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RESEARCH ARTICLE

Association between high-risk pregnancy and environmental contaminants in the Metropolitan Region of Baixada Santista, Brazil

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Abstract

The Metropolitan Region of Baixada Santista (MRBS) is a highly contaminated area. High-risk pregnancy is one factor that leads to a higher chance of both morbidity and mortality of the mother-fetus binomial. The purpose of this study is to analyze the association between exposure to environmental contaminants and high-risk pregnancy. Case–control study, using a probabilistic and random sample composed of 201 high-risk pregnant women (cases) and 201 no high-risk pregnant women (control) followed up during prenatal care at a Public Hospital. The instrument used was a self-administered questionnaire. Contaminated areas data were obtained from the Environmental Company of the São Paulo State. The participants were georeferenced by their place of residence. Descriptive analysis, Chi-square test, and univariate and multiple logistic regression analysis were performed. The multiple logistic regression model demonstrated that living in a contaminated area (OR = 1.565; 95%CI: 1.033; 2.370), preterm delivery in the current pregnancy (OR = 1.989; 95%CI: 1.239; 3.194), and more than 35 years old (OR = 2.822; 95%CI: 1.692; 4.706) are factors jointly related to high-risk pregnancy. Environmental contaminants play an important role in high-risk pregnancy, and mitigating measures are needed to improve the environment and reduce high-risk pregnancy.

Keywords High-risk pregnancy · Case–control study · Logistic regression · Environmental contamination · Public health · Georeferencing

Introduction

High-risk pregnancy is one where previous, habitual, and obstetric disease in current pregnancy lead to a higher chance of maternal–fetal morbidity and mortality (São Paulo 2018). Among the most prevalent pathologies that lead to pregnant women being classified as high risk are sickle cell anemias, systemic arterial hypertension, and diabetes mellitus (Brasil 2019). Thus, it is necessary to have the presence of a professional qualified to identify the risk factors present in the woman's life history and to follow up the pregnant woman, from the beginning to the end of pregnancy, in order to ensure healthy development, without tragic outcomes, which is one of the functions of prenatal care (PNC) (Tomasi et al. 2017).

According to the Ministry of Health (Brasil 2019), the pregnant woman assisted by the Unified Health System in Brazil (SUS), in her first medical consultation, will be classified as habitual, intermediate, or high-risk pregnancy. The

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first two categories (habitual and intermediate) are followed up at the Basic Health Unit (UBS), and the high-risk pregnant women are referred to specialized services. Throughout the PNC, if some unfavorable outcome trends are observed, both for the pregnant woman and for the conceptus, the pregnancy is directed to the high-risk PNC, where she will have the most appropriate assistance for her situation.

No pregnancy is the same, so it is of paramount importance to observe risk factors in a timely manner in order to not compromise the pregnant woman, fetus, and family bonds. The Ministry of Health (Brasil 2019) adapted the social health determinant model by Dahlgren and Whitehead (Buss and Filho 2007; Carrapato et al. 2017) to identify the risk factors to which a pregnant woman is exposed in order to reduce maternal and fetal mortality and morbidity. The Dahlgren and Whitehead (Buss and Filho 2007; Carrapato et al. 2017) determinants are proximal (individuals' lifestyle), intermediate (social and community networks), and distal (general socioeconomic, cultural and environmental conditions) (Brasil 2019).

Regarding the environment, the Sustainable Development Goals (SDGs) "Transforming Our World: The 2030 Agenda for Sustainable Development" highlight the goals of significantly reducing the release of chemical contaminants into air, water, and soil, minimizing their negative impacts on human health and the environment (USEPA 2015).

For environmental contaminants, there are no borders because they can quickly spread to all parts of the world; in the Metropolitan Region of Baixada Santista (RMBS), the port, trucks, industries, wind, and tide are responsible for its dispersion. The RMBS (Fig. 1) is in the central area of the State of São Paulo coast. Its territory is one of the oldest areas with urban occupation in Brazil, dating back to the sixteenth century and composed of nine municipalities: Peruíbe, Itanhaém, Mongaguá, Praia Grande, São Vicente, Cubatão, Santos, Guaruja, and Bertioga. It encompasses localities with good levels of wealth, which are not reflected in social indicators and environmental quality (Carriço and Saleme 2018) .

