Maternal exposure to air pollutants and birth weight in Tehran, Iran

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Abstract

Background Air pollution can cause various health outcomes, especially in susceptible groups including pregnant women. Low birth weight (LBW) is among the adverse birth outcomes and is one of the main causes of infant mortality. The aim of this study was to assess the association between air pollutants and LBW in Tehran, Iran.

Methods In this case-control study, 2144 babies born in three hospitals of Tehran (Iran) during 2011 to 2012 whose mothers were the residents of this city in last 5 years were considered. Of these, 468 infants with birth weight < 2500 g and 1676 with birth weight ≥ 2500 g were regarded as case and control groups, respectively. Gestational age was also considered for definition of cases (small for gestational age (SGA)) and controls (appropriate for gestational age). Land use regression models were used to assess exposure to particulate matter ≤ 10 μm in aerodynamic diameter (PM₁₀), sulfur dioxide (SO₂), nitrogen dioxide (NO₂) and volatile organic compounds (benzene, toluene, ethylbenzene, o-xylene, m-xylene, p-xylene (BTEX), and total BTEX) during pregnancy. Logistic regression model was applied to assess the association between air pollutants and LBW.

Results The concentrations of air pollutants were very high but similar in cases and controls. After adjustment for potential confounding variables, no statistically significant association was observed between air pollutants and LBW. The adjusted odds ratios (95% confidence interval) for PM₁₀, SO₂, and benzene were 0.999 (0.994–1.005), 0.998 (0.993–1.003), and 0.980 (0.901–1.067), respectively.

Conclusions No association was found between LBW and air pollutants. Further studies with more rigorous designs and access to more comprehensive information are suggested to assess the effect of other air pollutants, such as CO, O₃, PM_{2.5}, ultrafine particles, and oxidative potential of particles on birth outcomes.

Keywords Air pollution · Nitrogen dioxide · Sulfur dioxide · Particulate matter · Volatile organic compounds · Low birth weight

Background

Air pollution in large cities, especially in low- and middle-income countries (LMICs), seriously threatens the health of residents, particularly vulnerable people, including children, elderly, and pregnant women [1]. Epidemiological studies, mainly in high income countries (HICs), have evaluated the effects of air pollution on cardiovascular outcomes, respiratory system, and adverse birth outcomes [2–4]. However, little is reported from LMICs, especially from the Middle East and Iran.

Low birth weight (LBW) is defined as birth weight below 2500 g and is one of the adverse birth outcomes. Annually, more than 20 million infants, i.e. 15.5% of all births worldwide, are LBW. The prevalence of LBW is 7% in HICs and 16.5% in LMICs [5]. In Iran, the mortality rate of children under 5 and 1 year is 16.8 and 14.4 per thousand, of whom 10.3 per thousand die within the first month, and most of them

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are low weight infants [6]. LBW may affect the quality of life of the child in future, increase the rate of mortality and disability, slow down mental development, and cause neurological damage as well as behavioral and psychosocial disorders [7–9]. Many factors can affect birth weight. The most important factors include genetic, environmental factors, and fetal and maternal factors [7, 10]. Amongst the environmental factors, air pollution has received high attention in recent years as pregnant women and infants are considered as vulnerable groups and are sensitive to the effects of air pollution [1, 10].

