Reproductive outcomes in an area adjacent to a petrochemical plant in southern Brazil

Riscos reprodutivos em região próxima ao pólo petroquímico de Triunfo no Sul do Brasil

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Keywords
Petroleum industry.# Environmental exposure.# Infant, newborn.# Impacts on health.# Risk Factors. Infant, low birth weight. Case-control studies.

Abstract

Objective
To evaluate possible adverse reproductive outcomes in an area adjacent to a petrochemical plant in southern Brazil.
Methods
A review of 17,113 birth records of the main hospital of the municipality of Montenegro, southern Brazil, from 1983 to 1998 was carried out. Three groups of cases were selected: (1) newborns with major congenital malformations; (2) newborns with low birth weight (<2,500 g); and (3) stillborns (>500 g). A control was assigned to each case. Controls were the first newborns weighing ≥2,500 g without malformations and of case-matching sex. Mother's residence during pregnancy was used as an exposure parameter. Statistical analyses were performed using Chi-square test or Fisher test, odds ratio, 0.05 significance level, and 95% confidence interval.
Results
For unadjusted analysis, it was found a correlation between low birth weight and geographical proximity of mother's residence to the petrochemical plant (OR = 1.66; 95% CI = 1.01–2.72) or residence on the way of preferential wind direction (OR = 1.62; 95% CI = 1.03–2.56). When other covariates were added in the conditional logistic regression (maternal smoking habits, chronic disease and age), there was no association.
Conclusions
Despite final results were negative, low birth weight could be a good parameter of environmental contamination and should be closely monitored in the studied area.

Descritores
Indústria petroquímica.# Exposição ambiental.# Recém-nascido.# Impactos na saúde.# Fatores de risco. Recém-nascido de baixo peso. Estudos de casos e controles.

Resumo

Objetivo
Avaliar os possíveis riscos reprodutivos em uma região próxima a pólo petroquímico situado no Rio Grande do Sul.
Métodos
Foram analisados 17.113 registros de nascimentos ocorridos no principal hospital da região, localizado no município de Montenegro, RS, desde 1983 até 1998. Foram selecionados três diferentes grupos de casos: (1) recém-nascidos portadores de malformações congênitas maiores; (2) recém-nascidos com baixo peso ao nascer

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(<2.500 g); e (3) natimortos (>500 g). Para cada caso, foi atribuído um controle específico, que foi a primeira criança nascida viva, pesando 2.500 g ou mais, com ausência de malformações e tendo o mesmo sexo que o caso em questão. A residência materna durante a gravidez foi utilizada como um parâmetro para exposição. Para a análise estatística, foram usados os testes qui-quadrado ou Fisher, "odds ratio", nível de significância de 0,05 e intervalo de confiança de 95%.

Resultados

Foi encontrada correlação positiva para baixo peso ao nascer e para proximidade geográfica da residência materna ao Pólo Petroquímico ["odds ratio" (OR) = 1,66; 95% confidence interval (CI) = 1,01-2,72] ou residência na direção preferencial do vento ["odds ratio" (OR) = 1,62; 95% confidence interval (CI) = 1,03-2,56]. Quando outras variáveis foram incluídas na análise de regressão logística condicional (fumo, doenças crônicas e idade materna), essa associação desapareceu.

Conclusões

Apesar de os resultados finais terem sido negativos, o baixo peso ao nascer pode ser um bom parâmetro para medir a contaminação ambiental, mas deve ser monitorado na região estudada.

INTRODUCTION

Thirty percent of petrochemical production in Brazil are generated by the Southern Petrochemical Complex (Complexo Petroquímico do Sul – COPESUL). In 1997, 1.9 million of tons of raw petrochemical material was produced including hydrocarbons and volatile organic compounds (VOCs)* such as ethene, butadiene among others. In 1999 the plant was expanded and its production has increased to 3.0 million of tons per year.

Montenegro and Triunfo are two municipalities located in the southern state of Rio Grande do Sul, adjacent to a large petrochemical plant. Montenegro has an area of 467 km^2, population of approximately 49,000 inhabitants—29,000 living in urban areas and 20,000 in rural areas. Triunfo has an area of 834 km^2 and only 13,000 inhabitants, half of them living in rural areas.

The Southern Petrochemical Complex was settled in 1982. It is located approximately 15 km from Montenegro's urban center and 30 km from Triunfo's urban area and 50 km from Porto Alegre, the state capital. It is also situated by one of the affluent rivers of Guaíba hydrographic basin, the largest water net in Rio Grande do Sul, where specific programs for pollution control are in place.

The Fundação Estadual de Proteção Ambiental – FEPAM (State Institute for Environmental Preservation) has developed specific programs to evaluate possible ecotoxicity in the area near the petrochemical plant since 1983, and potential genotoxic substances have been identified.[21] Hence, a case-control study was conducted in the area to evaluate whether there is a relationship between adverse reproductive outcomes and mother's place of residence. Low birth weight newborns, stillborns and newborns with major malformations were selected as outcomes for analysis.

