2.5}	4.021	1.002	0.997–1.006	0.480
Lag 4	O ₃	8.192	0.992	0.984–1.000	0.057
	NO ₂	2.020	0.887	0.864–0.910	<0.001 [†]
	NO	6.926	0.894	0.865–0.925	<0.001 [†]
	SO ₂	6.887	1.006	0.996–1.016	0.212
	CO	4.652	0.757	0.480–1.192	0.229
	PM ₁₀	4.256	1.002	1.001–1.004	0.006 [†]
	PM _{2.5}	5.052	0.998	0.993–1.004	0.588
Lag 5	O ₃	8.386	0.974	0.962–0.987	<0.001 [†]
	NO ₂	7.819	0.893	0.870–0.916	<0.001 [†]
	NO	7.481	0.906	0.878–0.936	<0.001 [†]
	SO ₂	4.571	1.005	0.994–1.016	0.376
	CO	7.240	0.828	0.551–1.242	0.360
	PM ₁₀	4.112	1.003	1.001–1.005	0.001 [†]
	PM _{2.5}	4.692	1.000	0.995–1.005	0.917
Lag 6	O ₃	8.638	0.975	0.963–0.988	<0.001 [†]
	NO ₂	6.078	0.877	0.855–0.900	<0.001 [†]
	NO	8.757	0.902	0.873–0.932	<0.001 [†]
	SO ₂	4.461	1.009	0.999–1.019	0.088

(Continued)

Table 2 (Continued).

Lag	Pollutant	edf	Risk Ratio	95% CI	P-value*
	CO	6.236	0.926	0.639–1.343	0.687
	PM ₁₀	4.031	1.004	1.003–1.006	<0.001 [†]
	PM _{2.5}	4.526	1.002	0.999–1.006	0.222

Notes: [†]Statistically significant. *Adjusted for trend, seasonality, temperature, relative humidity and weekdays.

0.2, 0.3, 0.4, 0.2, 0.3 and 0.4%, respectively (Table 2 and Figure 1).

Besides, there was a significant and direct correlation between SO₂ and low birth weight at two (RR=1.014 (95% CI:1.004–1.023)) and three (RR=1.012 (95% CI:1.002–1.022)) day lags after exposure. Thus, the risk of admission due to low birth weight per 10 µg/m³ increase in SO₂ at 2- and 3-day lags increases by 1.4 and 1.2%, respectively (Table 2 and Figure 1).

There was a significant and indirect relationship between NO and NO₂ pollutants at 0–6-day lags and O₃ at 2-, 5- and 6-day lags and low birth weight (Table 2 and Figure 1). There was no significant relationship between exposure to PM_{2.5} and low birth weight at any time in 0–6-day lags (Table 2 and Figure 1).

Relationship Between Exposure to Air Pollutants and Preterm Labor

The results of fitting the multiple GAM model on the relationship between air pollutants and preterm labor are shown in Table 3 and Figure 2. This table indicates the information of different fitted models preterm labor with air pollutants corresponding to 0–6-day lags.

There was a significant and direct correlation between exposure to NO₂ and preterm birth at zero (RR=1.031 (95% CI:1.025–1.037)), one (RR=1.031 (95% CI:1.025–1.037)), two (RR =1.037 (95% CI:1.031–1.043)), three (RR=1.037 (95% CI:1.031–1.043)), four (RR=1.039 (95% CI:1.033–1.045)), five (RR=1.039 (95% CI:1.033–1.045)) and six (RR=1.038 (95% CI:1.032–1.038)) day lags after exposure. Thus, the risk of admission due to preterm birth per 10 µg/m³ increase in NO₂ at 0-, 1-, 2-, 3-, 4-, 5- and 6-day lags increases by 3.1, 3.1, 3.7, 3.7, 3.9, 3.9 and 3.8%, respectively (Table 3 and Figure 2).