Exposure to chemicals and air pollutants during pregnancy could lead to increased risk of adverse birth outcomes, including mortality during and after birth [4, 11–13]. Although the exact mechanism of the impact of air pollutants on fetal defects is unclear, studies indicate that air pollutants may have negative impacts on the maternal health through oxidative stress, inflammation, tissue hypoxia, and fetal growth retardation [14, 15]. For example, studies have shown that carbon monoxide binds to hemoglobin and reduces the oxygen capacity of the blood to organs, such as the central nervous system and fetus, leading to preterm birth, LBW, and intra-uterine fetal death [11, 13, 16, 17]. Sulfur dioxide (SO₂) is a colorless gas and upper respiratory irritant. Nitrogen dioxide (NO₂) is also a reddish-brown gas and a lower respiratory irritant; it is considered as one of the indicators of air pollution caused by vehicles and may result in respiratory diseases and adverse birth outcomes, such as preterm delivery [11, 12, 18]. Particulate matters may negatively impact the growth and function of the placenta, maternal and fetal health through oxidative stress, inflammation, and changes in systolic and diastolic blood pressure [3, 15]. Volatile organic compounds (VOCs) are another important air pollutant containing a wide range of hydrocarbons. Amongst the VOCs, there is a group of alkylbenzenes that are toxic and carcinogen, such as benzene, toluene, ethylbenzene and xylene (BTEX). The most important sources of BTEX are anthropogenic sources [19]. Exposure to BTEX compounds may cause neurological disorders, cancer, and pulmonary problems [20, 21]. However, few studies have investigated these compounds and their adverse birth outcomes [12, 22–24]. Benzene is one of the most dangerous chemicals classified as a carcinogenic substance that has negative effects on fetal blood cells [25].

The results of studies investigating the association of air pollutants and LBW are inconsistent; for example, studies in Spain and Germany found a significant association [23, 26] but no association has been reported in studies conducted in Brazil and Norway [27, 28]. As a result, further investigations are needed on this matter. On the other hand, assessment of exposure to air pollution is a major challenge in epidemiological air pollution studies. Most studies have used the data of monitoring stations to assess exposure to air pollutants, which do not usually represent variations in pollutants in the environment sufficiently. Moreover, some studies have used

interpolation methods, which may smooth the concentration levels of pollutants, might be unable to adequately describe hotspots, and may have some degree of exposure misclassification [29]. More recently, land use regression (LUR) models have been developed to address the abovementioned limitations where changes in small areas are identified very effectively. In fact, LUR is one of the most used exposure assessment method in epidemiological studies in recent years [22, 30, 31].

In recent decades, rapid industrialization and exhaust of millions of vehicles in Tehran, the capital of Iran, have caused air pollution, which is aggravated by natural topography and inversions during cold season. Studies have shown that almost all population in Tehran lives in areas where the World Health Organization (WHO) guidelines for air pollutants are not met [32–34]. The aim of this study was to assess the association between air pollutants and LBW in Tehran.

Methods

Study design and population

In this case-control study, three hospitals affiliated with Tehran University of Medical Sciences (Imam Khomeini, Arash, and Yas) were selected and the hospital records of live births in 2011–2012 were investigated. The records that contained the landline number and those mothers who were the resident of Tehran in last 5 years were included in the study. The total number of participants was 2144, of whom 468 infants with birth weight less than 2500 g were considered the case group and 1676 normal weight infants (birth weight $\geq$ 2500 g) comprised the control group. In some studies, birth weight is considered according to the gestational age. So, we also defined cases and controls using this definition and conducted extra analyses. Accordingly, 499 infants were selected as the case group (small for gestational age (SGA) defined as birth weight below the 10th percentile for gestational age) and 1645 infants as the control group (appropriate for gestational age). The collected information included maternal age (year), birth weight (gram), gestational age (week), birth order (the order of child born), and infant gender which were extracted from hospital clinical records. All mothers give their births at hospitals in Tehran, and cases and controls were selected from the same hospital, so there is not a risk of selection bias in case and control ascertainment. The study has been approved by institutional review board (92–01–46–22,330).

Assessment of air pollutants exposure

Resident telephone numbers were used to extract the geographical coordinates (X, Y) of the participants via the Tehran Central Post Office. Previously developed LUR