The Environmental Company of the State of São Paulo (CETESB), attentive to the SDGs, is responsible for the implementation of environmental and sustainable development policies in the State of São Paulo. According to CETESB, Santos and Cubatão are the sixth highest contaminated areas among the 45 studied areas in the State of São Paulo (CETESB 2018a).

Studies show the relationship between living in a contaminated area and problems caused to the reproductive system such as abortions, prematurity, low birth weight, and the decrease in the number of pregnancies in people living in contaminated areas (Sun et al. 2020; Mandakh et al. 2020; Hu et al. 2020; Mansouri and Reggabi 2021; Novelli et al. 2021). At RMBS, Guimarães et al. (2015) also related contaminated areas and problems in the reproductive system and reinforcing the need for further studies in the estuary region of Santos and São Vicente. Other studies conducted at RMBS have demonstrated the relationship between homes in contaminated areas and the occurrence of liver diseases (Carvalho et al. 2015), hypertension (Ribeiro et al. 2016), and breast cancer (Montanha et al. 2020); however, little is known about the effects of maternal exposure to environmental contaminants that may be leading to high-risk pregnancy.

In view of the above, this study aimed to evaluate the relationship between exposure to environmental contaminants and high-risk pregnancy in residents of RMBS.

Methods

This is a 1:1 case–control study, where the case group was composed of high-risk pregnant women, and the controls were pregnant women, without injuries or diseases, who were not diagnosed as high-risk pregnancy attended in the

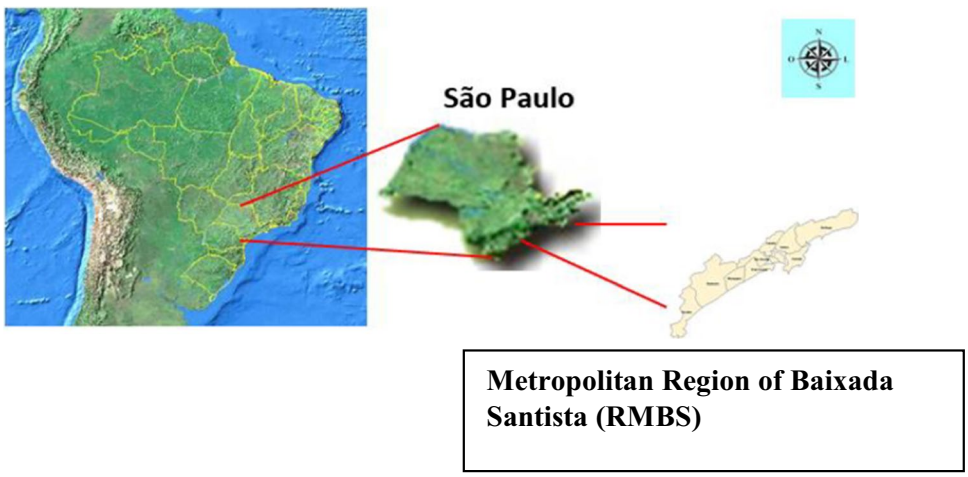

Fig. 1 Metropolitan Region of Baixada Santista

SUS at one RMBS public maternity. This site was chosen because all pregnant women were submitted to the same classification protocol and because it attended all RMBS municipalities.

The sample size calculation was performed based on the Bernoulli distribution, and considering the chance of risk pregnancy in 50%, a power of 80%, a significance level of 5%, and a delta of 5%, that is, the prevalence of pregnancy risk can vary between 45 and 55%. Based on this information and adding 20% due to losses, it was necessary that 402 pregnant women would be needed, and the sample was stratified with $n = 201$ pregnant women in each group (case and control). As inclusion criteria, the pregnant woman would be over 18 years of age, without alcohol and smoking habits (Campbell et al. 1995). A self-administered questionnaire was used, adapted for this project, which was pre-tested in order to ensure its consistency and reliability. The first step was the testing of the questionnaire, being applied at two different moments with an interval of 1 week in the 30 pregnant women. Kappa tests were used to assess the agreement in the answers, and Cronbach's alpha test was used to assess the internal consistency of the questionnaire. The Kappa test showed that the questions were adequate and with good understanding (Kappa = 0.95; $p < 0.001$), and Cronbach's alpha test showed that the questionnaire presented adequate internal consistency (Cronbach's alpha = 0.92, $p < 0.001$). The group of interviewers was previously trained and supervised.

