The Effect of Air Pollution on Low Birth Weight: A Cohort Study

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Abstract

Aim: The paper aims to determine the effects of maternal exposures to essential air pollutants on low birth weight (LBW) in Tehran, Iran.

Methods: One thousands neonates were randomly selected of all live singletons born during 2000-2002, to 18-35 years old house wives mothers, living in one of the selected regions of the study (inside the boundary of 5 kilometers radius from four air quality control stations of Tehran. Linear regression and logistic regression were used to estimate the effects of air pollution on low birth weight.

Results: Low birth weight ratio was increased by the accretion of carbon monoxide, sulfur dioxide, nitrogen dioxide, and Ozone in the third trimester of the pregnancies. There was no statistical significant trend in LBW ratios in case of particulate matters ≤10μgr/m (PM10). The logistic model confirmed that the highest risk for low birth weight was related to CO. Multiple regression revealed CO as the most effective air pollutant in lowering the birth weight.

Conclusions: Low birth weight rates increases in the presence of essential air pollutants. This signifies the risk of neonatal diseases, hospitalizations and infants' higher mortality rates. Additionally, it might increase the cost of care and treatment.

BACKGROUND

Low birth weight (LBW) is considered to be an important predictor of infant mortality and childhood morbidity in developed and developing countries [1 , 2]. Compared with normal weight newborns (2500 g), the mortality rate of low weight infants is 40 times as much [3]. Sensitivity and low immunity of these infants make them vulnerable to different diseases [unpublished thesis].

Birth weight represents an endpoint of intrauterine growth, which depends on maternal, placental, and fetal factors, as well as a sequence of constitutional and environmental influences [4]. An extensive list of risk factors for low birth weight has been determined including maternal age, parity, pregnancy weight, history of adverse pregnancy outcomes, low social class, and cigarette smoking [5 , 6]. Numerous studies have demonstrated that maternal smoking during pregnancy increases the risk for delivering low birth weight, preterm, and small-for-gestational- age infants (SGA) [7,8,9,10,11].

The first study in a human population conducted in Los Angles, California in the early 1970s, demonstrated a lower mean birth weight for babies whose mothers lived in areas of high air pollution [12]. A cross-sectional study in China [13] found that the use of coal stoves for heating was significantly associated with LBW or preterm birth. A cohort study of Chinese women living in Beijing found association between elevated levels of SO2 and total suspended particles (TSP) and an increased risk for low–weight delivery (< 2500 g) [14]. Finally, another cohort study in Los Angeles, California, found that exposure of pregnant mothers to higher levels of ambient CO during the last trimester has been associated with a significantly increased risk for low birth weight after adjustment for potential confounders including commuting habits in the monitoring area, sex of the child, levels of prenatal care, and age, ethnicity, and education of the mother [15].

In general, low birth weight is considered to be an important predictor of infant mortality and childhood morbidity and may continue to be a risk factor for morbidity in adulthood [16 , 17]. As some authors [18] have pointed out, however, low birth weight itself does not cause adverse health outcomes, but rather serves as a biomarker for the primary causal factors responsible for prenatal developmental disturbances that predispose to childhood disability. It is widely accepted that it is important to reduce exposure to risk factors for low birth weight whenever possible in order to decrease the associated burden of disability and disease. If birth weight is found to be sensitive to the toxic effects of air pollutants, it can be used as an easily monitored sentinel indicator for environmental hazard surveillance, available to any large population that routinely records birth information and ambient air pollution levels.

Nowadays, air pollution is the most important ecological and health problem of big cities. Tehran, because of its special geographical situation, heavy traffic, and existence of pollutant industries, is the first or second polluted city in the world [unpublished dissertation]. Regarding the intensity of air pollution in Tehran and potential influence of high levels of air pollutants on birth weight and infants health, we chose to study the effects of essential air pollutants [CO, SO2, NO2, O3, PM10] on low birth weight.

METHOD

It was a retrospective cohort study that assessed the effect of essential air pollutants (CO, SO2, NO2, O3, PM10) on low birth weight in Tehran.