The results also showed that there was a significant and direct correlation between exposure to NO and preterm birth at zero (RR=1.055 (95% CI:1.049–1.061)), one (RR=1.055 (95% CI:1.049–1.061)), two (RR=1.056 (95% CI:1.051–

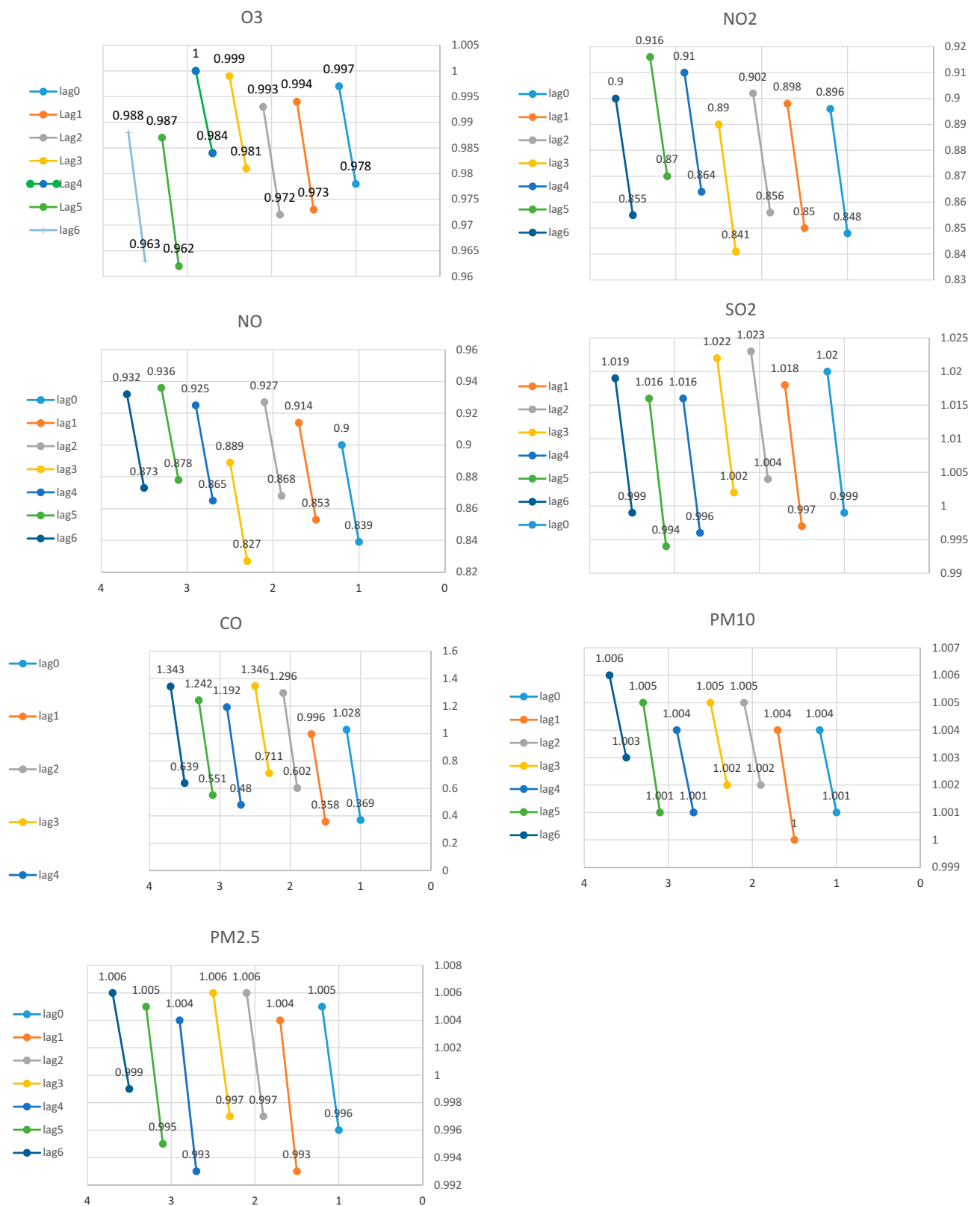


Figure 1 Risk ratio (95% confidence interval) of low birth weight associated with a 10-unit increase in air pollutant levels for different lags of lag 0–6 days.