At the end of the collection, which was carried out between February 2018 and March 2019, some municipalities only referred the cases, not having enough control for pregnant women to pair. Of the 9 nine municipalities of the RMBS, we ended up with 5 to be able to carry out the type of research proposed for a control; among the municipalities studied were Cubatão, Guaruja, Praia Grande, Santos, and São Vicente.

The questionnaire consisted of questions grouped into modules: Identification of the pregnant woman: address, age, color/race, marital status, time of the study, occupation time of residence, and number of rooms; Obstetric history: number of pregnancies, abortions, cesarean sections, and other risk factors that reinforce the diagnosis of referral to high-risk prenatal care; and Data on current pregnancy: planning, whether it is single or twin; beginning of prenatal care; number of consultations, normal tests, and tests performed during this period; guidance on childbirth; and possible risks.

Through the addresses informed by the pregnant women themselves through the questionnaire, the geocoding (Barcellos et al. 2008) of these addresses was performed to obtain the coordinates in Universal Transverse Mercator Projection (UTM) referenced to the SIRGAS 2000 Geodesic Reference System. CETESB through the contaminated area sheets (CETESB 2018a) provides the coordinates of such areas also in UTM projection; however, referenced to several Geodesic Reference Systems, thus being necessary the transformation of these coordinates to SIRGAS 2000.

The test and control cases were georeferenced by the residence of the pregnant women and cross-checked by the contaminated areas, placed in the QGIS version 3.4.9 software, and transformed into a point-in-point vector file in shapefile format. From these vector files with punctual features, it was possible to perform the spatial study with the objective of verifying the incidence of cases (tests and control) in the vicinity of contaminated areas (Resendes et al. 2007).

For this, in the QGIS software, the buffer tool was used to generate areas of influence with 1 km of radius of the contaminated areas. The areas of influence (buffer) allow verifying which of the pregnant women reported addresses that were within this radius. Along with the incidence in an area of influence, the time of residence factor of 3 or more years was used as an analysis parameter. Therefore, pregnant women who reported living for at least 3 years within the areas of influence of contaminated areas were considered residents of contaminated areas.

Descriptive analysis of all study variables was performed. The variables were transformed into qualitative and presented in terms of their absolute and relative values (Callegari-Jacques 2003), divided into socioeconomic data; scanners related to obstetric history, obstetric scans; and types of contaminants in contaminated areas. To evaluate the association between qualitative variables, the Pearson Chi-square test or Fisher's exact test (Contador and Senne 2016) was used.

The univariate and multiple logistic regression models were used to evaluate the risk factors for high-risk pregnancy. They were grouped to independent variables by the similarity of characteristics (socioeconomic, obstetric factors, environmental contamination risk factors classified by CETESB), and these variables to which they presented a value of $p < 0.20$ in the univariate analysis were included in the multiple models of each block. The following were significant variables per block that obtained $p \leq 0.05$ in the multiple models for the final logistic regression model (Kleinbaum et al. 2013). The tabulation was performed through the EXCEL program, and for the analysis, the Statistical Package for the Social Sciences (SPSS version 24) was used. The significance level was 5%.

The project was approved by the Research Ethics Committees of the Catholic University of Santos meeting the terms of CNS Resolutions 466/2012 and 510/16 of the National Health Council (Approval number: 79306417.0.0000.5536). All pregnant women who participated signed the Free and Informed Consent Form immediately after receiving detailed information about data collection. There were non-financial competing interests.

Results

In this study, the majority of the pregnant were aged between 18 and 34 years, had brown color, studied beyond elementary school, and were housewives (Table 1). The pregnant who worked were predominantly in the commerce, had a workload of up to 40 h per week, considered the sites appropriate, and did not manipulate fungicides, herbicides, insecticides, varnish, oil paint, solvents, glues or adhesives, acids, or abrasives.