models were used to estimate the exposure of study participants to the following pollutants: PM₁₀, SO₂, NO₂, benzene, toluene, ethylbenzene, *o*-xylene, *p*-xylene, *m*-xylene, and total BTEX (TBTEX) [33–35]. Briefly, in LUR, air pollution concentrations are measured at a number of monitoring sites (typically at >20 sites) within the city. Then, various variables within certain buffers around each monitoring station, such as population density, land use, traffic surrogates (e.g., density of streets, highways, bridges, roads, etc. within buffers), and/or distances to variety of features are extracted. Finally, a multiple linear regression is run and using the final set of predictors, air pollution concentrations could be predicted anywhere in the study area. In our study, the previously developed LUR models for PM₁₀, SO₂, and NO₂ were based on 21 to 23 regulatory monitoring network sites [33, 34], and the BTEX compounds were modeled based on measurements at 179 sites [35]. Also, the PM₁₀ and BTEX compounds were estimated per µg/m³ and SO₂ and NO₂ were estimated per ppb. The leave-one-out cross validation R square (as measure of model validity) in the applied LUR model were 0.48, 0.50, 0.57 and 0.61 for PM₁₀, SO₂, NO₂ and BTEX, respectively [33–35].

Statistical analysis

The characteristics of the study participants in both case and control groups were described by mean ± standard deviation (SD) or frequencies in number and percentage. The annual concentration of the air pollutants was also described.

The crude and adjusted logistic regression models were applied to assess the association between air pollutants and LBW and also SGA. Considering LBW, the adjusted variables include maternal age, gestational age, infant gender, and birth order while obviously gestational age was omitted from this list considering SGA. Odds ratios (ORs) with 95% confidence intervals (CIs) per 1 unit increase in the concentration of air pollutants were presented. *P*-values less than 0.05 were considered to be statistically significant. SPSS for Windows, version 16.0 (Chicago, SPSS Inc.) was used for the analyses.

Results

In this study, 2144 infants were investigated. Table 1 shows the characteristics of the mothers and infants. The mean (± SD) for gestational age was 37.3 (± 1.3) week in the cases and 38.5 (± 1.1) week in the controls.

The estimated annual mean ± SD concentration of PM₁₀ and benzene was 102.90 ± 21.71 µg/m³ and 7.34 ± 1.50 µg/m³ in the case group and 101.84 ± 22.50 µg/m³ and 7.30 ± 1.59 µg/m³ in the control group, respectively. The estimated concentration of other pollutants is shown in Table 2. As

shown in this Table, the concentration of pollutants was very similar in cases and controls.

There was a significant association between LBW and SO₂ and NO₂ before adjustment for the confounders (*P* < 0.05) and the estimated ORs were close to 1, suggesting a weak relationship (Table 3). However, after adjustment for the confounders, LBW had no significant association with PM₁₀, SO₂, NO₂, and BTEX. The ORs (95% CI) for PM₁₀, SO₂, benzene, and toluene were 0.999 (0.994–1.005), 0.998 (0.993–1.003), 0.980 (0.901–1.067), and 0.993 (0.973–1.014), respectively. After adjustment for confounders, SGA had no significant association with PM₁₀, SO₂, NO₂, and BTEX.

Discussion

Several studies have investigated adverse birth outcomes of air pollutants including LBW, preterm birth, abortion, and so forth. The aim of this study was to investigate the association between pollutants (PM₁₀, SO₂, NO₂, BTEX compounds) and LBW. We found a weak significant association between SO₂ and NO₂ and LBW before adjusting for confounders but the association was no longer significant (for SO₂, NO₂, and BTEX compounds) after adjustment.

Estarlich et al. conducted a cohort study on the association of NO₂ and benzene with birth length and weight in Spain. The results showed that exposure to NO₂ during pregnancy had a significant association with birth length, but this association was only observed in the second trimester of pregnancy with birth weight. Moreover, there was no significant association between benzene and the infant's length and weight [23]. We also found no relationship between benzene and LBW. In a cohort study, Slama et al. examined 271 non-smoking women for the relationship between benzene and head circumference, and birth weight in France, and found an association between exposure to benzene and 68 g reduction in average birth weight (95% CI: −135 to −1 g) [24]. Another study in Spain used the LUR model to assess the relationship between exposure to NO₂ and BTEX and birth weight. They observed a relationship between BTEX compounds and LBW only in women in the second trimester who spent <2 h/day in non-residential outdoor environments [22]. We did not have this information in our dataset and could not stratify the analysis for spent hours outside.

