Relationship between low birthweight and air pollution in the city of Sao Paulo, Brazil

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Keywords
Infant, low birth weight. Air pollution. Linear models. Morbidity.

Abstract

Objective
Air pollution has been investigated as a potential determinant for low birthweight. The aim of the present study was to study the effect of air pollution on birthweight.
Methods
We analyzed all deliveries by mothers living in the municipality of São Paulo, Southeastern Brazil, between 1998 and 2000. We estimated the prevalence of low birthweight according to newborn, mother, and delivery characteristics. Only births occurring in the most central districts of the city were analyzed, totaling 311.735 events. For the evaluation of the effects of air pollution, we excluded preterm and multiple deliveries. Pollutants analyzed were ozone (O_3), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), suspended particles (PM_{10}), and carbon monoxide (CO). The effect of maternal exposure to air pollution on birthweight was evaluated using linear and logistic regression.
Results
A total of 4.6% of newborns weighed less than 2,500 g at birth. Maternal exposure to CO, PM_{10}, and NO_2 during the first trimester of pregnancy was significantly associated with decreased birthweight.
Conclusions
Our results reinforce the notion that maternal exposure to air pollution during the first trimester of pregnancy may contribute to lesser weight gain in the fetus.

INTRODUCTION

Newborn health may be analyzed from different perspectives. One of these is birthweight, which is an important factor in the determination of neonatal morbidity and mortality and post-neonatal mortality, thus being of great importance for public health.[5] Hence, the World Health Organization (WHO) considers low birthweight as the most important single factor in infant survival.

Even though infant mortality has fallen substantially in both developed and developing countries, this decline has not been due to a reduction in the number of low birthweight children; instead, it is likely to have been caused by improvements in antenatal, delivery, and newborn care.[10,13,14]

Thus, in spite of the reductions in infant mortality, low birthweight (< 2,500 g) gains in importance due to the increase in the number of preterm births or of babies small for their gestational age.

In developed countries, unlike in developing ones, social inequities are less marked, and birthweight information systems more reliable. The mean weight of newborns is 3,500 g, and the number of low birthweight deliveries does not exceed 5%.[20]

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Based on a Master's dissertation presented at the Universidade de São Paulo, in 2004.
Received on 6/10/2004. Reviewed on 17/6/2005. Approved on 30/7/2005.

According to Datasus,* the Brazilian Ministry of Health Information System, in 2000, the proportion of low birthweight newborns in the country as a whole was 7.6%, ranging from 6.2% in the North Region to 8.5% in the Southeast Region. However, information for the North and Northeast Regions should be interpreted with caution, since the incomplete coverage of the National Live Birth Information System in these Regions may lead to underestimation (*Sistema de Informação Sobre os Nascidos Vivos* - SINASC).**

Preterm birth is more present in developed countries, where its specific determinants are placental abnormalities and cervical incompetence. On the other hand, newborns small for gestational age (SGA) are more common in developing countries. This is due to several factors, including insufficient calorie intake during pregnancy.[8]

In developed countries such as France and the United States, the incidence of preterm births is 6%.[11] In Brazil, the proportion of preterm births in 2000 was 6.7% for the whole country and 7.4% in the municipality of São Paulo.*

Epidemiological studies are currently investigating the causes of lower birthweigth.[8] These include child's sex, mother's age, socioeconomic conditions, and antenatal care.[5,14,15] Maternal smoking and malnutrition may also influence birthweight. The main effects of smoking are on intra-uterine growth retardation rather than on preterm birth; on the other hand, low pre-pregnancy body mass index is one of the major causes of preterm delivery.[2,10]

More recently, several studies have been published indicating air pollution as a potential determinant for low birthweight. A Chinese study[21] has reported an association between maternal exposure to sulfur dioxide (SO_2) and total suspended particles (TSP) during the third trimester of pregnancy and low birthweight. In Seoul, South Korea, exposure to pollutants such as carbon monoxide (CO), nitrogen dioxide (NO_2), SO_2, and TSP during the first trimester of pregnancy was found to be a risk factor for low birthweight.[7] In the city of São Paulo, Southeastern Brazil, a recent study[6] has indicated that birthweight may be reduced when mothers are exposed to high levels of CO and particulate material (PM_{10}) in the first trimester of pregnancy. This was the first study conducted in Brazil to identify an association between low birthweight and air pollution.