Table 3 The Results of the Modified GAM of the Relationship Between Air Pollutants and Preterm Labor of Ahvaz (Increasing the Cases of Daily Low Birth Weight per Increasing 10 Units in a Daily Average of the Pollutant)

Lag	Pollutant	edf	Risk Ratio	95% CI	P-value*
Lag 0	O ₃	8.887	0.996	0.994–0.999	0.004 [†]
	NO ₂	8.643	1.031	1.025–1.037	<0.001 [†]
	NO	6.196	1.055	1.049–1.061	<0.001 [†]
	SO ₂	4.827	0.966	0.958–0.973	<0.001 [†]
	CO	8.679	1.457	1.369–1.551	<0.001 [†]
	PM ₁₀	7.605	1.000	0.999–1.001	0.971
	PM _{2.5}	7.109	1.004	1.003–1.005	<0.001 [†]
Lag 1	O ₃	8.790	0.996	0.993–0.999	0.004 [†]
	NO ₂	6.338	1.031	1.025–1.037	<0.001 [†]
	NO	8.703	1.055	1.049–1.061	<0.001 [†]
	SO ₂	4.138	0.962	0.954–0.969	<0.001 [†]
	CO	8.051	1.448	1.358–1.544	<0.001 [†]
	PM ₁₀	8.716	1.000	0.999–1.001	0.381
	PM _{2.5}	8.477	1.004	1.003–1.005	<0.001 [†]
Lag 2	O ₃	8.880	0.994	0.991–0.997	<0.001 [†]
	NO ₂	8.592	1.037	1.031–1.043	<0.001 [†]
	No	7.224	1.056	1.051–1.062	<0.001 [†]
	SO ₂	8.259	0.962	0.955–0.970	<0.001 [†]
	CO	8.799	1.451	1.365–1.542	<0.001 [†]
	PM ₁₀	7.124	0.999	0.997–1.000	0.006 [†]
	PM _{2.5}	8.375	1.004	1.003–1.005	<0.001 [†]
Lag 3	O ₃	8.873	0.997	0.995–1.000	0.022 [†]
	NO ₂	7.969	1.037	1.031–1.043	<0.001 [†]
	NO	6.001	1.057	1.051–1.062	<0.001 [†]
	SO ₂	5.211	0.959	0.952–0.967	<0.001 [†]
	CO	8.491	1.471	1.387–1.560	<0.001 [†]
	PM ₁₀	7.394	0.999	0.998–1.000	0.022 [†]
	PM _{2.5}	8.739	1.004	1.003–1.005	<0.001 [†]
Lag4	O ₃	8.803	0.997	0.995–1.000	0.021 [†]
	NO ₂	7.333	1.039	1.033–1.045	<0.001 [†]
	NO	8.738	1.057	1.051–1.062	<0.001 [†]
	SO ₂	4.224	0.963	0.956–0.971	<0.001 [†]
	CO	8.357	1.472	1.388–1.562	<0.001 [†]
	PM ₁₀	8.059	0.998	0.997–0.999	<0.001 [†]
	PM _{2.5}	8.862	1.003	1.002–1.005	<0.001 [†]
Lag 5	O ₃	8.766	0.995	0.992–0.998	<0.001 [†]
	NO ₂	7.987	1.039	1.033–1.045	<0.001 [†]
	NO	8.562	1.057	1.052–1.063	<0.001 [†]
	SO ₂	4.968	0.959	0.952–0.967	<0.001 [†]
	CO	8.366	1.455	1.369–1.546	<0.001 [†]
	PM ₁₀	6.915	0.997	0.996–0.998	<0.001 [†]
	PM _{2.5}	6.536	1.003	1.001–1.004	<0.001 [†]
Lag 6	O ₃	8.856	0.995	0.992–0.998	<0.001 [†]
	NO ₂	6.366	1.038	1.032–1.044	<0.001 [†]
	NO	7.450	1.057	1.051–1.062	<0.001 [†]
	SO ₂	3.975	0.959	0.951–0.966	<0.001 [†]

(Continued)

Table 3 (Continued).