Junger and Leon studied air pollution and term birth weight in Brazil but did not observe any significant association between air pollutants (PM₁₀ and NO₂) and LBW; the adjusted OR for NO₂ was 0.96 (95% CI: 0.90–1.03) [27], which was similar to our findings and also similar to the results of a study in Norway [28]. Morello-Frosch et al. conducted a similar study in California, and found no significant association between SO₂ and reduction in full term birth weight (adjusted

Table 1 Characteristics of the study participants based on two different definitions; birth weight or gestational age (Mean $\pm$ SD or frequency (%))

Variable		Birth weight		Gestational age	
		Cases (<i>n</i> = 468)	Controls (<i>n</i> = 1676)	Cases (<i>n</i> = 499)	Controls (<i>n</i> = 1645)
Maternal age (year)		28.8 $\pm$ 4.9	28.1 $\pm$ 5.1	28.6 $\pm$ 4.9	28.2 $\pm$ 5.1
Gestational age (week)		37.3 $\pm$ 1.3	38.5 $\pm$ 1.1	37.8 $\pm$ 1.3	38.4 $\pm$ 1.2
Infant gender	Girl	237 (50.6)	798 (47.6)	249 (49.9)	786 (47.8)
	Boy	231 (49.4)	878 (52.4)	250 (50.1)	859 (52.2)
Birth order	1	290 (62)	987 (58.9)	323 (64.7)	954 (58)
	2	120 (25.6)	469 (28)	121 (24.2)	468 (28.4)
	3	28 (6)	104 (6.2)	26 (5.2)	106 (6.4)
	4	3 (0.6)	19 (1.1)	4 (0.8)	18 (1.1)
	Missing	27 (5.8)	97 (5.8)	25 (5)	99 (6)

OR = 1.02, 95% CI: 0.99–1.06). However, they reported a relationship between NO₂ and LBW (adjusted OR = 1.03, 95% CI: 1.01–1.05) [36], which is consistent with the results of a study by Bell et al. [16]. In Amsterdam, a cohort study was conducted on 7600 births to investigate the relationship between air pollution and birth outcomes. Similar to our study, the LUR was used to assess maternal exposure to air pollutants and the results showed no significant association between NO₂ and outcomes such as term birth weight [30]. However, in another cohort study conducted in Valencia, Spain, Ballester et al. found a relationship between NO₂ and SGA in the second trimester of pregnancy. The adjusted OR was 1.37 (95% CI: 1.01–1.85) that was contrary to our finding [37]. Liu et al. examined the relationship between SO₂, NO₂, CO, and O₃ and birth outcomes in Vancouver, Canada, and found a significant relationship between maternal exposure to SO₂ and LBW (OR = 1.11, 95% CI: 1.01–1.22) but no relationship was found between LBW and other pollutants [38]. Hooven et al. conducted a cohort study to investigate the

relationship between living near heavy traffic and adverse birth outcomes in pregnant women. Their results showed that maternal exposure to air pollutants in the place of residence did not increase adverse birth outcomes [39].

In the present study, there was no significant association between PM₁₀ and LBW before and after adjustment for confounders. Some studies have reported an association between PM₁₀ and adverse birth outcomes [40, 41]. For example, Mannes et al. examined 138,056 live births in Sydney to assess the impact of NO₂, PM_{2.5}, PM₁₀, CO and O₃ on birth weight during three years. The data of monitoring stations were used to determine exposure to these pollutants. They observed significant associations between CO and reduced birth weight, and PM₁₀ had a weak relationship with reduced birth weight in the second trimester (OR = 1.01, 95% CI: 1.00–1.04) [40]. However, Nascimento and Moreira found no relationship between PM₁₀ and LBW in Brazil [42]. In another study by Dugandzic et al. in Canada, no statistically significant association was found between PM₁₀ and O₃ and

Table 2 The estimated annual concentration of air pollutants for cases and controls based on two different definitions; birth weight or gestational age