Table 1 Descriptive analysis of socioeconomic and housing data of pregnant women living RMBS per risk group

Variables	Control *N* (%)	Case *N* (%)	*p* value[&]
?Age (years)			
≥ 35	27 (13.4)	62 (30.8)	˂0.001
18–34	174 (86.6)	139 (69.2)	
Race			
White	91 (45.3)	81 (40.3)	Fisher 0.229
Black	12 (6.0)	18 (9.0)	
Brown	95 (47.3)	98 (48.8)	
Asiatic	1 (0.5)	4 (2.0)	
Indigenous breed	2 (1.0)	-	
Studied beyond elementary school			
No	26 (12.9)	25 (12.4)	0.881
Yes	175 (87.1)	176 (87.6)	
Ocupação			
Housewife	112 (55.7)	106 (52.7)	0.548
Works out of the house	89 (44.3)	95 (47.3)	

[&]Chi-square test and Fisher accurate test

Georeferencing presents the results obtained from cases and controls that were within the buffer and of these how many were considered in contaminated areas, that is, with length of stay greater than or equal to 3 years (Fig. 2). With this, we were able to differentiate pregnant women who lived in a contaminated area or not, both for the cases and for the controls. Most cases resided in contaminated areas, defined by CETESB, and were exposed to automotive fuel and aromatic solvents.

Regarding the reproductive profile, most pregnant women had less than 4 pregnancies; the current pregnancy was unique and unplanned; the PN was started before 12 weeks of gestation, with 7 or more prenatal consultations; they were normotensive, with normal glycemia, had no syphilis, and no HIV nor urinary infection. They were instructed about the place of delivery ($p < 0.001$) and considered their PN care between excellent and good ($p < 0.001$). Hypertensive syndrome, diabetes mellitus (DM), or both (71%) predominated in high-risk pregnant women ($p < 0.001$).

In the univariate and multiple logistic regression model (Tables 2 and 3) were observed 3 times more likely to have high-risk pregnancy if they were over 35 ($p < 0.001$) years of

