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Exposure to pollution during pregnancy and occurrence of miscarriage

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Abstract: A cross-sectional study was carried out to estimate the prevalence of miscarriages in a population of 360 women distributed in areas exposer to higher and lower vehicle traffic air pollution on the Island of São Luís, MA, Brazil, and identify associated variables. Participants were interviewed and bivariate and multivariate logistic regressions were conducted. The overall miscarriage prevalence was of 15.83%, totaling 25.56% (n=180) in the higher exposure area and 6.11% (n=180) in the lower exposure area. Maternal alcohol consumption (OR=3.11), STIs during pregnancy (OR=2.74), living in a high-exposure area (OR=8.32), having suffered physical or psychological distress during pregnancy (OR=4.25) and repeated miscarriages (OR=39.11) were all associated to the miscarriage outcome. The findings reported herein thus indicate potential vehicle traffic air pollution contribution as a risk factor in the etiology of miscarriages.

Keywords: Miscarriage; atmospheric pollution. vehicle traffic. epidemiology. early pregnancy loss.

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São Paulo. Vol. 25, 2022

Original Article

DOI: http://dx.doi.org/10.1590/1809-4422asoc20200134r2vu2022L2OA

Introduction

Air pollution is defined by the World Health Organization (WHO) as the contamination of internal or external environments by any chemical, physical, or biological agent that modifies natural atmosphere characteristics, representing one of the main global environmental challenges today. This type of pollution is responsible for seven million premature deaths, 3.7 million of which are attributed to outdoor air pollution (WHO, 2014).

Air pollution is associated to decreased life expectancy and increased morbidity and mortality, mainly due to respiratory and cardiovascular diseases (DADBAKHSH et al., 2015; DASTOORPOOR et al., 2016; 2018; GOUDARZI et al., 2015; GOUDARZI et al., 2016; HASHEMI et al., 2014; KHANJANI et al., 2012; VAHEDIAN et al., 2017).

A review on particulate matter (PM) impacts on human health has demonstrated associations between exposure to this type of pollutant and several diseases, including premature deaths, hospital admissions, asthma attacks, chronic bronchitis, cancer, cardiovascular diseases and diabetes (KIM; KABIE; KABIR, 2015). Projections by the Organization for Economic Co-operation and Development indicate that particulate matter, one of the main types of air pollutants, will be the second cause of premature death in 2050 (OECD, 2012).

Consistent evidence indicates that maternal exposure to air pollution also contributes to increased risk adverse birth outcomes, *i.e.*, low birth weight (LBW) (PEDERSEN et al., 2013), prematurity (LI et al., 2016), fetal deaths (FAIZ et al., 2012), preeclampsia (DADVAND et al., 2013), intrauterine growth restriction (PARKER et al., 2005) and miscarriages (ENKHMAA et al., 2014; MORIDI et al., 2014; DASTOORPOOR et al., 2016; 2017; DI CIAULA; BILANCIA, 2015; GREEN et al., 2009; HA et al., 2018; HOU et al., 2014; LEISER et al., 2019; MORDI; ZIAEI; KAZEMNEJAD, 2014; PEREIRA et al., 1998).

Miscarriages are the most common pregnancy complication, ensuing in 6.5% to 21% of all pregnancies, with 75% of cases arising between the 7^{th} and 15^{th} pregnancy weeks. Its etiology is multifactorial and heterogeneous and still not fully understood and may result from genetic factors (chromosomal anomalies and gene mutations), exposure to environmental toxins (drugs and ionizing radiation) and infectious agents (viruses and bacteria) and uterine abnormalities (malformations, fibrosis and cervical insufficiency), as well as and other paternal and maternal factors, such as chronic diseases (BRASIL, 2009; 2011; 2012).

One systematic review of observational studies evaluated the effects of air pollution exposure on the occurrence of unfavorable reproductive outcomes. The findings suggest that exposure to air pollutants such as PM, carbon monoxide (CO) and cooking smoke may be associated with increased stillbirth and miscarriage risks. Exposure to PM_{10} throughout pregnancy was associated with increased miscarriage risks, while exposure to $PM_{2.5}$ and PM_{10} in the third trimester seems to increase the risk of stillbirths. Exposure to CO during the first trimester is associated with increased miscarriage risks, and during the third trimester, with increased stillbirth risks (GRIPPO et al., 2018).

Several studies have examined the effects of air pollution on human health through indirect exposure measures, such as vehicular traffic exposure. In this regard, different vehicular traffic indicators have been employed to characterize atmospheric pollution, *i.e.*, analyzing distances of certain places, such as homes or schools, to roads, assessing vehicle density or road length/density in census sectors or buffers, employing vehicle flows on roads of interest or using a combination of several indicators (HABERMANN; MEDEIROS; GOUVEIA, 2011).