Pollutants	Birth weight		Gestational age	
	Cases (<i>n</i> = 468)	Controls (<i>n</i> = 1676)	Cases (<i>n</i> = 499)	Controls (<i>n</i> = 1645)
NO ₂ (ppb)	44.87 $\pm$ 12.01 ^a	46.26 $\pm$ 13.74	44.96 $\pm$ 11.90	46.26 $\pm$ 13.80
SO ₂ (ppb)	30.40 $\pm$ 24.56	34.65 $\pm$ 29.80	31.38 $\pm$ 25.49	34.43 $\pm$ 29.68
PM ₁₀ (μg/m ³)	102.90 $\pm$ 21.71	101.84 $\pm$ 22.50	102.20 $\pm$ 21.35	102.03 $\pm$ 22.62
Benzene (μg/m ³)	7.34 $\pm$ 1.50	7.30 $\pm$ 1.59	7.34 $\pm$ 1.55	7.30 $\pm$ 1.58
Toluene (μg/m ³)	24.06 $\pm$ 5.95	24.20 $\pm$ 6.34	24.18 $\pm$ 6.11	24.16 $\pm$ 6.30
Ethylbenzene (μg/m ³)	5.44 $\pm$ 1.09	5.41 $\pm$ 1.14	5.45 $\pm$ 1.12	5.41 $\pm$ 1.13
<i>p</i> -xylene (μg/m ³)	5.40 $\pm$ 0.95	5.43 $\pm$ 1.01	5.41 $\pm$ 0.98	5.43 $\pm$ 0.99
<i>m</i> -xylene (μg/m ³)	9.73 $\pm$ 2.16	9.68 $\pm$ 2.29	9.73 $\pm$ 2.23	9.68 $\pm$ 2.27
<i>o</i> -xylene (μg/m ³)	5.93 $\pm$ 1.38	6.01 $\pm$ 1.41	5.97 $\pm$ 1.43	6.00 $\pm$ 1.39
TBTEX (μg/m ³)	57.16 $\pm$ 11.99	57.07 $\pm$ 12.79	57.21 $\pm$ 12.27	57.06 $\pm$ 12.72

^a Data presented as Mean $\pm$ SD

Table 3 The association between air pollutants with LBW, and SGA using logistic regression model

Outcome	Pollutants	Crude OR (95%CI)	P value	Adjusted OR ^a (95%CI)	P value
LBW	NO ₂ (ppb)	0.992 (0.984–1.000)	0.048	0.995 (0.985–1.005)	0.339
	SO ₂ (ppb)	0.994 (0.990–0.998)	0.005	0.998 (0.993–1.003)	0.344
	PM ₁₀ (μg/m ³)	1.002 (0.998–1.007)	0.366	0.999 (0.994–1.005)	0.846
	Benzene(μg/m ³)	1.013 (0.949–1.081)	0.693	0.980 (0.901–1.067)	0.644
	Toluene(μg/m ³)	0.996 (0.980–1.013)	0.671	0.993 (0.973–1.014)	0.533
	Ethylbenzene(μg/m ³)	1.025 (0.936–1.122)	0.598	0.990 (0.880–1.113)	0.863
	<i>p</i> -xylene(μg/m ³)	0.964 (0.868–1.069)	0.486	0.909 (0.795–1.039)	0.160
	<i>m</i> -xylene(μg/m ³)	1.011 (0.966–1.058)	0.636	0.997 (0.941–1.056)	0.915
	<i>o</i> -xylene(μg/m ³)	0.958 (0.889–1.032)	0.256	0.939 (0.852–1.034)	0.200
	TBTEx(μg/m ³)	1.001 (0.992–1.009)	0.894	0.997 (0.987–1.008)	0.615
SGA	NO ₂ (ppb)	0.992 (0.984–1.000)	0.059	0.999 (0.990–1.007)	0.749
	SO ₂ (ppb)	0.996 (0.992–1.000)	0.039	0.999 (0.994–1.003)	0.518
	PM ₁₀ (μg/m ³)	1.000 (0.996–1.005)	0.881	0.998 (0.993–1.003)	0.497
	Benzene(μg/m ³)	1.016 (0.954–1.083)	0.618	1.020 (0.947–1.098)	0.599
	Toluene(μg/m ³)	1.000 (0.984–1.016)	0.969	0.999 (0.981–1.018)	0.938
	Ethylbenzene(μg/m ³)	1.035 (0.947–1.130)	0.448	1.034 (0.933–1.146)	0.522
	<i>p</i> -xylene(μg/m ³)	0.976 (0.882–1.081)	0.645	0.960 (0.853–1.081)	0.500
	<i>m</i> -xylene(μg/m ³)	1.010 (0.966–1.055)	0.672	1.011 (0.960–1.064)	0.683
	<i>o</i> -xylene(μg/m ³)	0.985 (0.917–1.059)	0.685	0.977 (0.897–1.064)	0.595
	TBTEx(μg/m ³)	1.001 (0.993–1.009)	0.817	1.001 (0.992–1.010)	0.880