METHODS

A case-control study was carried out and all birth records registered from 1983 to 1998 in the main hospital of the area, located in the municipality of Montenegro, were reviewed. This is a referral hospital for the Latin America Collaborative Study on Congenital Malformations (Estudo Colaborativo Latino-Americano de Malformações Congênitas – ECLAMC). Three groups of cases were selected: (1) newborns with major congenital malformations; (2) newborns with low birth weight (<2,500 g); and (3) stillborns (>500 g). A control was assigned to each case. Controls were the first newborns weighing ≥2,500 g without malformations and of case-matching sex.

All medical records were reviewed to collect mother's demographic data and clinical description of the newborns. Demographic characteristics were compared to available ECLAMC from six other regions with similar economic and cultural characteristics. For congenital malformations analysis all newborns with at least one major malformation diagnosed during hospital stay were initially included. Then, only newborns with one of 15 birth defects routinely monitored by ECLAMC were selected, i.e., the ones of easy clinical diagnosis and thus subjected to less ascertainment bias. These birth defects categories included cases with both

*http://www.copesul.com.br - Avaitable in 2000.

isolated malformations and multiple anomalies. Expected values of birth prevalence rate of congenital anomalies were obtained from the ECLAMC data during the 1982–1995 period. These data came from a sample of 2,595,064 births studied in 59 hospitals of eight Latin American countries.

Exposure categories were created for each birth based on geographical distance of mother's residence from the petrochemical plant at the time of birth. Three regions were arbitrarily defined according to the plan proximity: Region 1—the nearest, in a perimeter of approximately 10 km from the plant; Region 2, intermediate, distant 10 to 20 km from the plant and including the municipality of Montenegro; and Region 3, reference or unexposed area, extending beyond 30 km from the plant (Figure A). The regions were further subdivided according to the prevailing wind direction in Region A (prevailing wind tunnel); Region B (lateral to A) and Region C, the same as Region 3, unexposed region (Figure B). Cases and controls were compared according to mother's residence during pregnancy in the three regions , having as reference Region 3 and C, respectively.

Initially crude comparisons between cases and controls were performed for the following maternal variables: residence, age, chronic diseases, smoking, previous abortions, parity and gestational age, using Chi-square test or Fisher test when expected values were less than 5. Odds ratio were calculated using significance level of 0.05 and confidence interval of 95%. Conditional regression analysis was then performed for mother's residence including the most significant variables: smoking, maternal age, and chronic diseases. All analyses were performed using SPSS version 8.0.

RESULTS

In these 15 years of study, 17,113 births were registered in the Montenegro hospital. Hospital records were complete for 90% of all newborns with low birth weight (n=990), 85% of stillborns (n=230) and 85% of malformed newborns (n=160). This represents 70% of all expected births for this region during the study period (Table 1). Fetal death mortality rate was 1.7% and low birth weight was seen in 6.8% of all livebirths. These frequencies are not different from that observed in the ECLAMC for six other Brazilian hospitals located in economically and developmentally similar regions.

The observed and expected frequencies for the selected 15 congenital malformations are shown in Table 2. Lower than expected rates were observed for anencephaly, Down syndrome and nonsyndromal multiple congenital anomalies patterns (two or more apparently unrelated defects). There was no temporal variation for these congenital malformations. When the defects were plotted in the region map no cluster for any anomaly was seen.

Table 1 - Demographic characteristics of the sample of newborn.

Characteristics	Montenegro		ECLAMC		p-value
	N	%	N	%	
Total births	17.113	-	389.618	-	-
Live births	16.826	98.30	382.419	98.2	-
Stillbirths	287	1.70	7.199	1.8	NS
Birth weight <2,500 g	1.147	6.80	52.131	13.4	NS
Malformed live births	170	1.01	-	-	-
Malformed stillbirths	18	6.30	-	-	-

ECLAMC: Estudo Colaborativo Latino-Americano de Malformações Congênitas
NS: non significant

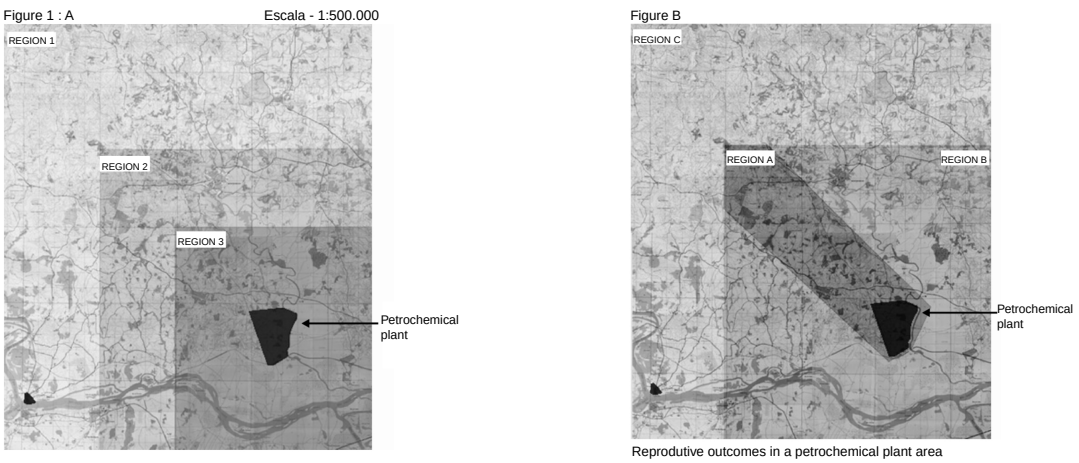

Figure 1 - A) Geographical distance of mother's residence from the petrochemical plant. B) Prevailing wind direction.