Lag	Pollutant	edf	Risk Ratio	95% CI	P-value*
	CO	8.304	1.492	1.404–1.585	<0.001 [†]
	PM ₁₀	8.193	0.998	0.997–0.999	<0.001 [†]
	PM _{2.5}	8.744	1.004	1.002–1.005	<0.001 [†]

Notes: [†]Statistically significant. *Adjusted for trend, seasonality, temperature, relative humidity and weekdays.

1.062)), three (RR=1.057 (95% CI:1.051–1.062)), four (RR=1.039 (95% CI:1.033–1.045)), five (RR=1.057 (95% CI:1.051–1.062)) and six (RR=1.057 (95% CI:1.052–1.063)) day lags after exposure. Thus, the risk of admission due to preterm birth per 10 µg/m³ increase in NO at 0-, 1-, 2-, 3-, 4-, 5- and 6-day lags increases by 5.5, 5.5, 5.6, 5.7, 5.7, 5.7 and 5.7%, respectively (Table 3 and Figure 2).

The results also showed that there was a significant and direct correlation between exposure to CO and preterm birth at zero (RR=1.457 (95% CI:1.369–1.551)), one (RR=1.448 (95% CI:1.358–1.544)), two (RR=1.451 (95% CI:1.365–1.542)), three (RR=1.471 (95% CI:1.387–1.560)), four (RR=1.472 (95% CI:1.388–1.562)), five (RR=1.455 (95% CI:1.369–1.546)) and six (RR=1.492 (95% CI:1.404–1.585)) day lags after exposure (Table 3 and Figure 2).

Finally, there was a significant and direct correlation between exposure to PM_{2.5} and preterm birth at zero (RR=1.004 (95% CI:1.003–1.005)), one (RR=1.004 (95% CI:1.003–1.005)), two (RR=1.004 (95% CI:1.003–1.005)), three (RR=1.004 (95% CI:1.003–1.005)), four (RR=1.003 (95% CI:1.002–1.005)), five (RR=1.003 (95% CI:1.001–1.004)) and six (RR=1.004 (95% CI:1.002–1.005)) day lags after exposure. Thus, the risk of admission due to preterm delivery per 10 µg/m³ increase in PM_{2.5} at 0-, 1-, 2-, 3- and 6-day lags increases by 0.4% and that of the 4- and 5-day lags increases by 3% (Table 3 and Figure 2).

A significant and inverse relationship was found between exposure to O₃, SO₂ and PM₁₀ and preterm birth (Table 3 and Figure 2).

Discussion

Air pollution has been investigated in many studies as a factor damaging fetal development.^{20,53,54} The purpose of this study was to investigate the short-term effects of air pollution on hospital admissions due to low birth weight and preterm labor in Ahvaz. Rapid cell growth and limitation of limb metabolism, especially embryonic growth systems, are susceptible to exposure to air pollutants.²⁰