The mixture of gases released by vehicle exhausts, secondary pollutants formed in the atmosphere, evaporative emissions from vehicles and non-combustion emissions (*e.g.*, road dust, tire wear) is termed traffic-related air pollution (TRAP). Exposure to vehicular traffic using only distance as an indicator consists of using a Geographic Information System (GIS) to map a place of interest and its distance to one or more traffic lanes (MATZ et al., 2019). The TRAP model assumes that vehicle emissions on roads approximate a Gaussian (normal) distribution and that 96% of pollutants emitted by vehicular traffic are dispersed within 500 feet (150 m) of the center of the road, *i.e.*, the greater the road flow, the greater the vehicular pollutant emission, thus increasing contaminant concentrations in the urban space, especially in homes close to the busiest roads (PEARSON; WACHTEL; EBI, 2000).

São Luís, the capital of the state of Maranhão, is home to 1,101,888 inhabitants and an estimated vehicle fleet of 402,961, the equivalent of almost one car for every 2.73 inhabitants. A 169% increase in the vehicle fleet in the capital of Maranhão was noted between 2006 and 2018 alone (IBGE, 2020). Furthermore, Maranhão ranked first in fire outbreaks among federated Brazilian units in 2019, and recent January 2020 data indicate a record of forty-five outbreaks in Maranhão municipalities, with seven fire *foci* (15.6%) in the Amazon Biome, 37 (82.2%) in the Cerrado Biome and one (2.2%) in the Caatinga (MARANHÃO, 2020).

Considering the above and the scarcity of studies regarding this issue in Brazil, this study aimed to estimate the prevalence of miscarriages in two different areas, one exposed to higher air pollution and one to lower, originating from different emission sources and stratified as a function of vehicular traffic in the city of São Luís, Maranhão, Brazil. The specific aims of the study were to identify sociodemographic/economic, socio-environmental/lifestyle and reproductive factors associated with miscarriages.

Methods

A cross-sectional study was carried out regarding miscarriages among women of childbearing age living in high (exposed) and low (control) air pollution exposure areas home to industrial activities and vehicle traffic during the first half of 2019.

Sampling area and period

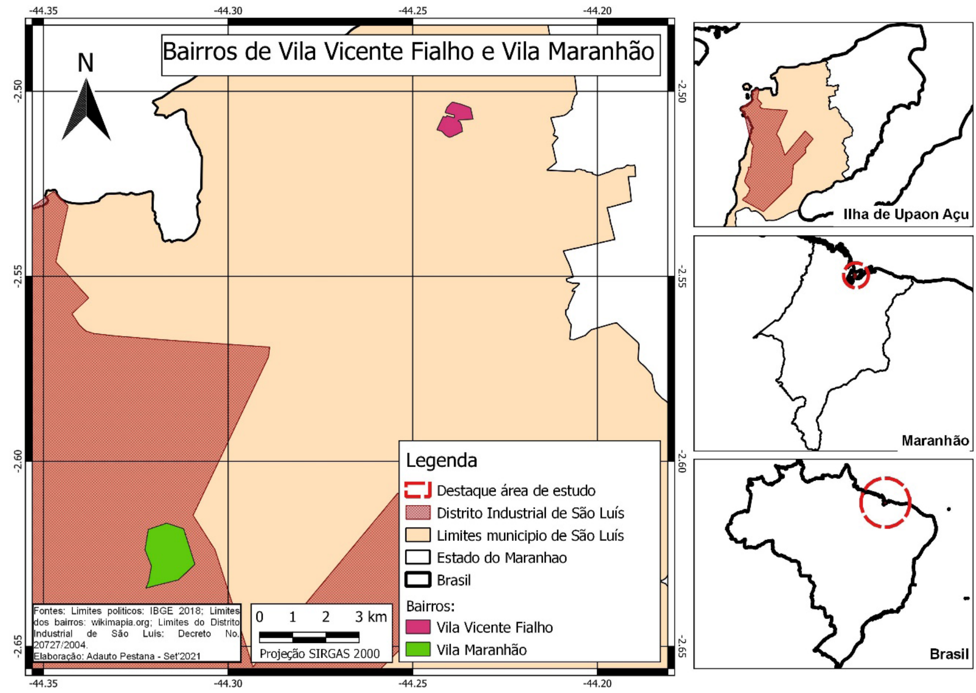
Two urban aggregation areas were chosen based on atmospheric pollution exposure during the first half of 2019. Vila Maranhão comprised the highest exposure area and Vila Vicente Fialho, the lowest (control). The following inclusion criteria for the study areas were considered: sociodemographic and economic similarities, one more intense

(Vila Maranhão) and one less intense (Vila Vicente Fialho) traffic lane and differential pollution levels due to industrial activities. Vila Maranhão, located on the banks of a BR highway, presents a greater flow of vehicles, both small, medium and large, throughout the day and week, while the flow is lower at Vila Vicente Fialho, higher during rush hours and lower on weekends, consisting of mainly small cars. In addition, the greatest traffic exposure coincides with an industrial district. A brief description of the selected areas follows:

1) Vila Maranhão (higher exposure area) – The Vila Maranhão community currently belongs to the Itaqui-Bacanga Sanitary District, located in the Industrial District of São Luís (Lat. 2° 37' 31'' S and Long. 44º 19' 04'' W). It is accessed through the BR-135 highway, located between the Federal Highway and the Carajás Railroad (EFC), comprising 6.48 km^2, located in the southwest region of the Island of Maranhão, approximately 22 km from the city center (Figure 1). The neighborhood comprises 1,494 households with 3,851 residents and is home to nineteen large and small industries according to a previous survey. Of these, four are fertilizer plants, three comprise cement and concrete plants, two industries extract sand, stone, gravel, two are asphalt plants, one is a thermoelectric plant which recycles oil, laminates, plastics, mortar, steel, logistics and one is a Vale company loading dock. Concerning air pollution, 51,452 annual tons of air pollutants have been estimated for this region, with an emphasis on PTS (79.06%), PM_{10} (55.28%) and $PM_{2.5}$ (45.81%), whose emissions are attributed to the local vehicle fleet (MARANHÃO, 2017; VIANA, 2015).

2) Vila Vicente Fialho (control/lower exposure traffic lane) – This neighborhood belongs to the Bequimão sanitary district, comprising a total of 1,093 households and 5,739 residents. No official records are available concerning industrial activities in this area (Figure 1).

Figure 1 – Areas selected for the study (higher and lower exposure to atmospheric pollution), São Luís, Maranhão



Source: The authors (2020)

Sample design

An alpha error of 0.05, reliability of 95%, relative risk of 2.0 and test power of 80% were considered for sample size calculations (LWANGA; LEMESHOW, 1991). A value of 17.7% was adopted as miscarriage rate in pollution-exposed areas (NOGUEZ et al., 2008). The sample parameters applied in this study are similar to an assessment that evaluated the same outcome in women living near an Industrial Park in the city of Rio Grande (RS), also in Brazil. Based on these factors, the calculated value was 180 women for each of our study groups (higher and lower exposures), totaling 360 participants. Participant selection was carried out by drawing lots from study participant homes considering the area covered by the local Family Health Strategy (ESF). First, streets were selected, followed by residences. Maps of the studied areas were consulted to this end, and the streets and houses of each area were then mapped. Data on women of childbearing age were obtained from the Basic Health Units in the high-exposure and control districts. Participants were recruited at their homes or, when absent, during Basic health Unit consultations.

Inclusion and exclusion criteria

Women of childbearing age (10-49 years), with at least one pregnancy and living a minimum of four years in one of the two study areas were included, while women who were not at home for three times during the home interview stage or who refused to participate in the study were excluded.

Study variables

Miscarriage self-reports in the previous year comprised the dependent variable of this study, defined by the Ministry of Health as the expulsion or extraction of a conception product weighing less than 500g and/or height of less than 25 cm, or less 22 weeks of gestation, with or without evidence of life (BRASIL, 2009; 2011).

Miscarriages were estimated by calculating the ratio between the number of women who suffered a miscarriage and the total number of interviewed women, and the total miscarriage prevalence was estimated at a 95% confidence interval.

The independent variables that made up the covariates of the study were as follows: block 1 (Sociodemographic and economic) - maternal age (years), maternal education (years), maternal employment (yes/no), maternal income (number of minimum wages), ethnicity (white/non-white), presence of a partner (yes/no) and paternal ethnicity (white/non-white); block 2 (Socio-environmental and lifestyles) - residence area (greater or lesser exposure), residence time (years), maternal smoking (yes/no), maternal alcohol consumption (yes/no), use of folic acid during pregnancy (yes/no), excessive consumption of coffee during pregnancy (yes/no), drug use (yes/no), distance from the source of traffic-related pollution (meters), paternal smoking (yes/no) and paternal alcohol consumption (yes/no) and block 3 (Reproductive) - parity (number of children), menarche (years), LBW history (yes/no), prematurity history (yes/no), stillbirth history (yes/no), age at first pregnancy (years), history of STI (yes/no), chronic disease (yes/no), violence during pregnancy (yes/no) and recurrent miscarriages (yes/no). These quantitative variables were dichotomized using the distribution median as the cut-off point, as they did not present a normal distribution.

Exposure to air pollutants was measured at two coverage levels, macro- and microexposure. Women who live in communities close to the industrial district of São Luís were considered exposed (macro-exposure). Residential proximity to traffic is an indirect exposure measure, used as a proxy for microexposure to traffic air pollutants.

To measure microexposure, the home addresses of each participant were consolidated using the web geolocation service available at https://pt.batchgeo.com/ and Google Earth. Inconsistencies in addresses provided by the participants were adjusted by comparisons using the free Open Street Maps database. The geolocation and distance calculations were performed in a free GIS environment, using the QGIS 3.10.1-A Coruña program. Individual exposure to traffic (microexposure) was evaluated by calculating the distances between participant home addresses and the nearest road with a large flow of vehicles. Thus, low exposure was considered for participants residing at 150 meters from a pollution source, and high exposure, less than 150 meters from a pollution source. In addition, distances from participant homes to the pollution source were stratified into categories and associated with miscarriage cases to assess the dose-response exposure gradient based on a review of validated methods to estimate pollution exposure (HABERMANN; MEDEIROS; GOUVEIA, 2011). Macro and microexposure effects were analyzed separately.