SUBJECTS

The research population included all the live newborns born to 18-35 years old housewives mothers after gestational age of 24 weeks, living inside the boundary of air polluted areas. They didn't have a history of pre-eclampsia, hypertension, cardiopulmonary, renal, collagen and endocrine diseases or genetic anemia. They weren't drug users during their pregnancies. Moreover, they hadn't experienced a history of placental disorders such as placental abruptia, placenta previa or placental tumors. They also had never given birth to low weight newborns and had never experienced twins' pregnancies. Their pregnancies had never lasted more than 42 weeks and the intervals between their pregnancies weren't less than 3 years. Additionally, there weren't any symptoms of congenital disorders in their newborns.

The research sample included 1000 newborns, randomly selected from the research population in two stages. Initially, three educative – therapeutic centers were randomly selected. Then, the sample size was determined in accordance with the number of deliveries in each center during 2000-2002. All the newborns that had been born during these years and had enjoined the inclusion criteria were listed in each center. Then the requested sample was randomly selected from the list.

SETTING

The setting was inside the boundary of 5 kilometers radius from four predetermined air quality control stations (Fatemi, Azadi, Bazar, Farhangsaraye Bahman), where the mothers had experienced their pregnancies.

The boundaries of considered regions were determined on the city map. Five kilometers radius from each station were marked and mothers residences were determined.

DATA GATHERING

Birth information was collected based on medical records after obtaining grants from the managers of responsible of health centers. Data recording sheet was used as tool. Validity of the research tool was assessed in terms of content validity and ten of nursing faculties established the validity of the instrument. The research tool included three parts. The first and the second parts were completed in the medical records departments of each health center. Each essential air pollutant mean including CO, NO2, SO2, O3, and PM10 was determined and recorded in the third part of the sheets. These data were recorded during the time frame, from gestational age of 24 weeks to delivery time. The twenty forth weeks of the gestational ages were recognized according to the first day of the last menstruations. Then the mean of each air pollutant was calculated based on the data received from air pollution monitoring stations.

Initially the researcher obtained enough information from the air quality control center and two environmental protection agencies about Tehran air pollution monitoring stations. This assessment revealed that there were only a few active air pollution monitoring stations in Tehran. Therefore, information obtained from four centers was just being used.

It is important to mention that the newborns birth weights were compared to the standard weight of the same birth ages. The weights were considered low if they were less than tenth percentile, and they were considered normal if they were more. Additionally, since there wasn't any information related to the heights and weights of the mothers in the beginning of their pregnancies, their socio-economic levels, and air pollution rates in their houses in the assessed records, the impact of these factors was not assessable in our study.

STATISTICAL METHODS

According to the rate of each essential air pollutant in gestational periods, the newborns were divided into two groups. To determine an increase in low birth weight ratio by increasing of essential air pollutants, each air pollutant range was divided into 3-5 sub ranges. Carbon monoxide rates was categorized into four sub ranges including < 4, 4-5.99, 6-8.99, and ≥9 PPM (part per million). Sulfur dioxide was categorized as < 10, 10-19.99, 20-29. 99 and ≥30 PPB (part per billion). Nitrogen dioxide was divided into three sub ranges including < 25, 25-49.99, and ≥50 PPB. Ozone was divided into three sub ranges including < 5, 5-9.99, and ≥10 PPB, and particulate matter < 10 µgr/m (microgram per cubic meter) was divided into five sub ranges including < 40, 40-49.99, 50-50.99, 60-69, 99, and ≥70 µgr/m .

We used Chi square to determine the relationship between birth weight and essential air pollutants, and each air pollutant after adjustment for gestational age and infant sex. The relationship between birth weight and each essential air pollutant, was assessed by Mantel Hanzel test (intervening factors were deleted).

We used independent t-test to compare birth weight means adjusted for each essential air pollutant, and two way analysis of variance to compare birth weight means adjusted for each essential air pollutant, gestational age, and infant sex. Chi square to trend was used to determine an increasing or decreasing trend in low birth weight ratio according to the accretion of each essential air pollutant. Finally, the rate of each essential air pollutant risk for low weight ratio and the effect of each air pollutant on birth weight mean was assessed by logistic regression model and multiple regression respectively.