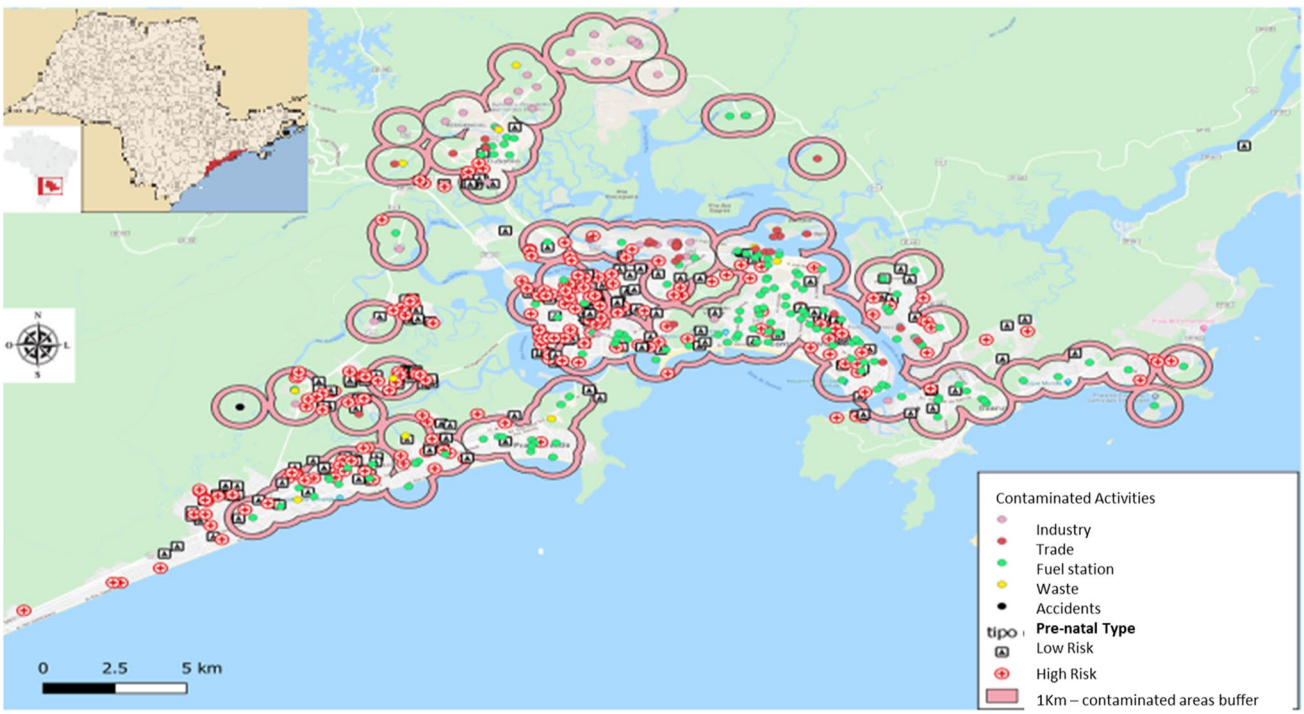

Fig. 2 Metropolitan Region of Baixada Santista with the activities of contaminated areas, low-risk, and high-risk pregnancy

Table 2 Analysis of reproductive risk factors in high-risk pregnancy

	Univariate			Multiple	
	OR	95%CI	*p* valor	OR	95%CI
Number of pregnancies					
More than 4	2.324	1.442–3.747	0.001	2.288	1.407–3.719
≤3	1	-		1	-
Previous abortions					
Yes	1.630	1.053–2.522	0.028		
No	1	-			
Cesarean					
Yes	1.667	1.110–2.505	0.014	-	-
No	1	-			
Preterm delivery in the current pregnancy					
Yes	2.004	1.263–3.178	0.003	1.853	1.156–2.971
No	1	-		1	-
More than 7 PN queries					
No	1.992	1.193–3.327	0.008	1.957	1.157–3.308
Yes	1	-		1	-

OR, odds ratio; *95%CI*, 95% confidence interval

Table 3 Logistic regression analysis of variables related to environmental contaminants found in the Metropolitan Region of Baixada Santista

	Univariate		
	OR	95%CI	*p* value
Live in contaminated area			
Yes	1.615	1.080–2.414	0.020
No	1	-	
Gas station activity			
Yes	1.824	1.170–2.844	0.008
No	1	-	
Aromatic solvents contaminant			
Yes	1.779	1.153–2.746	0.009
No	1	-	
Automotive fuel contaminant			
Yes	1.683	1.106–2.563	0.015
No	1	-	

OR, odds ratio; *95%CI*, 95% confidence interval

age (OR = 2.875; 95%CI:1.737–4.758) and 4 pregnancies or more pregnancies ($p < 0.001$). The univariate risk factors for high-risk pregnancy were having had less than 7 PNC visits ($p = 0.012$); having had a threat of premature labor in the current pregnancy ($p = 0.010$); living in contaminated areas ($p = 0.020$), with activity that led to contamination being fuel station ($p = 0.008$); and having as main exposure to aromatic solvents ($p = 0.009$) and automotive fuel ($p = 0.015$).

In the final multiple logistic regression model, where all variables selected in the univariate model were included, it was observed that living in contaminated areas, having had a threat of premature labor, and being 35 years of age or older (Table 4), are jointly important risk factors to be considered in high-risk pregnancy.

Discussion

This study demonstrated that being over 35 years of age is a risk factor for high-risk pregnancy; this profile of pregnant women over 35 years of age has been observed in Brazil, where between 2008 and 2018, there was an increase of 57.05% of births of mothers over 34 years of age, similar to the growth of 41.98% of pregnant women aged 34 years or older in RMBS (Brasil 2021). Today, women tend to become pregnant at an older age; this postponement of pregnancy causes age to increase the risk of chromosomal changes in the fetus; cardiovascular and metabolic diseases, such as hypertension, diabetes, and obesity; neoplasms; and fetal deaths (Brasil 2019). Therefore, it is important to monitor this group before it is even pregnant (Xie et al. 2020). Unfortunately, in our study, 69.7% of controls and 55.7% of cases did not plan this pregnancy.

The problem of having had 4 or more pregnancies lies in the risks of complications during pregnancy and in the course of labor, such as decreased muscle tone, resulting in the pendulum abdomen, which leads to dystocia, due to problems in fetal presentation (Montenegro and Rezende 2018) .