Sampling and data analysis

Data collection took place through household interviews in March, April and May 2019, using a structured research instrument developed by our group employing variables described in the literature on miscarriage, available in the supplementary material.

Concerning the exploratory analysis, variables were described according to their classification. Continuous variables were described by central tendency measures and dispersion, depending on their normality pattern, while qualitative variables were described by means of a simple frequency analysis and relative percentages. Due to the lack of normality of continuous variables, medians were used as a cut-off point for data dichotomization.

The strength of the associations between the miscarriage outcome and the assessed explanatory variables was measured by the Odds Ratio (OR) with a confidence interval of 95%.

A univariate logistic regression was used to obtain unadjusted odds ratios ($OR_{unadjusted}$). Variables with p values lower than 0.20 were maintained in the multivariate model to obtain the adjusted OR ($OR_{adjusted}$). Variables displaying statistical significance ($p<0.05$) or considered possible confounding variables regarding miscarriage were maintained in the final model. The Hosmer-Lemeshow goodnes of fit test was used to verify the goodness of fit between the variables of each block.

A simple logistic regression was performed to verify the relationship between distance from roads and intense vehicular traffic and miscarriages. Statistical analyses were performed using the STATA 15.0 program and sample calculations were performed employing the StatCalc application available in the Epi-Info 7 program.

Ethical aspects

This study was submitted and approved by the Dom Bosco Higher Education Unit (UNDB) Ethics Committee the under no. 3,138,034 and CAAE no. 05751118.8.0000.8707.

Results

Among the interviewed women with a history of at least one pregnancy, 57 reported at least one miscarriage in the previous year, an overall prevalence of 15.83% ($_{95\%}$CI 12.1% - 19.6%). A total of 180 participants resided in the higher exposure area, and 180, in the lower exposure area, with significantly different miscarriage prevalence values of 25.55% ($CI_{95\%}$ 19.2% - 31.9%) and 6.11% ($CI_{95\%}$ 2.6% - 9.6%), respectively ($p<0.0001$) and an 8.32-fold increased risk of miscarriage in the higher exposure area following the multivariate adjustment.

No significant differences between sociodemographic and economic variables were observed when comparing the high and low exposure groups.

The unadjusted effects of sociodemographic and economic variables on the miscarriage outcome indicated a significant association with low maternal education and low maternal income (Table 1).

Table 1 - Sociodemographic and economic factors associated by bivariate analysis (p<0.20) with miscarriage in women living in areas with higher and lower exposure to air pollution, São Luís (MA)

	Miscarriage		Bivariate Analysis	
Variable	**No**	**Yes**	**OR (CI95%)**	***p***
Maternal age (years)				
< 27.5	147 (81.67)	33 (18.33)	1.00	
≥ 27.5	156 (86.67)	24 (13.33)	0.68 (0.39 – 1.21)	0.195
Maternal education				
High school	245 (88.13)	33 (11.87)	1.00	
Elementary	58 (70.73)	24 (29.27)	3.07	<0.001
Maternal work				
No	211 (81.78)	47 (18.22)	1.00	
Yes	92 (90.20)	10 (09.80)	0.48 (0.24 – 1.00)	0.050
Maternal income (SW)*				
≥ 1	128 (93.43)	09 (06.57)	1.00	
< 1	175 (78.48)	48 (21.52)	3.90 (1.84 – 8.23)	<0.001
Ethnicity				
White	75 (80.65)	18 (19.35)	1.00	
Non-white	228 (85.39)	39 (14.61)	0.71 (0.38 – 1.32)	0.282
Partner presence				
Yes	265 (84.66)	48 (15.34)	1.00	
No	38 (80.85)	09 (19.15)	1.30 9 (0.59 – 2.88)	0.505
Paternal age (years)				
< 30	132 (83.02)	27 (16.98)	1.00	

≥ 30	171 (85.07)	30 (14.93)	0.86 (0.49 – 1.51)	0.596
Paternal ethnicity				
White	61 (83.56)	12 (16.44)	1.00	
Non-white	242 (84.32)	45 (15.68)	0.94 (0.47 – 1.89)	0.874

[a] Cut-off point based on the median of the distribution. OR: Odds Ratio; 95% CI: 95% confidence interval.
* SW (Minimum Wage). Source: The authors (2020)

Socio-environmental conditions and lifestyles were also positively associated with miscarriages, namely living in the high-exposure area, maternal and paternal smoking, maternal alcohol consumption and not using folic acid during pregnancy (Table 2).

