

# Influence of environmental contamination on pregnancy outcomes

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**Abstract** This study aims to compare pregnancy outcomes in four contaminated areas to those observed in a non-contaminated area of similar socioeconomic status. A cross-sectional study was carried out. A structured and pre-tested questionnaire was administered to population-based samples of 788–920 families in each of the five studied areas. The exposure assessment used was an ecological measure. Using logistic regression, odds of several pregnancies outcomes (pregnancy occurrence, miscarriage, stillbirth, prematurity, low birth weight, congenital malformation, and multiple births) were estimated after adjustment for potential confounders such as socioeconomic, demographic, and substance abuse factors. We adopted a statistical significance level of 5 %. In three of the four exposed areas, pregnancy occurrence was reduced in comparison to the control area (Area 2, odds ratio (OR)=0.68, 95 % CI=0.54–0.86; Area 3, OR=0.76,

95 % CI=0.60–0.97; Area 4, OR=0.71, 95 % CI=0.56–0.90). Also, a significantly increased odds of miscarriage for living in Area 3 (OR=1.83, 95 % CI=1.07–3.12) was found. The other pregnancy outcomes were not significantly elevated in the exposed areas. In conclusion, this study shows evidence of reduced pregnancy occurrence and increased miscarriage occurrence in some of the contaminated areas, compared to the control area.

**Keywords** Pregnancy · Miscarriage · Stillbirth · Preterm birth · Low birth weight · Congenital malformation · Multiple births · Environmental pollution

## Introduction

The Santos and São Vicente Estuary region is located southeast in São Paulo State, Brazil, inside the Santos metropolitan area, and represents an important example of environmental degradation by industrial pollution along the Brazilian coast. This estuary region hosts a large number of petrochemical, steel, and fertilizer production plants since the 1950s. According to the Environmental State Agency—CETESB, this industrial activity has contaminated the Santos and São Vicente Estuary mainly with dust, heavy metals, organochlorine compounds, polychlorinated biphenyls (PCBs), polycyclic aromatic hydrocarbons (PAHs), dioxins, and furans (CETESB 2001).

Epidemiology has provided evidence that fetuses, newborns, and children are probably more sensitive to environmental toxic substances than adults (Bosetti et al. 2010). Until recently, it was believed that low-level chemicals exposure in everyday life did not pose a risk for fertility, reproduction, or development. However, environmental toxins exposure may interfere in fertility and pregnancy outcomes, even before conception (Nieuwenhuijsen et al. 2013; Chalupka and Chalupka 2010).

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The literature has been evaluating risks to health arising from fetal environmental contamination. Identification of risk factors for the pregnant woman and her fetus is imperative for reducing fetal and neonatal morbidity and mortality (Leite and Schüller-Faccini 2001).

This study aimed to investigate the associations between several pregnancy outcomes (pregnancy occurrence, miscarriage, stillbirth, premature birth, low birth weight, congenital malformations, and multiple births) and living in contaminated areas of the Santos and São Vicente Estuary region.

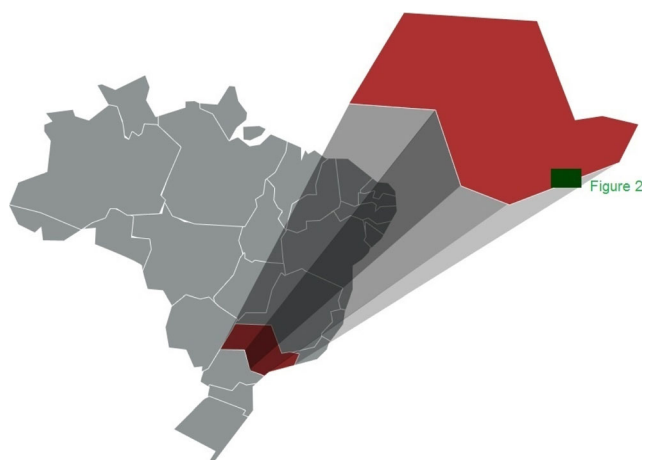
**Material and methods**

**Design**

This cross-sectional study was part of a larger and extensive project entitled “Epidemiological study on resident population in metropolitan area of Santos – Santos Estuary: Evaluation of effect and exposure indicators to environmental contaminants” whose aims were to estimate health effects associated with exposure to environmental contaminants among residents of Santos metropolitan area—Santos and São Vicente Estuary (Fig. 1).

**Selected areas and population sample**

Five areas were selected with similar socioeconomic status and access to health, education, and mobility services according to the Brazilian Institute of Geography and Statistics (IBGE), four in contaminated areas and one as control. Based on the report “Santos and São Vicente Estuarine System” of CETESB (2001), which aimed to assess water, sediment, and aquatic organisms contamination in Santos and São Vicente estuary and Santos Bay, contaminated areas were identified and used as an ecological measure of exposure.



**Fig. 1** Study area in São Paulo State, Brazil

The Area 1 was Água Fria and Pilões communities in Cubatão city, areas with an irregular industrial landfill (waste deposition area without protective measures to the environment and public health) and a petrochemical landfill. Area 2 was Cubatão city center, an area near the industrial pole of Cubatão city. Area 3 was the continental area of São Vicente city, an area with irregular chemical and pesticides industry landfills. Area 4 was Vicente de Carvalho region, in Guarujá city, an area near chemical industry and port. Area 5 (control area) was in Bertioga city, without evidences of environmental contamination and with *similar* socioeconomic profile of other areas (CETESB 2001).