Having performed 7 or fewer PN consultations has shown to be a risk factor for high-risk pregnancy in the univariate model This only confirms the importance of good control in the PN—the more opportunity to see the pregnant woman, the greater the chance of detecting any problem earlier, although nowadays the quality of consultations is more relevant than the number of them, with the professional having due attention to timely care and the team paying attention to the absences of pregnant women in the consultations and trying to verify the reason and, if necessary, make home visits (São Paulo 2018). Mario and collaborators (2019) agree that the quality of PN is not only measured by the number of consultations, but when it started, the requested

Table 4 Analysis of the final multiple risk factors for the high-risk pregnancy

	OR	95%CI
Living in a contaminated area	1.565	1.033–2.370
Preterm delivery in the current pregnancy	1.989	1.239–3.194
More than 35 years old	2.822	1.692–4.706

OR, odds ratio; *95%CI*, 95% confidence interval

tests, pressure, and weight verification. These items had high percentages in our study.

The pregnant women in this study considered the PN between excellent and good, but some of them had less than 7 consultations; this is a problem in these pregnant women, given that 71% of the cases had diseases such as diabetes, hypertension, or both, and this may have been one of the reasons that led to premature labor, which could have led pregnant women to have 7 consultations or less of PN.

Preterm labor is when contractions and uterine cervix modification occur before 37 weeks of gestation (Brasil 2016). The time of pregnancy is important for the fetus, not influencing the body of the pregnant woman. Thus, depending on the very distant prematurity of 37 weeks, we will have a low-weight newborn with immature organs for the functions they should perform after birth. (Montenegro and Rezende 2018). Many factors lead to preterm delivery, among them we have maternal age, access to inadequate PN, gestational diabetes, and gestational hypertension (Brasil 2019); all those mentioned were found in this study.

Albrecht et al. (2019) report that there is a difference between the concepts of hypertensive pregnant women because they are generally premature and underweight, different from pregnant women with diabetes, where the conceptus is large for gestational age and can reach a more advanced gestational age.

According to the Brazilian Guidelines on Arterial Hypertension–2020, to be considered gestational hypertension, making the manual verification (gold standard), with two measures altered in an interval of 4 h, with systolic pressure equal to or greater than 140 mmHg (millimeters of mercury) and/or atolic greater than or equal to 90 mmHg. Preeclampsia is the presence of altered pressure from the 20th week of gestation, with or without increased proteinuria or more severe signs; and eclampsia, when it causes convulsion without another defined cause (Barroso et al. 2021).

Some scientific evidence that has been studied and proven in people who had a higher risk of having hypertension is in relation to exposure to environmental contaminants such as lead, drought seasons, and having preeclampsia (Moyene et al. 2016); cadmium in high concentrations (Pinheiro Júnior et al. 2020); air pollutants (Chuang et al. 2017); preeclampsia and small fetuses for gestational age (Mandakh et al. 2020); exposure to PM2.5 (Sun et al. 2020), mainly in the first and third trimesters of pregnancy can lead to hypertensive disorders during pregnancy (Zhang et al. 2020a).

As in hypertension, diabetes mellitus can occur before or during pregnancy. The Brazilian Diabetes Society reports that genetic, biological, and environmental factors are listed among the genetic, biological, and environmental factors (Forti et al. 2019).

Regarding environmental factors and diabetes during pregnancy, studies have shown the association between exposure to environmental contaminants mainly in the 1st trimester of pregnancy (Zhang et al. 2020b); biocides (DDE and HCB) (Mansouri and Reggabi 2021), dioxins (Novelli et al. 2021), metals such as cadmium (Cd) and limit, lead (Pb) (Soomro et al. 2019); living in places with large vehicle displacements (Choe et al. 2018); exposure to increases in the level of PM2.5 in the second trimester (Choe et al. 2019); increase in the level of nitrogen dioxide (NO2) in the first trimester (Hu et al. 2020); and exposure between 3 months before pregnancy and the first trimester of benzene pregnancy (Williams et al. 2019).

Benzene is one of the components of gasoline; according to Fonseca et al. (2017), gasoline is chemically composed of hydrocarbons containing aromatic solvents such as benzene, toluene, ethylbenzene, and xylees (BTEX), as well as other mixtures that can also contaminate the environment. For Lima et al. (2017), in Brazil, we have the mixture of ethanol in gasoline, which can lead to greater damage, due to higher concentrations when leakage occurs, due to the increased solubility of BTEX in water.