The population of São Paulo is exposed to high concentrations of air pollution, and, spite of improvements in sanitation and healthcare, the prevalence of low birthweight has remained high in the last 22 years. We may thus hypothesize that air pollution is affecting the intra-uterine development of children born in this city. Hence, the aim of the present study was to study the effects of air pollution in the city of São Paulo on birthweight, according to maternal exposure in the three trimesters of pregnancy.

METHODS

We analyzed all babies born to mothers living in the Municipality of São Paulo between 1998 and 2000 with completed live birth declarations. This information was obtained from the SINASC, which is based on the Live Birth Declaration (*Declaração de Nascidos Vivos* - DN).

The following inclusion criteria were observed: term birth (gestational age 37-41 weeks); single birth (not twin birth); being born in a hospital, and birthweight between 1,000 and 5,500 g. Birthweight was restricted to these values in order to exclude children of more extreme birthweights. These children are likely to come from high-risk pregnancies, where the contribution of air pollution to birthweight would be less important.

We considered as low birthweight children born weighing less than 2,500 g and with gestational age between 37 and 41 weeks, that is, small-for-gestational-age term babies. Only the more central districts of the City of São Paulo were included, leading to a total 311,735 births.

The more central region of the city was prioritized due to the greater concentration of air-quality monitoring stations. Thus, the peripheral districts of the Municipality of São Paulo were excluded.

The Environmental Sanitation Technology Company (*Companhia de Tecnologia de Saneamento Ambiental* – Cetesb) provided daily records of the concentration of sulfur dioxide (SO_2), particulate material (PM_{10}), carbon monoxide (CO), ozone (O_3), and nitrogen dioxide (NO_2). We considered all 14 stations operating in São Paulo, although not all stations provided measures of all pollutants. Information on the concentration of PM_{10} and SO_2 were obtained from 14 and six monitoring stations, respectively. We obtained data on O_3 from six monitor-

*Datasus. Disponível em: http://tabnet.datasus.gov.br/cgi/dettohtm.exe?sinasc/cnv/nvbr.def [29 abr 2003]
**Novaes HMD, Almeida MF, Ortiz LP. O que são os nascimentos de baixo peso ao nascer? Disponível em: http://www.saudepublica.bvs.br/itd/level3.php?channel=mort_faq2e7_14 [29 abr 2003]

Table 1 - Prevalence, odds ratio (OR), and confidence intervals (95%CI) for low birthweight among all live births, according to maternal, newborn, pregnancy, and delivery characteristics. Municipality of Sao Paulo, 1998-2000.

Variables	N=595,559	Prevalence of low birthweight	OR	95% CI	p
Year of birth					-
1998	196,791	9.07	-	-	
1999	204,911	8.71	-	-	
2000	193,857	8.94	-	-	
Gender*					<0.001
Male	304,113	8.11	1.00	-	
Female	291,394	9.73	1.22	1.20-1.24	
Race*					<0.001
White	191,095	8.40	1.00		
Black	4,905	9.70	1.17	1.06-1.29	
Asian	1,936	8.26	0.98	0.83-1.16	
Mulatto	77,384	9.37	1.13	1.09-1.16	
Amerindian	370	8.65	1.03	0.72-1.48	
Preterm*					<0.001
Yes	34,688	56.09	20.06	19.58-20.54	
No	524,746	5.99	1.00	-	
Mother's schooling*					<0.001
None	7,772	10.59	1.37	1.27-1.48	
Incomplete elementary	231,231	9.16	1.16	1.13-1.20	
Complete elementary and secondary	180,971	8.51	1.07	1.04-1.11	
University	74,144	7.97	1.00	-	
Place of occurrence*					0.002
Hospital	590,085	8.92	1.00	-	
Other health facility	1,868	8.08	0.90	0.76-1.06	
Home	1,635	13.76	1.63	1.42-1.88	
Others	440	5.68	0.61	0.41-0.92	
Type of delivery*					0.119
Vaginal	315,969	8.90	1.00	-	
C-section	270,794	9.02	1.01	1.00-1.03	
Antenatal appointments*					<0.001
None	12,952	19.48	3.27	3.12-3.42	
≤6	185,157	10.80	1.64	1.60-1.67	
>6	235,581	6.89	1.00	-	

*The number of cases lacking information for variables sex, race, birthweight, preterm birth, mother's schooling, place of occurrence, type of delivery, and number of antenatal care appointments was, respectively: 52, 319,869, 8,112, 36,125, 101,441, 1,531, 8,796, and 161,869.

ing stations and on NO_2 and CO from seven stations.