Table 2 - Socio-environmental factors and lifestyles associated by bivariate analysis (p<0.20) with miscarriage in women living in areas with higher and lower exposure to air pollution, São Luís (MA)

	Miscarriage		Bivariate Analysis	
Variable	**No**	**Yes**	**OR (CI95%)**	***p***
Area				
Control	169 (93.89)	11 (06.11)	1.00	
Exposed	134 (74.44)	46 (25.56)	5.27	<0.001
Living time (years)				
< 12	142 (83.53)	28 (16.47)	1.00	
≥ 12	161 (84.74)	29 (15.26)	0.91 (0.51 – 1.610	0.754
Maternal smoking				
No	290 (86.31)	46 (13.69)	1.00	
Yes	13 (54.17)	11 (45.83)	5.33 (2.25 – 12.62)	<0.001
Maternal alcohol consumption				
No	277 (86.02)	45 (13.98)	1.00	
Yes	26 (68.42)	12 (31.58)	2.84 (1.33 – 6.03)	0.007
Folic acid use				
No	48 (72.73)	18 (27.27)	2.45 (1.29 – 4.63)	0.006
Yes	255 (86.73)	39 9 (13.27)		
Abuse of coffee				
No	182 (85.45)	31 (14.55)	1.00	

Yes	121 (82.31)	26 (17.69)	1.26 (0.71 – 2.23)	0.424
Drugs consume				
No	294 (84.48)	54 (15.52)	1.00	
Yes	09 (75.00)	03 (25.00)	1.81 (0.47 – 6.92)	0.383
Housing				
Brick house	276 (85.45)	47 (14.55)	1.00	
Others	27 (72.97)	10 (27.03)	2.17 (0.98 – 4.79)	0.054
Paternal smoking				
No	225 (88.58)	29 (11.42)	1.00	
Yes	78 (73.58)	28 (26.42)	2.78 (1.55 – 4.97)	0.001
Father alcoholism				
No	138 (87.34)	20 (12.66)	1.00	
Yes	165 (81.68)	37 (18.22)	1.54 (0.85 – 2.79)	0.146

[a] Cut-off point based on the median of the distribution. OR: Odds Ratio; 95% CI: 95% confidence interval. Source: The authors (2020)

Miscarriages were also associated with chronic disease, suffering from physical or psychological violence during pregnancy, a history of STI and recurrent miscarriages. Age at first pregnancy over 18 was considered a protective factor, reducing miscarriage risks by 44% (Table 3).

Table 3 - Reproductive factors associated by bivariate analysis ($p<0.20$) with miscarriage in women living in areas with higher and lower exposure to air pollution, São Luís (MA)

	Miscarriage		Bivariate Analysis	
Variable	**No**	**Yes**	**OR (CI95%)**	**p**
Parity				
< 2	97 (83.62)	19 (16.38)	1.00	
≥ 2	206 (84.43)	38 (15.57)	0.94 (0.52 -1.72)	0.845
Menarche age (years)				
< 13	147 (84.97)	26 (15.03)	1.00	
≥ 13	156 (83.42)	31 (16.58)	1.12 (0.64 – 1.98)	0.688
LBW history*				
No	275 (84.10)	52 (15.90)	1.00	

Yes	28 (84.85)	05 (15.15)	0.94 (0.34 – 2.56)	0.910
Prematurity history				
N0	272 (85.27)	47 (14.73)	1.00	
Yes	31 (75.61)	10 (24.39)	1.87 (0.86 – 4.07)	0.115
Stillbirth history				
No	293 (84.93)	52 (15.07)	1.00	
Yes	10 (66.67)	05 (33.33)	2.82 (0.95 – 8.57)	0.068
First pregnancy age (years)				
< 18	116 (79.45)	30 (20.55)	1.00	
≥ 18	187 (87.38)	27 (12.62)	0.56 (0.31 – 0.99)	0.045
STI history*				
No	278 (86.88)	42 (13.13)	1.00	
Yes	25 (62.50)	15 (37.50)	3.97 (1.93 – 8.13)	0.000
Chronic disease				
No	275 (86.48)	43 (13.52)	1.00	
Yes	28 (66.67)	14 (33.33)	3.19 (1.60 – 6.55)	0.001
Violence in pregnancy				
N0	281 (87.65)	41 (12.35)	1.00	
Yes	12 (42.86)	16 (57.14)	9.46 (4.18 – 21.41)	<0.001
Recurrent miscarriage				
N0	295 (89.39)	35 (10.61)	1.00	
Yes	08 (26.67)	22 (73.33)	23.18 (9.60 – 55.9)	<0.001

[a] Cut-off point based on the median of the distribution. OR: Odds Ratio; 95% CI: 95% confidence interval.
* LBW (Low Birth Weight) * STI (Sexually Transmitted Infection). Source: The authors (2020)

After the multivariate adjustment including variables with p<0.2, maternal alcohol consumption (OR=3.11, p=0.018), STI during pregnancy (OR=2.74, p= 0.033), living in the high-exposure Vila Maranhão area (OR=8.32, p<0.001), having suffered physical or psychological violence during pregnancy (OR=4.25, p=0.026) and repeated miscarriages (OR= 39.11, p<0.001) remained in the final model, whereas no sociodemographic and economic variables remained in the final model after the multivariate step.

The descriptive analysis concerning home distance from vehicle flow paths indicated 19 (10.56%) residences located less than 150 m from the pollution source in the Vicente Fialho neighborhood and 45 (25%) in Vila Maranhão. The minimum distance from roads was 0 m and the maximum, 4,898m, with a means of 672.28m, standard deviation of 626.35m and median of 549.5m.