RESULTS AND DISCUSSION

Most of the maternal ages were between 20-24 years (38%) and most of gestational ages were ≥37 weeks (87.3%). The majority of infants were females (50.4%) and most of them had normal weights (85.3%). The rate of low birth weight was 14.7%.

11.7% , 10.6% , 12.4% , 23.9% , and 71.8 % of the mothers had been exposed to ≥9 PPM of CO, ≥30 PPB of SO2, ≥50 PPB of NO2, ≥10 PPB of O3, and ≥70 µgr/ m of PM10 respectively. Tables 1 through 3 describe the sample in short.

Figure 1

Table 1: Mean maternal age, gestational age, and infant weight

Characteristics	Mean	± SD
Maternal age (years)	24.88	4.62
Gestational age (weeks)	38.69	2.69
Weight of infant (g)	2912.53	533.30

Figure 2

Table 2: Rates of low (

Characteristics	Number	(%)
Weight status		
Low weight	147	14.7
Normal weight	853	85.3
Sex of infant		
Male	496	49.6
Female	504	50.4

Figure 3

Table 3: Mean CO, SO2, NO2, O3 and PM10 in fetal period

Air pollutant	Mean	± SD
CO (PPM)	6.13	2.87
SO2 (PPB)	15.80	19.70
NO2 (PPB)	33.64	28.73
O3 (PPB)	5.93	4.38
PM10 (µgr/m 3)	110.74	118.59

The results indicated that low weight ratio had been increased by the accretion of carbon monoxide ($X^2 = 8.60$, P= 0.003). This finding has been supported by other researchers [15, 19]. The biological mechanisms whereby air pollution might influence birth weight remain to be determined. Nevertheless, it is known that CO crosses the placental barrier and that the hemoglobin in fetal blood has 10 times more affinity for binding CO than does adult hemoglobin. Moreover, some animal studies have indicated that fetal growth might be retarded by the direct toxic effects of CO and/or nicotine and other substances generated by burning cigarettes [20].

In our study there wasn't a statistically significant difference in case of sulfur dioxide, however, some researchers have found significant differences [14 , 21]. This difference might be related to the assessment criterion. The criterion in our study was the standard rate of SO2, while Bobak and Leon [21] had considered the frequency distribution of this pollutant in the assessed areas as criterion. In some studies [14] indoor coal stoves were the sources of sulfur monoxide.

We didn't find a significant relationship between low birth weight ratio and increasing rates of nitrogen dioxide. Some other researchers didn't find the relationship as significant as well [21, 22]. In the early 1970s, a study of 533 non – smoking women who all delivered in the same maternity hospital in Los Angeles reported a lower mean birth weight for babies than mothers who lived in areas of higher air pollution. When the measures of air pollution exposure consisting CO, NO2, and O3 levels recorded at the monitoring station nearest to a woman's residence were averaged over the entire pregnancy, only CO levels were significantly linked to decreased birth weight. Trimester – specific results, however, showed that increased levels of all three pollutants contributed to lower birth weight [23].

In our study there was a statistically significant relationship between increasing rates of PM10 and low weight ratio [$X^2 = 6.43$, P=0.011]. Wang and colleagues found a significant exposure – response relationship between maternal exposures to TSP during the third trimester of pregnancy and infant birth weight [14].

We assessed the exposure – response relationship between maternal exposures to essential air pollutants and newborn's low weight ratio after adjustment for gestational age and infant sex. Findings revealed that gestational age was not an intervening factor for carbon monoxide. Ritz and Yu [15] also didn't find the relationship as significant, but there was a statistically significant relationship between male newborns' low weights and carbon monoxide in our study ($X^2 = 5.109$, P= 0.024). Some authors contended that augmentation of humans X chromosomes increases their resistance to stressful situations. In other words, male sex intensifies carbon monoxide toxicity [24]. We found a significant exposure – response relationship between maternal exposures to sulfur monoxide and infant birth weight in gestational age of 37 weeks or more ($X^2 = 6.339$, P= 0.012). The results of Mantel Hanzel test also confirmed that without adjustment for gestational age, no significant relationship would manifest. Other researchers also found the same results [14]. We didn't find a statistically significant relationship between maternal exposures to SO2 and infant low birth weight, after adjustment for infant sex.