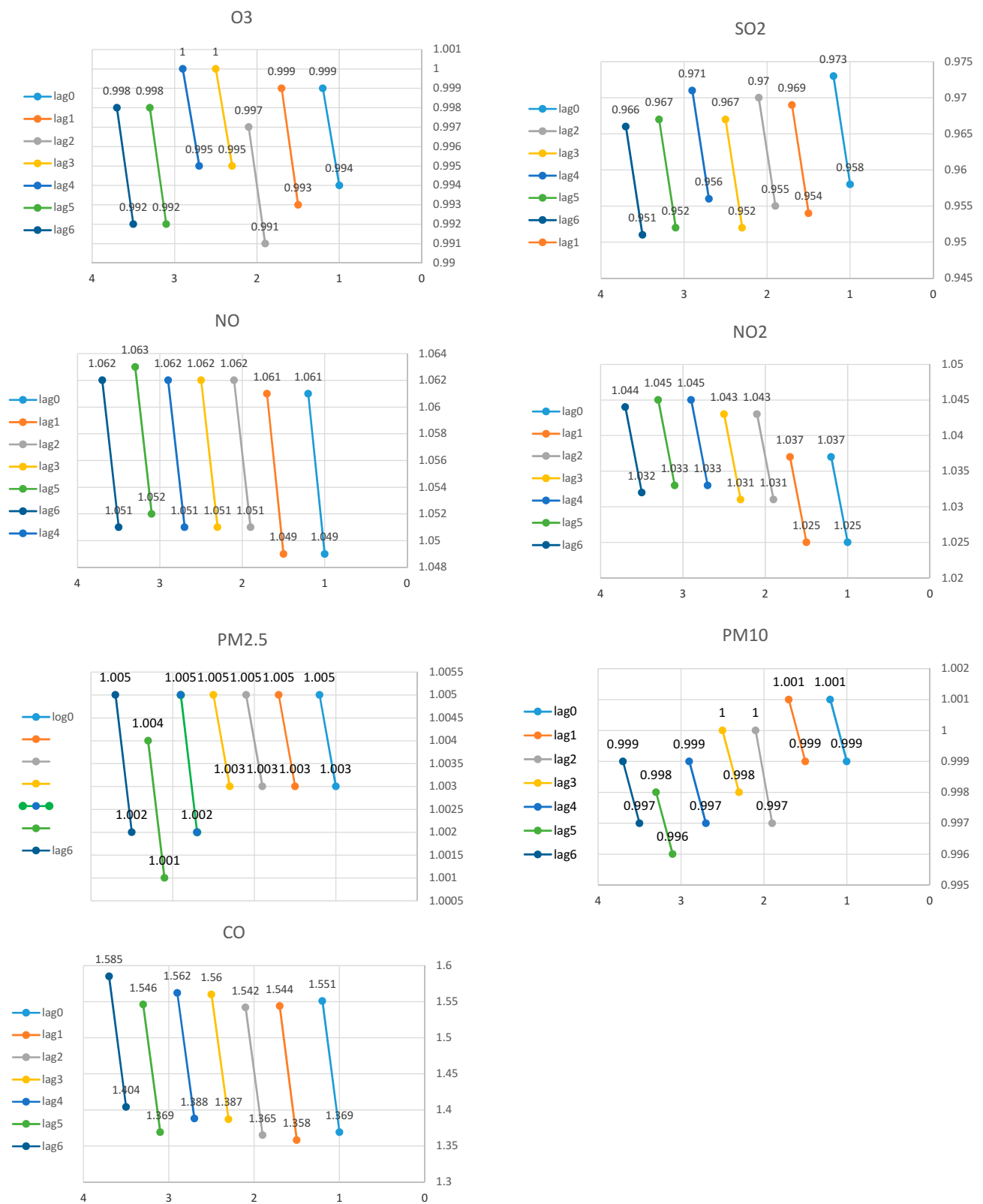


Figure 2 Risk ratio (95% confidence interval) of preterm labor associated with a 10-unit increase in air pollutant levels for different lags of lag 0–6 days.

The production of free radicals caused by pollution could create an inflammatory response that increases blood concentration and decreased placental perfusion caused by changes in blood viscosity may be associated with undesirable outcomes of pregnancy including low birth weight and preterm labor.⁵⁵

Low Birth Weight

The results showed that there is a direct and significant relationship between exposure to PM₁₀ and low birth weight. In this regard, numerous studies have confirmed the relationship between exposure to PM₁₀ and low birth weight.^{56,57} The results of a study in Mongolia showed that the exposure to PM₁₀ was associated with a 12.2 g weight reduction in the newborn.⁵⁸ However, in Salam et al, no correlation was observed between the increase in PM₁₀ and low birth weight;⁵⁹ however, exposure to PM₁₀ may cause its passage through the blood, increased blood viscosity and activated systemic oxidative stress followed by impaired fetal growth.⁶⁰