The criteria used by CETESB to establish if the pollutants concentration found in fresh water sediment samples (Area 1 and 2) or in brackish water sediments samples (Area 3 and 4) around an estuary region were above or below the limits to cause adverse effect on the biological community were based on the Canadian Environmental Quality Guidelines (Environment Canada 1999) (Table 1).

Exposed and non-exposed population samples in each area were estimated based on the most rare studied event, congenital malformations prevalence in Brazil and resident population by census district in neighborhoods as the 2000 IBGE census. Thus, 820 families were randomly selected from a database constructed from the count of residences conducted in each neighborhood included in the study (Fig. 2).

**Data information**

A structured questionnaire was applied personally in each residence. Interviewers were trained to ensure uniform application of the questionnaires, and they were supervised by field managers. The questionnaire was adapted to the study needs based on the morbidity questionnaire developed by researchers from National Cancer Institute—INCA (INCA 2003) and pre-tested in order to ensure consistency and applicability. The approach strategy in the selected households was to invite all residents to participate, including children and adults. The key informant had to be at least 18 years old and was able to *provide* accurate and detailed information *on* each other residents.

Interviews were conducted during weekends to avoid selection bias from January 2006 to June 2008 and everyone in the household was invited to participate giving additional personal information. The questionnaires application was supervised by a field manager with experience in similar work and responsible for periodic interviewer’s evaluation and systematic verification of the questionnaires *response* quality.

Data from childbearing age women, between 15 and 49 years old (as classified by the Brazilian Institute of Geography and Statistics—IBGE) were analyzed (Table 2). Pregnancy occurrence and pregnancy outcomes prevalence in the last 5 years were calculated for each area. Pregnancy

**Table 1** Ecological measure of exposure assessment in contaminated areas

|   | Area 1 | Area 2 | Area 3 | Area 4 |
|---|--------|--------|--------|--------|
| <b>Heavy metals</b>                     |        |        |        |        |
| Cadmium                                 | +      | +      | +      | +      |
| Chromium                                | +      | +      | -      | -      |
| Nickel                                  | +      | +      | +      | +      |
| Arsenic                                 | -      | +      | -      | -      |
| Copper                                  | -      | +      | +      | +      |
| Lead                                    | -      | -      | +      | +      |
| Mercury                                 | -      | -      | +      | +      |
| Zinc                                    | -      | -      | -      | +      |
| <b>Organochlorine compounds</b>         |        |        |        |        |
| Alpha-hexachlorocyclohexane             | -      | +      | +      | +      |
| Beta-hexachlorocyclohexane              | -      | -      | +      | +      |
| Delta-hexachlorocyclohexane             | -      | +      | +      | +      |
| Gamma-hexachlorocyclohexane             | -      | +      | +      | +      |
| <b>Polychlorinated biphenyls</b>        |        |        |        |        |
| Polychlorinated biphenyls               | -      | +      | -      | -      |
| <b>Polycyclic aromatic hydrocarbons</b> |        |        |        |        |
| Acenaphthene                            | +      | +      | -      | +      |
| Acenaphthylene                          | +      | +      | -      | +      |
| Anthracene                              | +      | -      | -      | -      |
| Benz(a)anthracene                       | +      | +      | -      | -      |
| Beonzo(a)pyrene                         | +      | +      | -      | -      |
| Chrysene                                | +      | +      | -      | -      |
| Dibenz(a,h)anthracene                   | +      | +      | -      | +      |
| Fluorene                                | +      | -      | -      | +      |
| Phenanthrene                            | +      | -      | -      | -      |
| Fluoranthene                            | +      | -      | -      | -      |
| Naphthalene                             | +      | -      | -      | -      |
| Pyrene                                  | +      | -      | -      | -      |

+ above the limits to cause adverse effect on the biological community, - below the limits to cause adverse effect on the biological community

**Table 2** Specific pregnancy questions included in the questionnaires

- Which resident women became pregnant?
- Which resident women *received* prenatal care?
- How many times these resident women became pregnant?
- In how many of these pregnancies these women had prenatal care?
- Which women had twins?
- What women had miscarriage?
- How many miscarriages these women suffered?
- How many premature babies these women had?
- How many babies weighting less than 2500 g these women had?
- How many born dead babies these women had?
- How many babies with congenital malformation these women had?

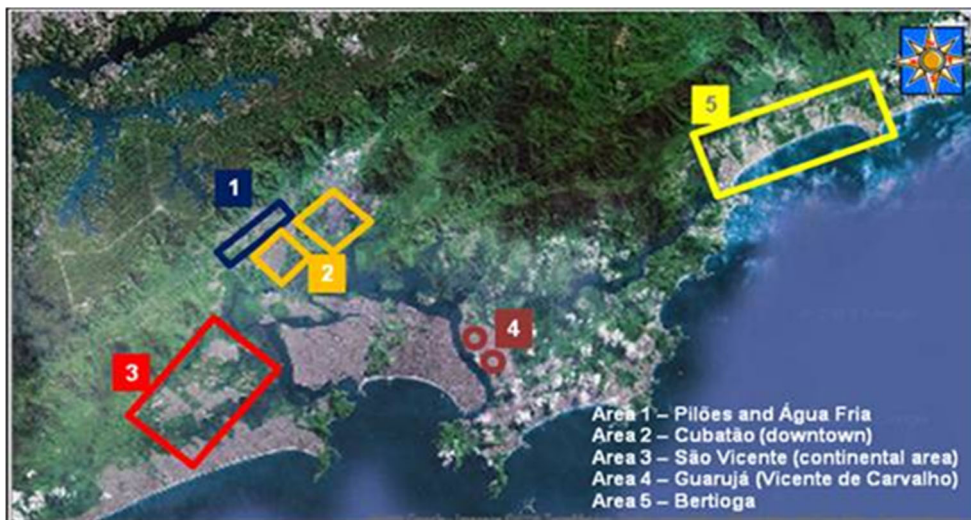
All questions were made considering the last 5 years before the interview date and in relation to all resident women between 15 and 49 years old

outcomes analyzed were: miscarriage—pregnancy loss below 20 weeks of pregnancy, stillbirth—pregnancy lost in 20 weeks of pregnancy or more, prematurity—live births with gestational age below 37 weeks, low birth weight—live birth weighting less than 2500 g, congenital malformations, and multiple births. Data from multiple births were excluded in the prematurity and low birth weight analyses.