We found a significant exposure – response relationship between maternal exposures to NO2 and infant low birth weight after adjustment for gestational age. ($X^2 = 7.08$, P=0.008). This relationship was significant in gestational age of 37 weeks and more. There was no significant relationship in case of infant sex.

There was also a significant exposure – response relationship between maternal exposures to Pm10 and infant low birth weight after adjustment for gestational age (37 weeks and more) [fisher – exact test (PF) = 0.04]. Mantel Hazel test also confirmed that any significant relationship would not manifest without adjusting for gestational age. Some studies have supported this finding in the last trimester of pregnancy [14] while other studies have not found it significant in the first trimester [14]. Some authors contended that fetal growth does not follow a uniform pattern. Rather, it represents different periods of growth spurts for different organs and anthropometric measurements [25]. Thus, the time, intensity, and duration of the negative factors affecting fetal growth will manifest themselves in differing patterns. Previous studies [25] indicate that the peak fetal length growth occurs first, around the 20 week of gestation, while peak weight growth occurs around 33 weeks of gestation. It is estimated that by the 28 week, length has reached 71 % of the mean length at term (41 weeks), while weight is only 32% of the full- term infant weight [26]. In other words, weight growth is predominantly a phenomenon of the third trimester.

There was a significant relationship between maternal exposures to PM10 and infant low birth weight in female infants (PF=0.03). Other researchers have found the same result in male infants [14]. However in our study, the results of Mantel Hanzel test determined that infant sex bad not been an intervening factor in the relationship between PM10 and infants low birth weight ($X^2 = 5.29$, P=0.021).

We determined and compared the infants' birth weight means according to essential air pollutants in fetal life period. Our findings revealed that maternal exposures to increased rates of CO, SO2 and NO2 in their 3rd trimester decrease the infants birth weight mean (CO, t = 2.11, P= 0.035; SO2, t = 2.96, P= 0.003; NO2, t = 3.16, P= 0.002).

Some researchers have found that when mothers have had exposed to tobacco smoke in their third trimesters, their newborns birth weight means had been decreased [27]. Moreover, some authors have found that infants born to smoking mothers weigh on average 200 g less than infants of non smokers [14]. The same authors [14] have found a significant relationship between maternal exposures to SO2 and reduction of infant birth weight mean. We didn't find a significant relationship between maternal exposures to PM10 and the birth weight means of the two groups of infants.

Two way analysis of variance revealed that the effects of gestational age and infant sex on birth weight means were independent of each other. This was the case in CO, SO2, and NO2. In other words, the mutual effects of gestational age or infant sex and CO, SO2, or NO2, on birth weight means were not statistically significant. But, there was a significant relationship in case of gestational age and PM10 (F= 4.48, P= 0.035). However, this relationship was not adjusted for different gestational ages. We didn't find a significant relationship between maternal exposures to PM10 and infant birth weight mean after adjustment for infant sex. However, there is some evidence that gestational age is the most important determinant of birth weight [28].

We determined the trends in the ratio of infant low birth weight according to increasing of each essential air pollutant. The findings revealed that low weight ratios have increased by accretion of CO (X^2 = 6.470, P= 0.011). Table 4 shows when CO is < 4 PPM, 4-5.99 PPM, 6-8 PPM and ≥9 PPM, low birth weight ratios are 8.5% , 13.7 %, 12.7 % and 22.9 % respectively. In other words, when CO was ≥9 PPM, risk of low birth weight was 3.2 times as much in comparison with CO ≤ 4 PPM.

An increasing trend was observed in LBW ratios with the maternal exposures to high levels of SO2 (X^2 = 3.619, P= 0.050). Table 4 shows that when SO2 levels are < 10 PPM, 10-19.99 PPM, 20- 29.99 PPM, and > 30 PPM, LBW ratios are 13.5 %, 13.5 %, 19.5 %, and 20. 2% respectively. In other words, when SO2 level is ≥30 PPM, risk of LBW is 1.6 times as much in comparison with 10 PPM of this air pollutant. A cohort study in Beijing also revealed that SO2 had contributed to an excess risk of low birth weight [14].