Results also showed that there is a significant and direct relationship between exposure to SO₂ and low birth weight. In other studies, an increased risk ratio of low birth weight has been confirmed by increasing SO₂. In a longitudinal study in Sao Paulo and a systematic study by Jacob et al, exposure to SO₂ was associated with an increased risk ratio of low birth weight.^{61,62} In a case-control study in China, the increased maternal exposure to SO₂ in the first month of pregnancy was associated with an increased risk ratio of low birth weight.⁶³ However, a study in China with a time-series approach showed that pregnant women's weekly exposure to SO₂ has no significant relationship with low birth weight.⁶⁴ However, according to the results of the present and several other studies that confirmed the finding, it seems that exposure to SO₂ pollutant can change blood viscosity due to an increase in coagulation factors.⁶⁵ Following the change in viscosity, the blood supply to the placenta, placental function⁶⁶ and placental oxygenation³⁹ are reduced, which can lead to low birth weight.

The results of the present study showed that the exposure of pregnant women to NO₂ reduces the risk ratio of low birth weight. In a Chinese time-series study, the exposure of pregnant women to NO₂ was not significantly related to low birth weight.⁶⁴ Salam et al did not observe any correlation between NO₂ and low birth weight as well.⁵⁹ Although the results of the studies show that exposure to NO₂ pollutants is associated with an increased risk

ratio of low birth weight,^{40,67-69} given the controversial findings on the effect of NO₂, further research is needed in this regard.

The results of this study showed that the exposure of pregnant women to O₃ reduces the risk of low birth weight. However, in other studies, it has been shown that exposure to O₃ has been associated with a reduction in birth weight.^{43,58,59}

Some studies have examined the effects of PM_{2.5} on preterm labor and low birth weight in sensitive exposure window.⁷⁰⁻⁷² Moreover, the results of this study showed that there is no significant relationship between exposure to PM_{2.5} and low birth weight. Recent studies have shown that exposure to PM_{2.5} is associated with a reduction in birth weight.^{24,41,73} However, in another paper for each 10µg/m³ increase in PM₁₀ and PM_{2.5}, low birth weight was reduced by 0.12 and 0.44% at 6- and 3-day lags, respectively.⁴⁵ In this study, only exposure to PM₁₀ showed a meaningful relationship with low birth weight. The inconsistency in the findings emphasizes the need for further research on low birth weight mechanism.

Regarding the observed reverse effects, it seems that the harvesting effect is involved in this issue. This effect means that if the increase in air pollutants in the first days of exposure leads to low birth weight, after prolonged exposure to air pollutants, decreased daily low birth weight is expected. In other words, the relationship between air pollution and low birth weight during an increase in the volatility of air pollutants is concentrated in only a few days.⁷⁴

Preterm Labor

The results of the analysis show that exposure to nitric oxides, including NO and NO₂, is associated with an increased risk of preterm labor. In this regard, the results of Dastoorpoor et al showed that for each 10µg/m³ increase in NO₂, the risk of preterm labor increases.⁴⁸ Additionally, the results of a systematic review and meta-analysis showed that increased NO₂ was associated with an increased risk of preterm labor.⁷⁵ Other studies confirm this finding.^{40,76,77} However, some studies do not confirm this finding.^{75,78-80}

In fact, exposure to NO₂ during pregnancy increases lipid peroxidation in the placenta and increases the incidence of postpartum fetal mortality and postpartum growth disorders.⁸¹ In addition, NO₂ is capable of oxidizing tissue components (eg, protein, fat) and suppressing antioxidant protective systems.⁸²

The results of the present study showed that there is a significant and direct correlation between exposure to CO and preterm labor. Accordingly, the results of the study in California showed that exposure to CO in the first and third trimesters of pregnancy was followed by 27 and 36% of preterm labor, respectively.⁸³ Other studies also found that increased CO is associated with an increased risk ratio of preterm labor.^{48,80,84} The adverse effects of exposure to CO on human health are due to the possible mechanism of CO for endothelial inflammation and immune system activation.¹