One of the sources of contamination of RMBS are fuel stations, and exposure to substances from gas stations is a relevant risk factor for high-risk pregnancy.

The fuel stations have storage tanks and supply pumps that can emit saturated vapors, various types of volatile aromatic hydrocarbons, which are inside the underground tanks of the station, as well as in the tanks of the vehicles, which come out to enter the liquid fuel in the supply. Another way is the lack of conservation of submerged tanks that can lead to the contamination of soil and groundwater; in addition, their vapors (volatile organic compounds (VOC)) can rise through the soil exposing the population around them. These gas stations are located in Brazil in commercial and residential areas, which can cause risks to the health of the workers of these establishments and the residents around them (Sousa 2015; USEPA 2015; Fonseca et al. 2017).

Terrés and collaborators (2010) had already described that there is a difference between pollutants released around the gas stations (unburned gasoline) and that which is emitted in urban air due to traffic. The high environmental temperatures, the architectural elements around the post, direction, and wind speed influenced the concentration of n-hexane and benzene in two of the posts surveyed, concluding that the population within a radius of 100 m is influenced specifically by the gas station. Alenezi and Aldaihan (2019) analyzed fuel distribution stations in Kuwait and nearby residences, and agree with Terrés and collaborators (2010) regarding total BTEX dispersion being higher in a wind-favor location.

According to the report of Vehicle Emissions in the State of São Paulo, the emission of VOC by exhausts and evaporative are controlled, helping to lower their allowed maximum limits. In 2017, despite the reduction of the

vehicular emission of VOC in the RMBS, the large circulation of trucks in the port and Cubatão was not considered, thus requiring the reduction of these pollutants in this region. But VOC during fuel supply is not controlled in Brazil, projecting a growth of this type of volatile compound according to the fleet and the type of fuel used (CETESB 2018b).

Although 97% of the contaminated areas referenced by (CETESB 2018a) in RMBS have compromised groundwater, CETESB does not monitor due to water salinity and difficulty in maintaining the equipment used for this control (CETESB 2018c), preventing the true radius of compromise.

Concerning the constant monitoring of air quality, it would also not be possible to be compared in this study. This is because in 2017, there were only five fixed monitoring points for air quality assessment in RMBS, two in Santos and three in Cubatão, two more mobile monitoring, one in Cubatão and another in Guaruja. The other municipalities of the RMBS do not have air quality monitors (CETESB 2020).

Although the SDGs have set a target by 2020 to achieve environmentally healthy management of chemicals and all wastes throughout their entire life cycle, according to agreed international frameworks, and significantly reduce their release to air, water, and soil to minimize their negative impacts on human health and the environment (Assembly 2015), what was observed in this research is that we still have much to go on.

Conclusion

Therefore, living in contaminated areas, preterm delivery in the current pregnancy, and being 35 years or older are risk factors strongly associated with high-risk pregnancy. Actions to avoid exposure to chemical pollutants present in environmental compartments, both in the prenatal program and in the environmental surveillance in health of contaminated areas, may contribute to reduce the morbidity and mortality of the mother-fetus binomial.

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Author contribution JMPAF was responsible for the conceptualization, data curation, formal analysis, investigation, project administration, and methodology and was a major contributor in writing the manuscript.

YAPP was responsible for formal analysis and contributor in writing and editing the manuscript.

JAV was responsible for geo-referenced analysis and data curation.

ARP was responsible for data curation and investigation.

CLAB was responsible for making the critical review.

ALFB was responsible for conceptualization, methodology, and critical review.

LCM was responsible for the conceptualization, data curation, formal analysis, project administration, and methodology and was a major contributor in revision and edition of the manuscript.

Data availability The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate The project was approved by the Research Ethics Committees of the Catholic University of Santos meeting the terms of CNS Resolutions 466/2012 and 510/16 of the National Health Council (Approval number: 79306417.0.0000.5536). All pregnant women who participated signed the Free and Informed Consent Form immediately after receiving detailed information about data collection. There were non-financial competing interests.

Consent for publication All authors read the final version of the manuscript and approved it.

Competing interests The authors declare no competing interests.

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