The five pollutants (O_3, PM_{10}, NO_2, CO, SO_2) were analyzed separately. We calculated the mean concentration of each pollutant in the three trimesters of pregnancy based on mean daily values, using the date of birth as a reference. For example, a child born with gestational age between 37 and 41 weeks on 30 November 2000 was considered as being 39 weeks old on this date. Based on the date of birth, the mean concentration of each pollutant in the nine months preceding birth (i.e., between March and November 2000) was calculated. We thus obtained mean pollutant concentrations for the first, second, and third trimesters of pregnancy for each individual child.

We first carried out a descriptive analysis, when we excluded babies born to mothers living in the city outskirts ant those not fulfilling the previously established inclusion criteria.

To examine the association between maternal exposure to pollution and low birthweight, we used univariate and multivariate linear and logistic regression. In linear regression, the outcome variable (birthweight) was analyzed as a continuous variable, whereas in logistic regression birthweight was dichotomized into birthweight <2,500 g and ≥2,500 g.

Regarding maternal exposure to pollutants, in linear regression we considered the trimester mean concentration of each pollutant in the respective trimesters of pregnancy, whereas in logistic regression each pollutant was analyzed by recoding into quartiles based on trimester means.

Univariate linear and logistic regression examined first the relationship between birthweight and maternal exposure to each pollutant in order to estimate the crude effect of this exposure on the child. The univariate logistic model was used also to identify the relationship between the outcome and each of the variables in the live birth declaration, in order to identify potential confounders and select variables for the multivariate models.

Variable "month of birth" was originally planned to be used in analysis for controlling for any possible seasonal effects on the relationship between air pollution and birthweight. However, our primary analyses showed a strong correlation between this variable

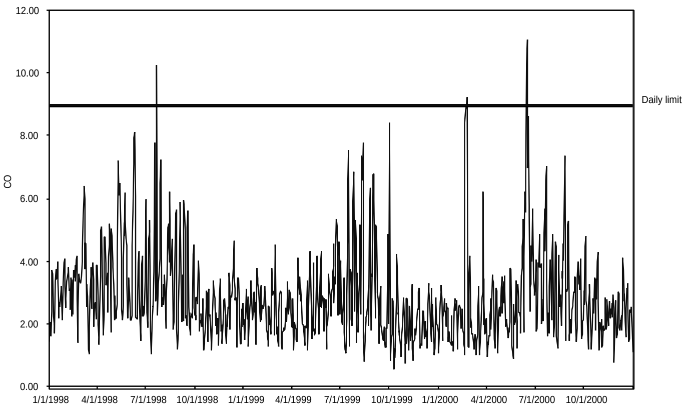

Figure - Daily mean CO concentration (ppm) in the Municipality of Sao Paulo, Brazil, between 1998 and 2000.

and air pollution, indicating colinearity between these variables. Thus, we chose not to include month of birth in the final model.

Statistical analysis was carried out using SPSS and Stata softwares.

RESULTS

Of the 595,559 births occurred between 1998 and 2000, 8.9% of babies were low birthweight. Table 1 shows that the prevalence of low birthweight was 56.1% among preterm babies, confirming preterm birth as an important risk factor (OR=20.1; 95%CI: 19.6-20.5). Absence of antenatal care was also important (OR=3.3; 95%CI: 3.1-3.4). Almost all deliveries took place in hospital environments. The frequency of vaginal delivery was slightly higher than that of cesarean sections.

The Figure shows the distribution of daily mean concentrations of CO. The peaks of concentration occur during winter, and some of these exceed the daily limit recommended by Cetesb.*

Of the total children studied, 4,6% were born weighing less than 2,500 g, and mean birthweight was 3,196 g. Table 2 presents the prevalence and odds ratios (OR) for low birthweight according to newborn, mother, pregnancy, and delivery characteristics. We found statistically significant associations between low birthweight and all variables studied ($p<0.001$).

Regarding maternal characteristics, we found greater prevalence of the outcome among younger (< 24 years) and older (> 35 years) mothers. Greater prevalence for extreme values was also seen in relation to the number of living children, i.e., in childless mothers or mothers with more than three children. As to maternal education, the greater the schooling, the lesser the risk of having a low birthweight child.