High levels of NO2 also contributed to increasing of LBW ratios. According to table 4, when NO2 level is < 25 PPB, 35-49.99 PPB , and ≥50 PPB , LBW ratio is 11.8 % , 17.3 % and 20.2 % respectively X^2 = 6.876, P= 0.009). In other words , in comparison to 25 and 50 PPB of NO2 , the latter, increases the risk of LBW, twice as much. This finding is logical because NO2 is moderately correlated with CO. This relationship is expected because a large percentage of both pollutants are produced by the same vehicular sources [15].

Figure 4

Table 4: Low weight distribution of absolute and relative frequency by CO, SO2, NO2, O3 and PM10 rates in fetal period.

	LBW(Yes)	LBW(No)	Total	Test results
	NO. (%)	NO. (%)	NO. (%)	
CO (PPM)				
< 4	11(8.5)	119(91.5)	130(100)	OR= 1.00
4-5.99	45(13.7)	284(86.3)	329(100)	OR= 1.71 χ2 t=6.470
6-8.99	42(12.7)	289(87.3)	331(100)	OR= 1.54 df=1
≥9	24(22.9)	81(77.1)	105(100)	OR= 3.21 P=0.011
Total	147(15.7)	853(85.2)	1000(100)	
SO2 (PPB)				
< 10	51(13.5)	328(86.5)	379(100)	OR= 1.00
10-19.99	57(13.5)	366(86.5)	423(100)	OR= 1.00 χ2 t=3.619
20-29.99	15 (19.5)	62 (80.5)	77 (100)	OR= 1.56 df=1
≥30	21(20.2)	83 (79.8)	104(100)	OR= 1.63 P=0.050
Total	147(14.7)	853(85.3)	1000(100)	
NO2 (PPB)				
< 25	59(11.8)	439(88.2)	498(100)	OR= 1.00 χ2 t= 3.619
25-49.99	41(17.3)	196(82.7)	237(100)	OR= 1.56 df =1
≥50	21(20.2)	83(79.8)	104(100)	OR= 1.88 P=0.050
Total	147(14.7)	853(85.3)	1000(100)	
O3 (PPB)				
< 5	67(13.0)	450(87.0)	517(100)	OR= 1.00 χ2 t= 4.590
5-9.99	29(22.3)	101(77.7)	130(100)	OR=1.93 df=1
≥10	37(18.2)	166(81.8)	203(100)	OR= 1.50 P=0.03
Total	147(14.7)	853(85.3)	1000(100)	

Figure 5

PM10(μgr/m 3)				
< 40	0 (0)	2 (100)	2 (100)	OR= 1.00
40-49.99	0 (0)	35(100)	35 (100)	OR= 7.84 χ2 t= 0.001
50-59.99	25(17.5)	118(82.5)	143(100)	OR=10.64 df=1
60.69.99	21(22.3)	73(77.7)	64(100)	
≥70	93(13.4)	603(86.6)	696 (100)	OR= 5.70 P=0.971
Total	147 (14.7)	853(85.3)	1000(100)	

An increasing trend was also observed in LBW ratios with the maternal exposures to high levels of O3. Table 4 demonstrates when O3 level is < 5 PPB , 5- 9.99 PPB, and > 10 PPB, LBW ratio is 13 % , 22.3 % and 18.2 % respectively (X^2 = 4.590, P= 0.03). In other words, compared with O3 levels of ≥ 10 PPB and < 5 PPB, the former increases the risk of LBW 1.5 times as much.

We didn't find a statistically significant trend in LBW in case of PM10 (Table 4).

The risk of each essential air pollutant, gestational age, and infant sex in LBW ratio was determined. Table 5 shows that this relationship is statistically significant in case of CO [(OR) = 2.12; 95 % (CI), 1.16-3.89]. We inserted the above mentioned variables in logistic model. As table 6 demonstrates, the risk of CO in accretion of LBW ratio is higher than other variables [(OR) = 2.17; 95 % (CI), 1.09 – 4.32]. Ritz and Yu [15] found a 22 % increase in LBW [(OR)= 1.22 ; 95 % (CI), 1.03- 1.44] among the children born to mothers who were exposed on average to more than 5.5 PPM CO (95 percentile for exposure) during the last trimester of pregnancy. Additionally, Bobak and Leon [21] found that each 50 micrograms of SO2 has increased the risk of LBW [(OR) = 1.10; 95% (CI), 1.02 – 1.17]. It seems that the difference between this finding and the results of our study (table 6) relates to the grouping of SO2 rates.