**Statistical analyses**

Pearson chi-square test was used to test association between studied variables *between all areas*. Logistic regression models were adopted to calculate odds ratio (OR) with 95 % confidence intervals (95 % CI) in order to estimate the association between residential exposure to contaminants and pregnancy outcomes, *comparing each contaminated area with the control area (baseline)*. The following variables were included in bivariate outcome-specific logistic regression

**Fig. 2** Analyzed areas in Santos and São Vicente Estuary. Source: Google Earth 6



models to identify potential confounders: time of residence in the region (less than 5 years or 5 or more years), age group (15 to 20 years, 21 to 30 years, 31 to 40 years, 41 to 49 years old), education (illiterate, elementary school, high school, college), marital status (married, single, widow), family income (three

or less minimum wages, more than three minimum wages), current and past occupational exposure, current and past use of alcohol and tobacco, prenatal *care*—for those who got pregnant in the studied period (seven or more medical visits, less than seven medical visits).

**Table 3** Childbearing age women’s sociodemographic characteristics according to analyzed areas

|                               | Areas <sup>a</sup> |                |                |                |                | Total           |
|-------------------------------|--------------------|----------------|----------------|----------------|----------------|-----------------|
|                               | Area 1<br>N (%)    | Area 2         | Area 3         | Area 4         | Area 5         |                 |
| <b>Age</b>                    |                    |                |                |                |                |                 |
| 15 to 20 years                | 134<br>(17.0)      | 147<br>(16.6)  | 150<br>(17.3)  | 142<br>(17.0)  | 161<br>(17.5)  | 734<br>(17.0)   |
| 21 to 30 years                | 261<br>(33.1)      | 279<br>(31.6)  | 278<br>(32.0)  | 279<br>(33.3)  | 331<br>(36.0)  | 1428<br>(33.3)  |
| 31 to 40 years                | 241<br>(30.6)      | 234<br>(26.5)  | 231<br>(26.6)  | 220<br>(26.3)  | 245<br>(26.6)  | 1171<br>(27.3)  |
| 41 to 49 years                | 152<br>(19.3)      | 223<br>(25.3)  | 209<br>(24.1)  | 196<br>(23.4)  | 183<br>(19.9)  | 963<br>(22.4)   |
| Total                         | 788<br>(100.0)     | 883<br>(100.0) | 868<br>(100.0) | 837<br>(100.0) | 920<br>(100.0) | 4296<br>(100.0) |
| <b>Education</b>              |                    |                |                |                |                |                 |
| Illiterate                    | 59<br>(7.6)        | 23<br>(2.7)    | 27<br>(3.2)    | 31<br>(3.8)    | 44<br>(4.9)    | 184<br>(4.4)    |
| Elementary school             | 451*<br>(57.9)     | 319<br>(36.8)  | 345<br>(40.4)  | 363<br>(44.5)  | 434<br>(48.5)  | 1912<br>(45.4)  |
| High school                   | 260<br>(33.4)      | 442<br>(51.0)  | 440<br>(51.5)  | 378<br>(46.3)  | 378<br>(42.3)  | 1898<br>(45.1)  |
| College                       | 9<br>(1.2)         | 83<br>(9.3)    | 43<br>(5.0)    | 44<br>(5.4)    | 38<br>(4.3)    | 217<br>(5.2)    |
| Total                         | 779<br>(100.0)     | 867<br>(100.0) | 855<br>(100.0) | 816<br>(100.0) | 894<br>(100.0) | 4211<br>(100.0) |
| <b>Marital status</b>         |                    |                |                |                |                |                 |
| Married                       | 500<br>(63.9)      | 455<br>(51.7)  | 461<br>(53.2)  | 439<br>(52.7)  | 525*<br>(57.3) | 2380<br>(55.6)  |
| Single                        | 272<br>(34.7)      | 400<br>(45.5)  | 390<br>(45.0)  | 384<br>(46.1)  | 381<br>(41.6)  | 1827<br>(42.7)  |
| Widow                         | 11<br>(1.4)        | 25<br>(2.8)    | 16<br>(1.8)    | 10<br>(1.2)    | 10<br>(1.1)    | 72<br>(1.7)     |
| Total                         | 783<br>(100.0)     | 880<br>(100.0) | 867<br>(100.0) | 833<br>(100.0) | 916<br>(100.0) | 4279<br>(100.0) |
| <b>Family income</b>          |                    |                |                |                |                |                 |
| Three or less minimum wages   | 638*<br>(86.2)     | 443<br>(53.6)  | 448<br>(57.9)  | 552<br>(71.2)  | 553<br>(65.2)  | 2634<br>(66.4)  |
| More than three minimum wages | 102<br>(13.8)      | 384<br>(46.4)  | 326<br>(42.1)  | 223<br>(28.8)  | 295<br>(34.8)  | 1330<br>(33.6)  |
| Total                         | 740<br>(100.0)     | 827<br>(100.0) | 774<br>(100.0) | 775<br>(100.0) | 848<br>(100.0) | 3964<br>(100.0) |