Regarding pregnancy and delivery characteristics (Table 2), we found that children born through vaginal delivery showed greater risk of low birthweight (OR=1.23; 95%CI: 1.19-1.28). Risk increases as the number of antenatal care appointments decreases and is greater upon the absence of antenatal care (OR=2.65; 95%CI: 2.40-2.92).

Multivariate linear regression showed that maternal exposure to all pollutants except for O_3 in the first trimester was associated with reduced birthweight (Table 3). This decrease was of 0.60 g; 0.47 g; 1.26 g, and 11.87 g, respectively, for every 1 $\mu g/m^3$ increase in mean maternal exposure to PM_{10}, NO_2, and SO_2 and each 1 ppm increase in CO, reaching statistical significance for all pollutants. During the second trimester of pregnancy, maternal exposure to CO and SO_2 was associated with an increase in birthweight. However, in the third trimester, this increase is observed along with exposure to all pollutants, all results reaching statistical significance (with the exception of exposure to O_3).

In multivariate logistic analysis, none of the pollutants showed statistically significant association with the outcome (Table 4). Moreover, we found no variation in risk for high pollutant concentrations. However, during the second trimester of pregnancy, exposure to PM_{10}, SO_2, O_3 appears as a protective factor, since in the first and third trimesters protection is associated with CO and O_3, respectively.

DISCUSSION

Low birthweight was associated with all maternal, newborn, pregnancy, and delivery characteristics studied. These results are in agreement with the data in the literature.[5,14,15]

Although it is difficult to isolate the effects of each individual pollutant due to the strong correlation between the different pollutants, exposure to CO is more relevant in terms of newborn weight. Although exposure to pollutants during the first trimester determined lower birthweight (-11.9 g), in the third trimester it was associated with weight gain. This is probably due to the seasonal component of air pollution: exposure during the first and second trimesters was almost always inversely associated with exposure during the third trimester.

*Companhia de Tecnologia de Saneamento Ambiental (Cetesb). Relatório de qualidade no Estado de São Paulo, 1999. São Paulo; 2000.

Table 2 - Prevalence, odds ratio (OR), and confidence intervals (95%CI) for low birthweight among the studied sample, according to maternal, newborn, pregnancy, and delivery characteristics. Municipality of Sao Paulo, 1998-2000

Variables*	N=311,735	Prevalence of low birthweight	OR	95% CI	p
Gender					<0.001
Male	158,782	3.86	1.00	-	
Female	152,942	5.40	1.42	1.37-1.47	
Mother's age (years)					<0.001
<20	48,070	5.80	1.50	1.42-1.58	
20-24	85,133	4.54	1.15	1.10-1.21	
25-29	82,489	3.96	1.00	-	
30-34	61,011	4.24	1.07	1.02-1.13	
35-39	28,376	4.92	1.26	1.18-1.34	
>39	6,447	7.35	1.93	1.74-2.13	
Mother's schooling					<0.001
None	3,784	5.87	1.89	1.64-2.18	
Incomplet elementary	110,974	5.10	1.63	1.54-1.73	
Complete elementary and secondary	98,195	4.32	1.37	1.29-1.45	
University	51,270	3.19	1.00	-	
Number of living children					<0.001
None	120,843	4.96	1.29	1.24-1.34	
1-3	132,225	3.89	1.00	-	
>3	58,667	5.55	1.45	1.39-1.52	
Number deceased children					<0.001
None	225,734	4.41	1.00	-	
One or more	12,079	5.96	1.38	1.27-1.49	
Type of delivery					<0.001
Vaginal	156.695	5.07	1.23	1.19-1.28	
C-section	153,180	4.15	1.00	-	
Antenatal appointments					<0.001
None	5,215	9.26	2.65	2.40-2.92	
≤6	86,913	5.44	1.49	1.43-1.56	
>6	132,999	3.71	1.00	-	

*The number of cases lacking information for variables sex, mother's age, mother's schooling, number of deceased children, type of delivery, and antenatal appointments was, respectively: 11,209, 47,512, 73,922, 1,860, and 86,608.