^a LBW; adjusted for maternal age, gestational age, infant gender, and birth order, SGA; adjusted for maternal age, infant gender, and birth order

LBW after adjusting for all confounders. The relative risk (RR) of PM₁₀ was 1.03 (95% CI: 0.94–1.14), which is consistent with the findings of our study [43]. Slama et al. and Bell et al. found a significant relationship between PM_{2.5} and LBW [26, 44].

Inconsistency in the results of the relationship between air pollutants and birth outcomes may be related to differences in the populations, sample size, study design, adjustment for confounding variables, air pollution sources and characteristics, and air pollution exposure assessment method [11, 13, 45]. This study was benefitted from the use of individual estimates predicted by the LUR models. However, there are some limitations for our models. First, the models for PM₁₀, SO₂, and NO₂ have been built based on small number of regulatory monitoring stations where their location and numbers might not be ideal for LUR. Second, although the LUR models for BTEX compounds were built based on a decent number of sites and locations, they were for measurements done in 2015–2016 [35]. Therefore, the spatial patterns of BTEX compounds might not be very similar to those of 2011–2012. Anyhow, a study in Canada has shown that spatial patterns of NO₂ did not change after seven years in Vancouver [46].

Another limitation of our study is that the available data in hospital records were used which vary from one hospital to another; therefore, those variables were extracted that were commonly available in all records. We did not have the data

of other LBW risk factors, including maternal weight and height, socioeconomic status, maternal nutrition, maternal education, maternal diseases, and maternal smoking; thus, our study suffers also from these limitations. Finally, the present study had a case-control design while prospective studies may better serve the purpose of this study.

Conclusions

This study was conducted to investigate the association between air pollutants and LBW in Tehran. Our study is unique for analyzing such association, especially for the BTEX species, in the Middle East. However, no significant association was found between PM₁₀, SO₂, NO₂, and BTEX compounds and LBW. Further research with more rigorous designs and access to more comprehensive information are recommended considering also other air pollutants, such as ultrafine particles, PM_{2.5}, oxidative potential of particles, CO, and O₃.

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Authors' contributions PN prepared the datasets, analyzed the data and interpreted the results and drafted the first version of the manuscript

which was supervised by MY. MY, KN, and RN contributed to study design. MY and HK contributed to statistical analysis and results interpretation for the study and assisted in drafting the manuscript. HA contributed to estimate the exposure of study participants to the pollutants with the Land Use Regression model. MY, HK, KN, RN and HA revised it critically for important intellectual content. All authors read and approved the final manuscript.

Compliance with ethical standards

Ethics approval and consent to participate Not applicable.

Consent for publication Not applicable.

Conflict of interest The authors declare that they have no conflict of interest.

Abbreviations *CI*s, Confidence intervals; *HIC*s, High income countries; *LBW*, Low birth weight; *LMIC*s, Low- and middle-income countries; *LUR*, Land use regression; *NO₂*, Nitrogen dioxide; *OR*s, Odds ratios; *PM₁₀*, Particulate matter $\leq 10 \mu\text{m}$ in aerodynamic diameter; *SD*, Standard deviation; *SGA*, Small for gestational age; *SO₂*, Sulfur dioxide; *VOC*s, Volatile organic compounds; *WHO*, World Health Organization

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