Concerning distance from the pollution source, non-significant associations between miscarriages and greater exposure distances to vehicular traffic in the 250m (OR=1.41, p=0.28), 400m (OR= 1.47, p=0.17) and 500m (OR=1.46, p=0.20) strata were observed. The other distance strata were not associated to any of the study variables, even when 1,000, 2,000, 3,000, 4,000 and 5,000 m distances were tested. No significant relationship was observed between increased the number of miscarriages and proximity to the emitting source when emitting source distances were analyzed concerning dose-response effects in relation to miscarriages (Table 4)

Table 4. Relationship between distance from emission source and number of spontaneous abortions in 360 women of childbearing age, São Luís, Maranhão

	Number of miscarriages n (%)		
Distance from the emission source (m)	**higher exposure area**	**lower exposure area**	**Total**
<150	09 (19.57)	01 (09.09)	10 (17.54)
150 a 300	07 (15.22)	00 (00.00)	07 (12.28)
300 a 450	11 (23.91)	04 (36.36)	15 (26.32)
450 a 600	04 (08.70)	01 (09.09)	05 (08.77)
600 a 750	03 (06.52)	04 (36.360	07 (12.28)
750 a 900	12 (26.09)	01 (09.09)	13 (22.81)
Total	**46 (100.0)**	**11 (100.0)**	**57 (100.0)**

Source: The authors (2020)

Discussion

The present study estimated miscarriages rates and tested the hypothesis of a multifactorial causality of this outcome, indirectly emphasizing air pollution contributions as an important factor. After applying multivariate modeling, significant associations with maternal alcohol consumption, STIs during pregnancy, living in the greatest exposure area (Vila Maranhão), having suffered physical or psychological violence during pregnancy and repeated miscarriages were detected, demonstrating the predictive power of lifestyles and reproductive behaviors concerning miscarriages.

The overall miscarriage rate in our sample was 15.38%. No official statistics or population-based studies on miscarriage rates are available in Brazil, although a cross-sectional study on 2,700 women of childbearing age conducted by Correia et al. (2018) in the state of Ceará, Brazil, reported similar miscarriage rates, between 12.5% and 13.8.

Early pregnancy loss is the most common early pregnancy (first trimester) complication, ranging up to 31%, although this value can decrease to 10% when considering only clinically recognized losses, decreasing to 1% in the second trimester (MAGNUS et al., 2019; WYATT et al., 2005).

The miscarriage rate in the macroexposure area was 25.56%, higher than reported by Noguez et al. (2008), who estimated a 17.7% rate in women living near the Industrial Park in the city of Rio Grande (RS) when evaluating 285 women of childbearing age who lived for at least two years exposed to high pollution levels. These differences between the studies can be attributed to regional, socio-environmental differences, in wind dynamics, terrain topography and pollutant dispersion pattern.

The effects of urban air pollution exhibit complex and specific local characteristics, arising not only from specific pollutant sources, *i.e.*, industrial and economic activities, type of fuel, urban traffic, but also from dispersion conditions, including day and night, weekly and yearly dispersion-concentration cycles (MOREIRA; TIRABASSI; MORAES, 2008).

Atmospheric dispersion depends on the characteristics of the pollutants themselves, such as how they are emitted into the environment (vehicle exhaust fumes, high or low chimneys), weather conditions (wind direction and speed, rain, thermal inversions) and local topography characteristics. During the dispersion process, besides dilution, pollutants can also change as a result of their chemical reactivity, and particles can be removed from the air by deposition (due to gravity or rain) or interception by plants or other obstacles (MOREIRA; TIRABASSI; MORAES, 2008).

In addition to the epidemiological approach, exposure to air pollutants has also been linked to miscarriages in animal models. Mohallem et al., (2005), for example, demonstrated that female mice that grew up exposed to atmospheric pollution had a lower number of live births and exhibited a higher failure uterine implantation process rate. Other studies using mice exposed to air pollution in the pre- and post-pregnancy periods reported that pollutants such as $PM_{2.5}$, NO_2, CO and SO_2 in the atmosphere increase the time required for mating, decrease fertility rates and number of pregnancies and increase the number of post-implantation pregnancy losses, also causing morphophysiological placenta and umbilical cord alterations (VERAS et al., 2008; VERAS et al., 2009).

Concerning factors adjusted by the multivariate logistic regression according to miscarriage rates, living in the higher exposure area (Vila Maranhão) significantly increased the risk of miscarriages, whereas the adjusted measure of association (OR_{adjust}) indicated an 8-fold miscarriage risk increase for Vicente Fialho residents (control area).

Recent studies have also demonstrated that exposure to air pollution during pregnancy is both acutely (HA et al., 2017; LEISER et al., 2019) and chronically (HA et al., 2017) associated to miscarriages. Furthermore, even when pollutants are below maximum permissible levels, they may still cause harmful human health effects (GAVINIER; NASCIMENTO, 2014).

On the other hand, residential proximity to traffic (microexposure) was not significantly associated with miscarriages, refuting the hypothesis that proximity of up to 150 meters from a road with a high flow of vehicles increases the risk of this outcome.