Moreover, there is a period of maximum weight gain which occurs between the 28th and 37th weeks of pregnancy (hormonal response). The placental corticotropin releasing hormone (CRH) participates in the peak of fetal glucocorticoids associated with fetal maturation at the end of the third trimester.[12] *In vitro*, placental CRH dose-dependently stimulates the release of adrenocorticotropic hormone (ACTH). CRH and ACTH secretion increases when uterine blood flow is restricted, and CRH is a potent uteroplacental vasodilator. This hormone is released into fetal circulation in response to fetal stress and under conditions leading to growth retardation.[18] CRH levels are often high in pre-eclampsia, fetal asphyxia, and preterm labor, as well as in several conditions causing growth restriction. Thus, whereas maternal exposure to pollutants during the first trimester may contribute towards fetal growth restriction, chronic exposure to air pollution throughout pregnancy may lead to fetal stress and increase the release of CRH during the later stages of pregnancy. The CRH released will increase fetal glucocorticoids, leading to maturation of the fetus in the third trimester, favoring weight gain during this period.

The difference observed between the results of logistic and linear models is probably due to the scale used in the latter, where the dependent variable is continuous rather than discreet, allowing for more detailed analysis. From this perspective, logistic regression is much more restrictive than the linear model.[3]

Studies of the effects of air pollution on low birthweight are not only scarce, they are also quite controversial. Some studies find no association,[1] others do not specify the period of exposure;[19] some find consistent associations for exposure during the third trimester of pregnancy,[22] while others fins such associations for exposure during the first trimester.[19] Our findings are in agreement with those of Ha et al[6] (2001), Yang et al[7] (2003), and Gouveia et al[22] (2004).

Table 3 - Regression coefficients and respective standard deviations and 95% confidence intervals for the concentration of air pollutants according to trimester means corresponding to trimesters of pregnancy (multiple linear regression*). Municipality of Sao Paulo, 1998-2000.

	Pollutants	Coefficient (SD)	95% CI
PM_{10}	1st trimester	-0.6 (0.1)	-0.8 to -0.4
	2nd trimester	0.04 (0.1)	-0.2 to 0.3
	3rd trimester	0.8 (0.1)	0.57 to 1.02
CO	1st trimester	-11.9 (1.9)	-15.5 to -8.2
	2nd trimester	4.9 (2.3)	0.5 to 9.3
	3rd trimester	12.1 (2.3)	7.6 to 16.6
NO_2	1st trimester	-0.5 (0.1)	-0.6 to -0.3
	2nd trimester	-0.02 (0.1)	-0.2 to 0.1
	3rd trimester	0.6 (0.1)	0.4 to 0.7
O_3	1st trimester	0.5 (0.1)	0.3 to 0.7
	2nd trimester	-0.7 (0.1)	-1.0 to -0.5
	3rd trimester	0.1 (0.1)	-0.1 to 0.2
SO_2	1st trimester	-1.3 (0.2)	-1.7 to -0.8
	2nd trimester	0.7 (0.3)	0.2 to 1.3
	3rd trimester	2.0 (0.3)	1.5 to 2.6

*Model adjusted for the following variables: antenatal care, maternal age and schooling, child's sex, type of delivery, number of living and deceased children, and year of birth.
SD: standard deviation

Gouveia et al[22] (2004) found a 23 g reduction in birthweight for each ppm increase in CO concentration, and a 13 g reduction for each 10 μg/m³ increase in PM_{10}concentration. These authors found no reduction associated with the remaining pollutants. In the present study, we found a reduction in birthweight of 12 g and 0.6 g for each ppm increase in CO concentration and for each 1 μg/m³ increase in PM_{10} concentration, respectively. Although the findings of these two investigations are similar, the variation in magnitude of the effects found may be due to methodological differences between the two studies. Whereas Gouveia et al[22] (2004) analyzed live births occurred in a one year period (1997), the present study analyzed a three year period (1998-2000). Furthermore, our sample was restricted to mothers living in more central areas, for whom exposure to air pollution may be more accurately estimated.