<sup>a</sup> Area 1 to 4, contaminated areas; Area 5, control area

\*  $p < 0.05$

**Table 4** Childbearing age women's habits and characteristics according to analyzed areas

|                                      | Areas <sup>a</sup> |                |                |                |                | Total           |
|--------------------------------------|--------------------|----------------|----------------|----------------|----------------|-----------------|
|                                      | Area 1<br>N (%)    | Area 2         | Area 3         | Area 4         | Area 5         |                 |
| <b>Time of residence</b>             |                    |                |                |                |                |                 |
| Less than 5 years                    | 103<br>(13.1)      | 66<br>(7.5)    | 99<br>(11.4)   | 68<br>(8.2)    | 211<br>(23.3)  | 547<br>(12.8)   |
| Five or more years                   | 683<br>(86.9)      | 815*<br>(92.5) | 767<br>(88.6)  | 763<br>(91.8)  | 696<br>(76.7)  | 3724<br>(87.2)  |
| Total                                | 786<br>(100.0)     | 881<br>(100.0) | 866<br>(100.0) | 831<br>(100.0) | 907<br>(100.0) | 4271<br>(100.0) |
| <b>Current occupational exposure</b> |                    |                |                |                |                |                 |
| Yes                                  | 25<br>(5.5)        | 31<br>(5.4)    | 43<br>(7.4)    | 15<br>(2.3)    | 43<br>(6.5)    | 157<br>(5.4)    |
| No                                   | 432<br>(94.5)      | 547<br>(94.6)  | 539<br>(92.6)  | 628*<br>(97.7) | 622<br>(93.5)  | 2768<br>(94.6)  |
| Total                                | 457<br>(100.0)     | 578<br>(100.0) | 582<br>(100.0) | 643<br>(100.0) | 665<br>(100.0) | 2925<br>(100.0) |
| <b>Past occupational exposure</b>    |                    |                |                |                |                |                 |
| Yes                                  | 29<br>(5.5)        | 25<br>(4.0)    | 29<br>(5.3)    | 24<br>(3.7)    | 30<br>(4.6)    | 137<br>(4.6)    |
| No                                   | 500<br>(94.5)      | 596<br>(96.0)  | 515<br>(94.7)  | 628<br>(96.3)  | 621<br>(95.4)  | 2860<br>(95.4)  |
| Total                                | 529<br>(100.0)     | 621<br>(100.0) | 544<br>(100.0) | 652<br>(100.0) | 651<br>(100.0) | 2997<br>(100.0) |
| <b>Current use of tobacco</b>        |                    |                |                |                |                |                 |
| Yes                                  | 164<br>(27.0)      | 122<br>(19.2)  | 119<br>(19.3)  | 143<br>(23.4)  | 161<br>(24.2)  | 709<br>(22.6)   |
| No                                   | 444<br>(73.0)      | 514*<br>(80.8) | 499<br>(80.7)  | 467<br>(76.6)  | 505<br>(75.8)  | 2429<br>(77.4)  |
| Total                                | 608<br>(100.0)     | 636<br>(100.0) | 618<br>(100.0) | 610<br>(100.0) | 666<br>(100.0) | 3138<br>(100.0) |
| <b>Past use of tobacco</b>           |                    |                |                |                |                |                 |
| Yes                                  | 87<br>(13.6)       | 71<br>(10.5)   | 78<br>(12.7)   | 46<br>(6.7)    | 92<br>(13.0)   | 374<br>(11.2)   |
| No                                   | 554<br>(86.4)      | 604<br>(89.5)  | 537<br>(87.3)  | 643*<br>(93.3) | 614<br>(87.0)  | 2952<br>(88.9)  |
| Total                                | 641<br>(100.0)     | 675<br>(100.0) | 615<br>(100.0) | 689<br>(100.0) | 706<br>(100.0) | 3326<br>(100.0) |
| <b>Current use of alcohol</b>        |                    |                |                |                |                |                 |
| Yes                                  | 128<br>(22.7)      | 95<br>(15.2)   | 141<br>(24.5)  | 118<br>(20.3)  | 157<br>(24.2)  | 639<br>(21.3)   |
| No                                   | 437<br>(77.3)      | 530*<br>(84.8) | 435<br>(75.5)  | 462<br>(79.7)  | 491<br>(75.8)  | 2355<br>(78.7)  |
| Total                                | 565<br>(100.0)     | 625<br>(100.0) | 576<br>(100.0) | 580<br>(100.0) | 648<br>(100.0) | 2994<br>(100.0) |
| <b>Past use of alcohol</b>           |                    |                |                |                |                |                 |
| Yes                                  | 56<br>(8.5)        | 20<br>(2.6)    | 30<br>(4.3)    | 15<br>(2.1)    | 44<br>(5.8)    | 165<br>(4.6)    |
| No                                   | 605<br>(91.5)      | 735*<br>(97.4) | 674<br>(95.7)  | 711<br>(97.9)  | 713<br>(94.2)  | 3438<br>(95.4)  |
| Total                                | 661<br>(100.0)     | 755<br>(100.0) | 704<br>(100.0) | 726<br>(100.0) | 757<br>(100.0) | 3603<br>(100.0) |

<sup>a</sup> Areas 1 to 4, contaminated areas; Area 5, control area\*  $p < 0.05$



Only those variables who presented statistical significant level equal or smaller than 0.20 in the bivariate outcome-specific logistic regression models were included in the adjusted outcome-specific multiple logistic regression models.