The results of the present study showed that there is a significant and direct relationship between exposure to PM_{2.5} and preterm labor. In this regard, Guan et al showed that for 10 µg/m³ increase in PM_{2.5} in the short- and long-term exposures, the risk of preterm labor increases by 0.52 and 3.13%, respectively.⁸⁵ The results of Liang et al showed that 1%, 6%, and 7% increases in risk of preterm labor and 20%, 18%, and 20% increases in risk of LBW, with each 10 µg/m³ increase in PM_{2.5} from trimester 1 to trimester 3, respectively.⁷¹ Other studies have shown that maternal exposure to high PM_{2.5} levels in the first trimester of pregnancy^{86,87} and length of pregnancy⁴⁰ are associated with preterm labor. However, there was no relationship between PM_{2.5} and preterm labor in the study of Sun et al.⁸⁸ However, the results of Rappazzo et al⁸⁹ and the systematic review and meta-analysis by Li et al⁹⁰ confirm this finding. It seems that exposure of pregnant mothers to PM_{2.5} during pregnancy has adverse effects on the growth, development and performance of the placenta.^{91,92}

The results of the present study showed that there is a significant and inverse relationship between exposure to PM₁₀ and preterm labor. In a time-series study in Rome, it was confirmed that exposure to PM₁₀ was not significantly associated with the outcome of preterm labor.⁹³ However, in other studies, exposure to PM₁₀ was associated with a direct and significant risk of preterm labor.^{48,63,69,94} The findings seem contradictory in this regard, and studies with more precise methods are required.

The results of this study showed a significant and inverse relationship between the exposure of pregnant women to O₃ and preterm labor. Findings of the relationship between exposure to O₃ and the increased risk of preterm labor are highly controversial. While many studies show a positive and significant relationship, some studies did not achieve such a result. In a study in 24

Canadian cities, exposure to O₃ at zero-, 1- and 6-day lag was associated with an increased risk of preterm labor.⁷⁵ Other studies also reported a significant relationship between O₃ exposure and preterm labor.^{95,96} However, there was no significant relationship between O₃ exposure and preterm labor in a time-series study by Darrow et al in Atlanta and Schifano et al in Rome, Italy.^{32,93} In the present study, there was a significant and inverse relationship between exposure to SO₂ and the risk of preterm labor. However, in other studies, daily exposure to SO₂ was associated with an increase in preterm labor.^{40,45,77} These contradictory findings show the need for more and more detailed studies.

Exposure to particulate air pollution during pregnancy can lead to acute inflammation in the lungs and other organs, including the placenta, which is associated with an increase in preterm labor.⁹⁷ Placenta has a unique role in transferring gas, nutrients and waste materials between mother and fetus.⁹⁸ High levels of exposure to particulate matter may increase the number of cells with immature chromatin.^{99,100} It can also be effective in reducing the birth weight of the baby with potentially harmful effects on DNA.¹⁰¹ The production of free radicals from air pollution can lead to inflammatory responses that can be associated with adverse pregnancy outcomes, including low birth weight and preterm labor, by increasing blood levels and decreasing placental perfusion due to changes in viscosity of the blood.⁵⁵ In addition, increased systemic inflammation may also contribute to the restriction of intrauterine growth due to interference in the transfer of nutrients to the fetus and the reduction of oxygen supply to the fetus.¹⁰¹

One of the strengths of this study is that for the first time, the relationship between pollutants and low birth weight was carried out during a ten-year period in Ahvaz. It is suggested to perform similar studies in other metropolitan areas where access to pollutant data and a larger population of people with pregnancy outcomes is provided to provide precise information on planning for prevention. Also, cohort studies aimed to investigate the relationship between pregnant women exposure in different trimesters of pregnancy and the consequences of preterm labor and low birth weight in other metropolises.

The incomplete recording of air pollutants by the sensors and the inherent limitation of the ecological study that make the results of this study hard to transmit to individual levels directly are among the limitations of this research.

Conclusion

The results of this study showed that there is a direct relationship between the exposure of pregnant women to PM₁₀, SO₂ and low birth weight as well as exposure to NO, PM_{2.5}, NO₂, CO and preterm labor. This evidence emphasizes the need to implement policies for reducing air pollution to decrease the risk of preterm labor and low birth weight.

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The authors report no conflicts of interest in this work.

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