Residential proximity to traffic is an indirect exposure measure used as a proxy for traffic air pollutant exposure, used mainly to characterize chronic exposure to these pollutants, given that residences may be continuously exposed, which would lead to gradual cumulative health effects over a person's lifetime (BRENDER; MAANTAY; CHAKRABORTY, 2011).

Results concerning links between residential proximity to traffic and miscarriages are controversial, first described by Green et al., (2009). These authors recruited pregnant women from a prepaid health plan in California into a prospective cohort study in 1990–1991, establishing traffic exposure measures for the 4,979 participants by using annual counts of daily averages of traffic near each participant home and home distances to major roads. The authors also reported no statistically significant associations between maximum annual average traffic up to 50 m and increased miscarriage risks in the general population.

In another prospective cohort, consisting of 19,309 women and a total of 35,025 pregnancies between 1990 and 2008 in 14 states in the United States, the distance of miscarriage cases from a high-traffic road was stratified into two categories, 0-199 meters and ≥ 200 meters. The authors indicate that living close to a main road was not associated with miscarriage risks (OR=1), regardless of the type of road (GASKINS et al., 2019). This may be attributed to the employed GIS methods, as some errors can occur when assigning exposure, due to address inconsistencies. This then requires manual adjustments, which may constitute a source of bias. Wind dynamics and geoclimatic factors may also explain the reported lack of associations, as they were not controlled for in that assessment. In addition, other polluting sources may also negatively affect the reproductive health of participants who suffered miscarriages. Besides methodological and logistical factors, other factors could also not be controlled in the analysis, including indoor pollution, total time women spend in their homes during pregnancy and pollution outside the neighborhood (transportation and occupational exposures). None of these parameters were considered, which could lead to issues regarding result interpretation.

Repeated miscarriages comprised the variable most strongly associated to the miscarriage outcome, increasing miscarriage risks 39-fold, although an overestimation trend was noted due to the low occurrence of this event. Similarly, a hospital-based case-control study conducted in Tubarão (SC, Brazil) also indicated that a previous history of miscarriage was associated with the miscarriage outcome following a multivariate factor adjustment (OR=2.14) (FRANÇA; SAKAE; KLEVESTON, 2018). Analogous results are also described in the literature, in which the chance for a history of previous miscarriages ranges from about 80% to almost 3-fold higher (BUSS et al., 2006; CHAVES et al., 2011).

Maternal alcoholism increased the risk of the miscarriage outcome 3-fold, observed in about 32% of women who miscarried in our sample. In another cross-sectional study on 433 adult puerperal women and their fetuses attending a public maternity hospital in Rio de Janeiro, from 1999 to 2006, 18.2% of women who used alcohol during pregnancy reported a history of miscarriages (FREIRE; PADILHA; SAUNDERS, 2009). The alcohol that the mother ingests during pregnancy crosses the placental barrier, also exposing the through maternal blood contact. Fetal alcohol exposure is higher due to a slower metabolism and elimination system, and the amniotic fluid remains impregnated with unmodified alcohol (ethanol) and acetaldehyde (an ethanol metabolite) (FREIRE et al., 2005).

Ethanol induces the formation of free oxygen radicals capable of damaging cellular proteins and lipids, which increases apoptosis and impairs cell divisions and specialization. Ethanol also inhibits retinoic acid synthesis, a substance that regulates embryonic development. The consumption of 20 grams of alcohol (500 mL of beer, for example) seems to be enough to suppress fetal breathing and movements (CHAUDHURI, 2000).

In addition, alcoholic beverage ingestion during pregnancy directly affects live births, due to to Fetal Alcohol Syndrome (FAS), characterized by central nervous system damage, resulting in neurological and craniofacial anomalies, prenatal and postnatal growth deficiency, behavioral dysfunctions and associated malformations. About 6% of women give birth to a child with FAS among alcoholics (FREIRE et al., 2005)

A total of 38% of women who suffered miscarriages in the present study reported the presence of a sexually transmitted infection (STI) during pregnancy, with a 2.74 risk of a miscarriage outcome. Oakeshott et al. (2002) evaluated the association between bacterial vaginosis or chlamydial infection and miscarriage before 16 weeks of gestation in a prospective community-based cohort, reporting the role of bacterial vaginosis as a miscarriage predictor after 13 weeks of gestation and a relative risk of 3.5 for this outcome. The main mechanisms by which infections can induce miscarriages include the production of toxins or cytokines (tumor necrosis factor alpha), which induce uterine contractions or damage to the fetal-placental unit, fetal infection, resulting in fetal death or risk of malformations, placental infection, with subsequent placental insufficiency and fetal death, chronic endometrial infection, interfering with embryo implantation, and amnionitis, which causes first-trimester miscarriages, as well as third-trimester preterm deliveries (GIOVANNI et al., 2011).

Pregnant women who reported having suffered some type of violence during pregnancy exhibited a 4-fold increased risk for miscarriages. Violence, whether physical, sexual, psychological or emotional, becomes even more serious when a woman is pregnant, with significant consequences for the health of the mother-child dyad, such as low birth weight, abortions, childbirth and childbirth. premature and even maternal and fetal deaths, according to the World Report on Violence and Health by the WHO (PAHO, 2002).