Questionnaires containing errors, in blank, or when the interviewed did not answer were excluded from analysis. Statistic Package for Social Sciences 17.0 version—SPSS were used in all analyses, and a 0.05 significance level was adopted.

**Results**

From the 4100 expected interviewed houses in all areas, 3920 were interviewed (95.61 % response rate). In all areas, 4296 childbearing age women were interviewed (788 in Area 1, 883 in Area 2, 868 in Area 3, 837 in Area 4, and 920 in Area 5). Table 2 describes sociodemographic characteristics of those women according to analyzed area.

Women’s median age was 30 years in Area 1, 31 in Area 2, 31 in Area 3, 30 in Area 4, and 30 in Area 5. The majority of women did elementary and high school, with different distribution between the areas. Areas 2, 3, and 4 had more women with high school education than Area 1 and 5. Area 1 showed more illiterate women than the other areas. In addition, Area 1 showed the lowest percentage of women with college education compared to the other areas. Although more than half of childbearing age women were married, a great number of women had never been married. Less than 2 % of women were widowed in all areas. Statistical significant association was found between living in Area 1 and family income of three or less minimum wages. The majority of women had family income of three or less minimum wages, but it was observed that Area 1 showed lower family income than the other areas (Table 3).

A large percentage of women live in the same region for more than 5 years. However, statistical significant association was found between living in Area 2 and living for more than 5 years. The majority of women did not have contact with chemical products or dust on work. A statistical significant association was found between living in Area 4 and did not have occupational exposure. In relation to past occupational exposure, the higher percentage of nonexposure was found. Statistical significant association was found between living in Area 2 and not smoking. The majority of women did not smoke. A higher percentage of women did not smoke in the past either. The majority of women did not drink at all. An even higher percentage of women did not drink in the past (Table 4).

In the last 5 years, 1362 women in childbearing age got pregnant. Association between living in Area 2 and did not get

pregnant was statistical significant. No association between living in any area and prenatal care was found. Almost every pregnant woman did prenatal care (Table 5).

No association were found between living in any studied area and occurrence of multiple birth, miscarriage, prematurity, low birth weight, stillbirth, and congenital malformation (Table 6).

Table 7 shows, respectively, the crude OR among pregnancy outcomes and women living area. Pregnancy occurrence were reduced among childbearing age women in three contaminated areas (Areas 2, 3, and 4) when compared to the control area.

In analyses that adjusted for maternal age group and education, and family income, similar findings were observed (Area 2—OR=0.68, 95 % CI 0.54–0.86, Area 3—OR=0.76, 95 % CI 0.60–0.97, and Area 4—OR=0.71, 95 % CI 0.56–0.90) (Fig. 3).

One contaminated area (Area 3—OR=1.83, 95 % CI 1.07–3.12) also had more childbearing age women with miscarriage than the control area (Fig. 4).

All other adjusted analysis did not shown significant changes in the crude OR for multiple births, prematurity, low birth weight, stillbirth, and congenital malformation.

**Discussion**

Areas 1 and 5 (control) had a higher prevalence of women of childbearing age who became pregnant than in other areas. A

**Table 5** Pregnant women and prenatal care in the last 5 years according to analyzed areas

|                            | Areas <sup>a</sup> |                |                |                |                | Total           |
|----------------------------|--------------------|----------------|----------------|----------------|----------------|-----------------|
|                            | Area 1<br>N (%)    | Area 2         | Area 3         | Area 4         | Area 5         |                 |
| <b>Pregnant</b>            |                    |                |                |                |                |                 |
| Yes                        | 314<br>(44.2)      | 230<br>(28.6)  | 247<br>(34.1)  | 245<br>(33.2)  | 326<br>(42.4)  | 1362<br>(36.4)  |
| No                         | 397<br>(55.8)      | 573*<br>(71.4) | 477<br>(65.9)  | 492<br>(66.8)  | 442<br>(57.6)  | 2381<br>(63.6)  |
| Total                      | 711<br>(100.0)     | 803<br>(100.0) | 724<br>(100.0) | 737<br>(100.0) | 768<br>(100.0) | 3743<br>(100.0) |
| <b>Prenatal assistance</b> |                    |                |                |                |                |                 |
| Yes                        | 301<br>(96.8)      | 227<br>(99.1)  | 231<br>(96.3)  | 235<br>(97.1)  | 308<br>(95.7)  | 1302<br>(96.9)  |
| No                         | 10<br>(3.2)        | 2<br>(0.9)     | 9<br>(3.8)     | 7<br>(2.9)     | 14<br>(4.3)    | 42<br>(3.1)     |
| Total                      | 311<br>(100.0)     | 229<br>(100.0) | 240<br>(100.0) | 242<br>(100.0) | 322<br>(100.0) | 1344<br>(100.0) |

<sup>a</sup> Areas 1 to 4, contaminated areas; Area 5, control area

\* *p*<0.05

significant reduced pregnancy occurrence in Areas 2, 3, and 4 was found compared with the control area, adjusted for maternal age, maternal education, and family income.