Figure 6

Table 5: Distribution of odds ratios (ORs) and 95% Confidence intervals (CIs) for low birth weight by essential air pollutants

Variables	OR	CI
CO	2.12	1.16-3.89
NO2	0.79	0.30-2.07
O3	1.26	0.73-2.19
PM10	498.62	0.000-5.39×1013

In the final stage of analysis, we assessed the effect of each essential air pollutant on mean birth weight (Table 7). The results of multiple regression analysis revealed that CO has had the highest effect on reduction of the mean birth weight (P= 0.05, B= - 105.52). Moreover, gestational age was the most effective factor in the infant's mean weight gain (P= 0.000, B= 118.01).

Figure 7

Table 6: Logistic model of odds ratios (OR s) and 95 % confidence intervals (CIS) for low birth weight

Variables	OR	CI
Gestational age	0.69	0.64-0.74
Infant sex	1.19	0.70-2.02
CO	2.17	1.09-4.32
NO2	0.87	0.28-2.62
O3	1.59	0.85-2.91
PM10	281.84	0.000-3×0.004×1013

Figure 8

Table 7: Regression model of birth weight by different factors

Variables	Effect		Significance
Gestational age	118.01		0.000
Infant sex	23.213		0.51
CO	-105.52		0.05
NO2	27.49		0.70
O3	-11.45		0.80
PM10	-113.97		0.48
Invariable figure		1362.65	

[In tables 5, 6 and 7, the results related to SO2 were similar to NO2]

The biological mechanism whereby air pollution is associated with Low birth weight remains to be determined. Respiratory health effects of inhaled pollutants depend on their depth of penetration, deposition, and retention in the lung, as well as on the subsequent biological responses induced by the deposited material (29). In comparison, a mechanism for air pollution to affect birth weight is less straightforward. Fetal growth is influenced by maternal, placental, and fetal factors. Air pollution may affect maternal respiratory or general health, which may in turn impair utero-placental and umbilical blood flow, trans placental glucose, and total insulin, the major determinants for fetal growth (30). Therefore all the air pollutants which we studied might have been absorbed into the maternal bloodstream, have been crossed placental barrier, and have resulted in toxic effects on the fetus.

CONCLUSION

This study was limited to singleton live births to assess the effect of air pollution in a more homogenous sample. While we studied the effects of all essential air pollutants on low birth weight , and we included gestational age and infant sex in our models , but certainly, more extensive studies with more intervening variables are needed to explain the effect of air pollutants on low birth weight.

We believe that one of the most efficient and cost- effective strategies for evaluating pollution – related effects is to screen large populations broadly using existing air pollution monitoring records. Once an exposure-outcome association has been established, in – depth assessments can be conducted on a subset of individuals with the outcome of interest (e.g., mothers who have given birth to term low birth babies) , matching them with controls and interviewing each to collect the personal information needed to evaluate the influence of factors such as occupation, time spent in the area of residency, time commuting, nutrition during pregnancy , and indoor sources of pollution. This information, combined with a small validation study of exposure assessment via personal monitors, should serve to refine our understanding of pollutant effects and interaction, resolving many of the questions and uncertainties that could not be addressed in other studies.

However, regarding the results of this study we suggest the responsible centers for air pollution control in Tehran, to use effective strategies to reduce air pollution and maintain maternal and fetal health and development. Moreover, our findings are indicative of the necessity of executing teaching programs for pregnant women. These programs must orientate these women towards dangerous effects of air pollutants on their infants.

AUTHORS' CONTRIBUTIONS

Fatemeh Oskuie participated in the design of the study and data analysis, coordinated the study and drafted the manuscript. Afrooz Bagherzadeh proposed the design of the study, collected the data and performed the statistical analysis. Zohreh Feizi participated in the design and coordination of the study. Mahmood Mahmoodi was the statistical consultant. Hamid Peyrovi helped in writing the paper and revised the drafts.

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