Some limitations are noted in our study. Exposure to air pollution was attributed as a function of the participants' zip code and, therefore, we could not measure air pollution at a lower aggregation level or total exposure in all daily activities. In addition, data on atmospheric pollutant concentrations are not public, under the responsibility of Organ state environmental agencies. Furthermore, we could not determine exactly the gestational age of the miscarried fetuses, so no tests concerning effect differences concerning exact gestation age at the time of exposure could be performed. Case classification errors are also a possibility, as spontaneous pregnancy losses during the first few weeks of pregnancy may not be reported if the woman is unaware of the pregnancy. These factors limit the absolute number of self-reported cases and may underestimate miscarriage rates.

Based on the design adopted herein, miscarriages were more prevalent in the higher air pollution exposure areas and some lifestyle and reproductive variables, such as maternal alcohol consumption, STIs during pregnancy, having suffered physical violence or psychological during pregnancy and repeated miscarriages comprise important predictors in the causal chain of this outcome.

Final considerations

Our findings point to a contribution of air pollution as a miscarriage predictor for women living in air pollution exposure areas, as reported previously in the literature.

Miscarriage-associated factor (maternal alcohol consumption, the occurrence of STIs during pregnancy, living in Vila Maranhão, having suffered physical or psychological violence during pregnancy and repeated miscarriages) effects may be amplified in the presence of atmospheric pollutants, bearing in mind that miscarriages comprise an outcome with socio-emotional and economic impacts.

In this context, improvements in the socioeconomic conditions of the studied population and strict monitoring of pollutant emissions could contribute to the reduction of adverse reproductive outcomes and the improvement of general health conditions.

Although some methodological limitations were identified, the association strengths between the miscarriage outcome and the investigated explanatory variables were high after a multivariate adjustment, contributing as evidence to environmental exposure as a risk factor for adverse reproductive outcomes.

The investigation of other variables, such as environmental exposure, may contribute to a better understanding of the multifactorial chain in miscarriage etiology and serve as a model for the development of primary prevention strategies through risk factor modifications. Furthermore, other types of observational designs, as well as the use of biomarkers and/or bioindicator species, may confirm the association between air pollutant exposure and the miscarriage outcome and aid in better understanding pollution effects on human health.

Acknowledgments

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) - Finance Code 001.

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Submitted on: 10/07/2020
Accepted on: 04/01/2022
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AMBIENTE & SOCIEDADE 25 anos años years

Exposição à poluição durante a gestação e ocorrência de abortamento espontâneo

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Resumo: Realizou-se um estudo transversal para estimar a prevalência de abortamento espontâneo em 360 mulheres distribuídas em área de maior e menor exposição à poluição atmosférica proveniente do tráfego de veículos na Ilha de São Luís-MA e identificação de variáveis associadas. As participantes foram entrevistadas e os dados coletados foram submetidos à regressão logística bivariada e multivariada. A prevalência geral de aborto espontâneo foi 15,83%, correspondendo a 25,56% (n=180) na área de maior exposição e 6,11% (n=180) na área de menor exposição. Associaram-se ao aborto espontâneo o etilismo materno (OR=3,11), a presença de IST na gestação (OR=2,74), viver na área de alta exposição (OR=8,32), ter sofrido violência física ou psicológica na gestação (OR=4,25) e a ocorrência de abortamento de repetição (OR=39,11). Os resultados apontam para uma possível contribuição da poluição do ar proveniente do tráfego de veículos como fator de risco na etiologia do aborto espontâneo.

***Palavras-chave*:** Aborto espontâneo; Poluição atmosférica. Tráfego veicular. Epidemiologia. Perda gestacional precoce.

São Paulo. Vol. 25, 2022

Artigo Original

AMBIENTE & SOCIEDADE
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SciELO

Exposición a la contaminación durante el embarazo y ocurrencia de aborto espontáneo

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Resumen: Se realizó un estudio transversal para estimar la prevalencia de aborto espontáneo en 360 mujeres distribuidas en un área de mayor y menor exposición a la contaminación del aire por el tránsito vehicular en la Isla de São Luís-MA e identificación de variables asociadas. Los datos recolectados en las entrevistas se sometieron a regresión logística bivariada y multivariante. La prevalencia general de aborto espontáneo fue de 15,83%, correspondiente al 25,56% (n=180) y 6,11% (n=180) en las zonas de mayor y menor exposición. Aborto espontáneo se asoció con consumo materno de alcohol (OR=3,11), la presencia de ITS durante el embarazo (OR = 2,74), vivir en el área de alta exposición (OR=8,32), haber sufrido violencia física o psicológica (OR=4,25) y la ocurrencia de abortos repetidos (OR=39.11). Los resultados apuntan a una posible contribución de la contaminación atmosférica por el tráfico de vehículos como factor de riesgo en la etiología del aborto espontáneo.

Palabras-clave: Aborto espontáneo; contaminación atmosférica; tráfico vehicular; epidemiología; pérdida precoz del embarazo.

São Paulo. Vol. 25, 2022

Artículo original