**Table 6** Pregnancy outcomes in the last 5 years between childbearing age women according to analyzed areas

|                                | Areas <sup>a</sup> |                |                |                |                | Total            |
|--------------------------------|--------------------|----------------|----------------|----------------|----------------|------------------|
|                                | Area 1<br>N (%)    | Area 2         | Area 3         | Area 4         | Area 5         |                  |
| <b>Miscarriage</b>             |                    |                |                |                |                |                  |
| Yes                            | 43<br>(14.1)       | 32<br>(14.3)   | 46<br>(19.7)   | 36<br>(15.1)   | 42<br>(13.6)   | 199<br>(15.2)    |
| No                             | 261<br>(85.9)      | 191<br>(85.7)  | 187<br>(80.3)  | 203<br>(84.9)  | 266<br>(86.4)  | 1108<br>(84.8)   |
| Total                          | 304<br>(100.0)     | 223<br>(100.0) | 233<br>(100.0) | 239<br>(100.0) | 308<br>(100.0) | 1307<br>(100.0)  |
| <b>Stillbirth</b>              |                    |                |                |                |                |                  |
| Yes                            | 5<br>(1.7)         | 2<br>(0.9)     | 6<br>(2.6)     | 7<br>(2.9)     | 2<br>(0.6)     | 22<br>(1.7)      |
| No                             | 297<br>(98.3)      | 219<br>(99.1)  | 227<br>(97.4)  | 232<br>(97.1)  | 316<br>(99.4)  | 1291<br>(98.3)   |
| Total                          | 302<br>(100.0)     | 221<br>(100.0) | 233<br>(100.0) | 239<br>(100.0) | 318<br>(100.0) | 1313<br>(100.0)  |
| <b>Prematurity<sup>b</sup></b> |                    |                |                |                |                |                  |
| Yes                            | 24<br>(8.2)        | 13<br>(6.2)    | 19<br>(8.5)    | 8<br>(3.4)     | 20<br>(6.6)    | 84<br>(6.7)      |
| No                             | 270<br>(91.8)      | 196<br>(93.8)  | 204<br>(91.5)  | 224<br>(96.6)  | 281<br>(93.4)  | 1175<br>(93.3)   |
| Total                          | 294<br>(100.0)     | 209<br>(100.0) | 223<br>(100.0) | 232<br>(100.0) | 301<br>(100.0) | 1259<br>(100.0)  |
| <b>LBW<sup>b</sup></b>         |                    |                |                |                |                |                  |
| Yes                            | 22<br>(7.7)        | 11<br>(5.2)    | 11<br>(5.0)    | 9<br>(3.9)     | 18<br>(6.1)    | 71<br>(5.7)      |
| No                             | 265<br>(92.3)      | 199<br>(94.8)  | 207<br>(95.0)  | 219<br>(96.1)  | 279<br>(93.9)  | 1,2169<br>(94.3) |
| Total                          | 287<br>(100.0)     | 210<br>(100.0) | 218<br>(100.0) | 228<br>(100.0) | 397<br>(100.0) | 1240<br>(100.0)  |
| <b>Congenital malformation</b> |                    |                |                |                |                |                  |
| Yes                            | 4<br>(1.3)         | 2<br>(0.9)     | 3<br>(1.3)     | 2<br>(0.8)     | 5<br>(1.6)     | 16<br>(1.2)      |
| No                             | 301<br>(98.7)      | 227<br>(99.1)  | 231<br>(98.7)  | 238<br>(99.2)  | 311<br>(98.4)  | 1308<br>(98.8)   |
| Total                          | 305<br>(100.0)     | 229<br>(100.0) | 234<br>(100.0) | 240<br>(100.0) | 316<br>(100.0) | 1324<br>(100.0)  |
| <b>Multiple births</b>         |                    |                |                |                |                |                  |
| Yes                            | 6<br>(1.9)         | 10<br>(4.4)    | 7<br>(3.0)     | 5<br>(2.1)     | 6<br>(1.9)     | 34<br>(2.6)      |
| No                             | 302<br>(98.1)      | 217<br>(95.6)  | 230<br>(97.0)  | 236<br>(97.9)  | 312<br>(98.1)  | 1297<br>(97.4)   |
| Total                          | 308<br>(100.0)     | 227<br>(100.0) | 237<br>(100.0) | 241<br>(100.0) | 318<br>(100.0) | 1331<br>(100.0)  |