The limitations of the present study include the fact that mean concentrations were evaluated for each trimester. A shorter period may have been more appropriate, providing a better representation of exposure. Also, the present study considered the mean concentration of pollutants for each region, and CO levels may vary considerably between different areas of the city. Thus, individual exposure may have been under or overestimated by the mean level of pollutants measured by all monitoring stations. Moreover, important risk factors for low birthweight, such as smoking and maternal malnutrition, were not controlled for, since these information are not present in the Live Birth Declaration. Nevertheless, this secondary source of information contemplates most of the determinants of the outcome. Regarding the differences observed between the prevalence of live births according to place of residence, which ranged from 8.9% to 4.6%, we found that the exclusion of the outer districts was not a limiting factor for the analysis of the outcome, since this prevalence remained virtually unaltered after the exclusion of these districts. When we excluded only the city's outer districts, prevalence of low birthweight was 8.8%; when we excluded only preterm, post-term, and twin births, considering the entire municipality, the proportion fell to 4.8%.

One of the biological mechanisms involved in the retardation of fetal growth are alterations that take place in the placenta. These include pathologic-anatomic and morphometric alterations (lighter and smaller placentas among SGA newborns), placental infarction, and chronic villitis.[4,16,17]

The biological mechanisms behind the relationship between air pollution and low birthweight are still poorly understood. One hypothesis is that air pollution may lead to pathologic-anatomic and morphometric alterations, as well as to placental infarction and villitis. Pollutants may interfere with oxygen transportation, and may also increase blood viscosity by generating an inflammatory response.[2,9] This is believed to have a toxic effect on the fetus, caused by the reduction of fetal oxygen supplies due to decreased oxygen transportation capacity or alterations in blood viscosity.

The effective implementation of pollution control measures will allow for an increase in the number of healthy newborns. With adequate weight and normal growth potential, these children will

Table 4 - Odds ratio (OR) and confidence intervals (95%CI) for low birthweight according to quartiles of air pollutant concentration in each trimester of pregnancy (multiple logistic regression*). Municipality of Sao Paulo, 1998-2000.

Pollutants	Quartile	1st Trimester OR	1st Trimester 95% CI	2nd Trimester OR	2nd Trimester 95% CI	3rd Trimester OR	3rd Trimester 95% CI
PM_{10}	1st		1		1		1
	2nd	1.01	(0.94-1.07)	0.99	(0.93-1.05)	1.01	(0.94-1.08)
	3rd	1.03	(0.97-1.10)	0.97	(0.91-1.04)	1.00	(0.94-1.07)
	4th	1.01	(0.95-1.08)	0.97	(0.91-1.04)	0.99	(0.93-1.05)
CO	1st		1		1		1
	2nd	0.98	(0.92-1.04)	1.02	(0.95-1.08)	1.03	(0.97-1.10)
	3rd	0.98	(0.91-1.05)	1.03	(0.96-1.10)	0.95	(0.89-1.02)
	4th	0.98	(0.91-1.06)	0.97	(0.90-1.05)	1.03	(0.96-1.11)
SO_2	1st		1		1		1
	2nd	1.04	(0.97-1.11)	0.97	(0.91-1.04)	1.03	(0.96-1.10)
	3rd	1.03	(0.96-1.10)	0.95	(0.89-1.01)	1.04	(0.98-1.11)
	4th	1.01	(0.95-1.07)	0.97	(0.91-1.03)	1.01	(0.93-1.07)
NO_2	1st		1		1		1
	2nd	0.99	(0.93-1.06)	1.01	(0.93-1.07)	1.06	(0.98-1.13)
	3rd	1.00	(0.94-1.07)	0.98	(0.92-1.05)	0.98	(0.92-1.05)
	4th	1.00	(0.93-1.08)	0.98	(0.91-1.05)	0.99	(0.93-1.06)
O_3	1st		1		1		1
	2nd	1.03	(0.96-1.09)	0.99	(0.93-1.06)	0.95	(0.89-1.02)
	3rd	0.99	(0.92-1.07)	0.98	(0.91-1.07)	0.95	(0.88-1.02)
	4th	1.01	(0.92-1.08)	0.99	(0.91-1.08)	0.98	(0.91-1.05)

*Model adjusted for the following variables: antenatal care, maternal age and schooling, child's sex, number of living and deceased children, type of delivery, and year of birth consequently have greater chance of survival.

The continuity of investigations of the effects of air pollution on newborn health should be encouraged. Further studies including data from primary sources and measuring exposure closer to the mother's place of residence should be conducted.

ACKNOWLEDGEMENTS

We would like to thank the Fundação Sistema Estadual de Análise de Dados and the Companhia de Tecnologia e Saneamento Ambiental (Cetesb), for providing access to the data on live births and air pollution, respectively.

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