<sup>a</sup> Areas 1 to 4, contaminated areas; Area 5, control area

<sup>b</sup> Excluded multiple births data

**Table 7** Crude odds ratio of gestational outcomes between childbearing age women according to analyzed areas

|  | OR   | 95 % CI    | p value |
|--|------|------------|---------|
| <b>Pregnancy occurrence<sup>a</sup></b>    |      |            |         |
| Area 1                                     | 1.07 | 0.87–1.33  | 0.50    |
| Area 2                                     | 0.54 | 0.44–0.67  | 0.00    |
| Area 3                                     | 0.70 | 0.57–0.86  | 0.00    |
| Area 4                                     | 0.67 | 0.54–0.83  | 0.00    |
| <b>Multiple births<sup>a</sup></b>         |      |            |         |
| Area 1                                     | 1.03 | 0.33–3.23  | 0.95    |
| Area 2                                     | 2.39 | 0.85–6.69  | 0.09    |
| Area 3                                     | 1.58 | 0.52–4.77  | 0.41    |
| Area 4                                     | 1.10 | 0.33–3.65  | 0.87    |
| <b>Miscarriage<sup>a</sup></b>             |      |            |         |
| Area 1                                     | 1.04 | 0.66–1.65  | 0.85    |
| Area 2                                     | 1.06 | 0.64–1.74  | 0.81    |
| Area 3                                     | 1.55 | 0.98–2.46  | 0.05    |
| Area 4                                     | 1.12 | 0.69–1.81  | 0.63    |
| <b>Low birth weight<sup>a, b</sup></b>     |      |            |         |
| Area 1                                     | 1.28 | 0.67–2.45  | 0.44    |
| Area 2                                     | 0.85 | 0.39–1.85  | 0.69    |
| Area 3                                     | 0.82 | 0.38–1.78  | 0.62    |
| Area 4                                     | 0.63 | 0.28–1.44  | 0.28    |
| <b>Premature birth<sup>a, b</sup></b>      |      |            |         |
| Area 1                                     | 1.24 | 0.67–2.31  | 0.48    |
| Area 2                                     | 0.93 | 0.45–1.91  | 0.84    |
| Area 3                                     | 1.30 | 0.68–2.51  | 0.42    |
| Area 4                                     | 0.50 | 0.21–1.16  | 0.10    |
| <b>Stillbirth<sup>a</sup></b>              |      |            |         |
| Area 1                                     | 2.66 | 0.51–13.81 | 0.24    |
| Area 2                                     | 1.44 | 0.20–10.32 | 0.71    |
| Area 3                                     | 4.17 | 0.83–20.88 | 0.08    |
| Area 4                                     | 4.76 | 0.98–23.15 | 0.05    |
| <b>Congenital malformation<sup>a</sup></b> |      |            |         |
| Area 1                                     | 0.82 | 0.22–3.10  | 0.77    |
| Area 2                                     | 0.54 | 0.10–2.85  | 0.47    |
| Area 3                                     | 0.80 | 0.19–3.41  | 0.77    |
| Area 4                                     | 0.52 | 0.10–2.71  | 0.44    |

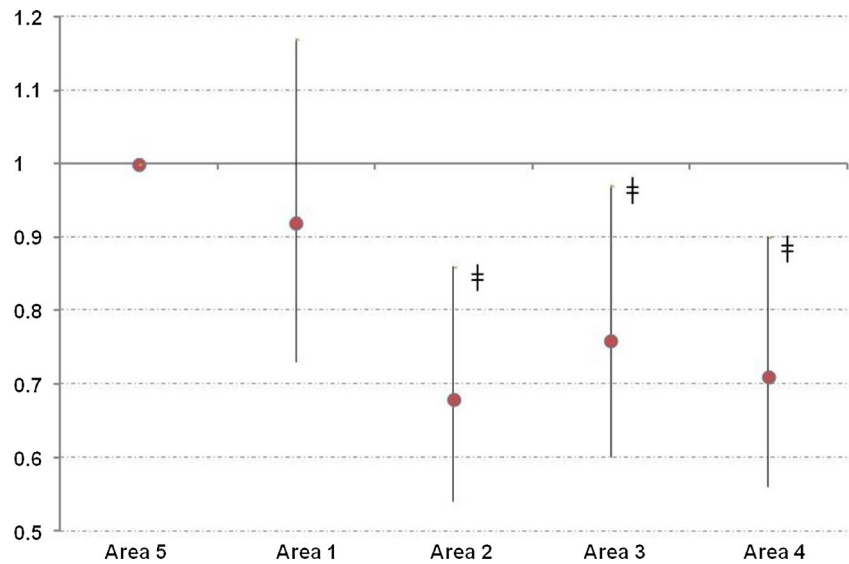
<sup>a</sup> Baseline: Area 5 (Bertioga—control area)

<sup>b</sup> Excluded multiple births data

The contaminated areas also had more miscarriages than the control area. A significant increased miscarriage odds ratio in Area 3 was found compared to the control area, adjusted for years of living in the region, age and maternal education, family income, and past history of maternal smoking.

Male and female reproductive systems are susceptible to environmental factors, which may impact on tissues development and also in adults’ reproductive functions, such as

**Fig. 3** Adjusted odds ratio of pregnancy occurrence according to analyzed areas. † $p < 0.05$



decrease in men’s and women’s fertility (Woodruff and Walker 2008). In the Netherlands, Burdorf and colleagues (2011) show an increase risk of longer time to pregnancy among women with occupational exposure to phthalates.

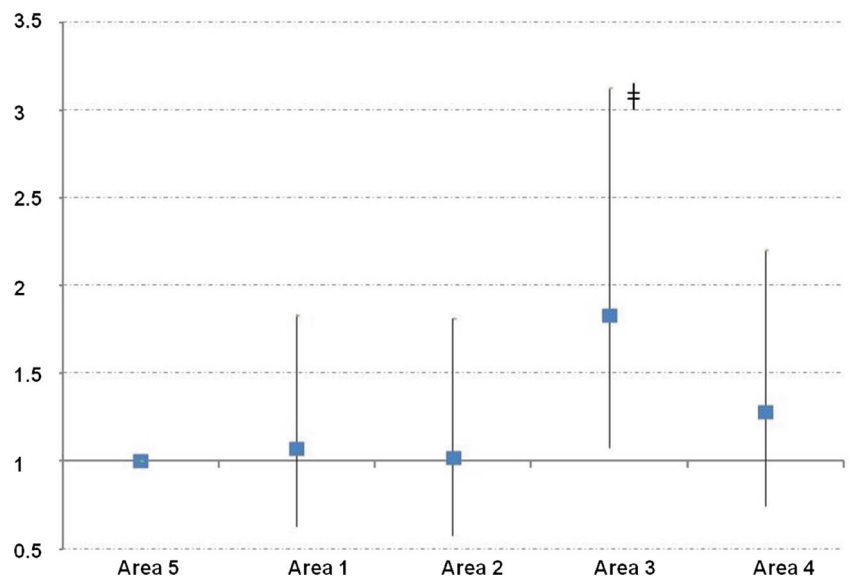
In Brazil, fertility has been rapidly declining since the 1960s second half, reaching in 2004 a 2.1 total fertility rate, population replacement limit level considered by WHO. Fertility rate decrease may be associated with several factors, such as increasing urbanization, reducing child mortality, improving education levels, and increased contraceptive methods use, among others (IBGE 2009). The general fecundity rate in São Paulo State was 51.88 live births per 1000 childbearing age women in the year 2010. Higher rates were found in all four cities that the studied areas belong (56.78 in Cubatão—Area 1 and 2, 56.41 in São Vicente—Area 3, 58.36

in Guarujá—Area 4, and 65.50 in Bertioga—Control area) (SEADE 2015).

There are differences in the fertility age structure according to women socioeconomic status, with the highest fertility in the less educated groups and in the most economically disadvantaged ones (Martins and Almeida 2001). The Human Development Index (HDI) of the four cities, where the studied areas are included, were classified as medium development and were similar for the year 2010 (0.730 in Bertioga, 0.737 in Cubatão, 0.768 in São Vicente, and 0.751 in Guarujá) (SEADE 2015).

Korrick and colleagues (2011) showed an increased risk of miscarriage associated with dichlorodiphenyldichloroethylene (DDE) serum levels in mothers. Toft and colleagues (2004) indicated in a review that exposure to organochlorine compounds may induce miscarriage in women.

**Fig. 4** Adjusted odds ratio of miscarriage according analyzed areas. † $p < 0.05$





About 15 % of pregnancies end in miscarriages. Including cases that go unnoticed or are not recognized, this percentage reaches up to 50 % of all conceptions (Korrick et al. 2011). Noguez and colleagues (2008) found no association between miscarriages and living near an industrial area in southern Brazil. In contrast, Thakur and colleagues (2010) found a higher miscarriage incidence in polluted areas with heavy metals and organochlorine compounds in India.

Associations between environmental contaminants and pregnancy outcomes such as miscarriage, premature birth and low birth weight have been investigated by several authors (Younglai et al. 2005; Windham and Fenster 2008; Green et al. 2009; Shirangi et al. 2010). Green and colleagues (2009) showed association between residential proximity to traffic and miscarriage occurrence. A recent review carried out by Shirangi and colleagues (2010) produced evidence that suggested an association between pesticides exposure near homes and increases in adverse reproductive outcomes, like congenital malformations, low birth weight, prematurity, and miscarriage.

Several studies show that premature birth occurrence is more frequent among poor populations (Barros et al. 2008, 2011; Gray et al. 2008). The complex variables network involved in the low birth weight occurrence has its genesis in precarious conditions of life and work in a considerable part of Brazilian population (Minagawa et al. 2006). Mother's age, marital status, and education, parity, and prenatal care are highlighted as risk factors for low birth weight and prematurity in several Brazilian surveys (Monteiro et al. 2000).

Prenatal care is an important protective factor against perinatal mortality (De Lorenzi et al. 2001), premature birth, and low birth weight (Belford 2005). Almost all pregnant women had prenatal care in the last 5 years. Nevertheless, the questionnaire used in this study did not evaluate the quality of this care and we cannot rule out that differences in care quality may have influenced the comparisons between study areas.

Although the present study had a cross-sectional design and used ecological assessment of exposure, data from important risk factors of adverse pregnancy outcomes such as occupational exposure, alcohol, and tobacco consumption were collected covering the entire life of the women and it were considered in the analysis. Low birth weight data may have been misclassified by the absence of gestational age adjustments.

The used data from self-reported morbidity questionnaire choice rather than medical records data are due to the fact that, in general, medical records are incompletely filled out and often have imprecision diagnosis in Brazil (Coeli 2010). This is the main difficulty in secondary data use especially in studies assessing environmental contamination. Despite the restrictions of self-reported morbidity use, the results presented are consistent and considered probably underestimated (Alves et al. 2007).

In studies of environmental contamination in pregnant women, occupational exposure is an important factor that must be controlled (Leite and Schüller-Faccini 2001). Occupational exposure to chemicals has been reported as an important risk factor on pregnancy, interfering in perinatal morbidity and mortality profile (Younglai et al. 2005). Alcohol is a teratogenic substance, which interferes with fetal development (Freire et al. 2005). Alcohol consumption is associated with miscarriage, preterm birth, and low birth weight (Mullally et al. 2011; Kesmodel et al. 2002). Smoking in pregnancy causes harm not only to the pregnant woman but also to the fetus (Windham and Fenster 2008). Smoking effects during pregnancy include low birth weight, premature births, and miscarriages (Jakab 2010).

Poor pregnancy outcomes have been shown to be elevated among socioeconomic disadvantaged women (Morgen et al. 2008; Ugwuja et al. 2011). All studied areas in our study are inhabited by low and/or very low income families who are already at elevated risk of poor pregnancy outcomes for that reason. The hypothesis of a relationship between contaminants exposure located in the region and adverse pregnancy outcomes should be investigated in future studies.

## Conclusions

Pregnancy occurrences were significantly reduced in *three of the* four contaminated areas compared to the control area, adjusted for important pregnancy risk factors.

Odds of miscarriage were almost twice as large in Area 3 than in the control area, after controlling for important pregnancy risk factors.

Increased odds of stillbirth, premature birth, low birth weight, congenital malformation, and multiple births were not found in the contaminated areas compared to the control area.

Identifying the decreased pregnancy occurrence and increased miscarriage prevalence in known contaminated areas (by chlorine compounds and heavy metals) should subsidize local public health managers in planning and prevention care in order to minimize the population exposure risk to these contaminants.

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**Competing interests** None.

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