Table 3 presents crude comparisons between cases and controls of mother's residence and potential risk factors. More than expected cases of low-birth weight were observed for maternal residence during pregnancy in Region 1 (adjacent to the petrochemical plant) (OR=1.66; 95% CI = 1.01-2.72) and Region A (preferential wind direction) (OR=1.62; 95%CI = 1.03–2.56). Though observed odds ratios were still higher in Region 2 than in Region 3, they were not statistically significant. The same was observed for Region B when compared to Region C. Positive associations were also seen for other risk factors: mater-

Table 2 - Observed and expected frequency of congenital anomalies from Montenegro Hospital.

Congenital anomaly type	Montenegro N	Rate*	ECLAMC Rate*	Expected N**
Anencephaly	5	2.90	6.80	12 (6-21)
Spina bifida and/or cephalocele	10	5.80	9.00	15 (8-25)
Hydrocephaly	16	9.30	6.50	11 (5-20)
Microcephaly	2	1.20	2.60	4 (1-10)
Microphtalmia and/or anophtalmia	5	2.90	1.60	3 (1-9)
Microtia and/or anotia	6	3.50	4.20	7 (3-14)
Cleft lip and/or cleft palate	24	14.00	14.20	24 (15-36)
Gastrointestinal tract atresias	8	4.70	4.20	7 (3-14)
Imperfurate anal membrane	6	3.50	4.00	7 (3-14)
Ambiguous genitalia	4	2.30	1.90	3 (1-9)
Hypospadia	18	10.50	8.20	14 (8-23)
Limb reduction defects	18	10.50	6.20	11 (5-20)
Down syndrome	13	7.60	15.40	23 (15-35)
Nonsyndromal MCA	23	13.40	27.80	47 (35-63)
Pathogenic syndromes	24	14.00	10.10	17 (10-27)

*Rates given per 10,000 births
**95% confidence limits (Poisson)
MCA: multiple congenital anomalies

Table 3 - Potential maternal risk factors for low birth weight, stillbirths and congenital malformations.

Variable	Cases N	Cases %	Controls N	Controls %	OR	CI	p-value
Low birth weight							
Maternal age (years)							
≤18	160	16.2	129	13.0	1.34	1.03-1.74	0.023
19-34	711	71.8	768	77.6			
≥35	119	12.0	93	9.4	1.38	1.02-1.87	0.028
Chronic disease	36	3.6	19	1.9	1.95	1.08-3.56	0.018
Smoking	387	39.1	245	24.7	2.07	1.69-2.53	<0.001
Geographic distance*							
Region 1	65	6.6	46	4.6	1.66	1.01-2.72	0.034
Region 2	829	83.7	831	83.9	1.17	0.86-1.58	0.295
Region 3	93	9.4	109	11.0			
Wind direction**							
Region A	83	8.4	60	6.1	1.62	1.03-2.56	0.028
Region B	811	81.9	817	82.5	1.16	0.86-1.58	0.311
Region C	93	9.4	109	11.0			
Stillbirths							
Maternal age							
≤18	28	12.2	28	12.2	1.09	0.60-2.00	0.756
19-34	160	69.6	175	76.1			
≥35	42	18.2	27	11.7	1.70	0.97-2.99	0.047
Chronic disease	23	10.0	4	1.7	6.55	2.10-22.77	<0.001
Smoking	57	24.8	52	22.6	1.20	0.76-1.90	0.407
Geographic distance*							
Region 1	9	3.9	7	3.1	0.78	0.22-2.72	0.659
Region 2	183	79.6	200	86.9	0.55	0.31-1.00	0.035
Region 3	38	16.5	23	10.0			
Wind direction**							
Region A	21	9.1	13	5.6	0.98	0.38-2.54	0.959
Region B	171	74.4	194	84.4	0.53	0.29-0.96	0.025
Region C	38	16.5	23	10.0			
Malformations							
Maternal age (years)							
≤18	16	10.0	13	8.1	1.43	0.62-3.30	0.368
19-34	114	71.2	132	82.5			
≥35	30	18.8	15	9.4	2.32	1.13-4.77	0.012
Smoking	43	26.9	37	23.1	1.22	0.71-2.10	0.438
Geographic distance*							
Region 1	4	2.5	7	4.4	0.37	0.07-1.72	0.132
Region 2	130	81.2	135	84.4	0.62	0.30-1.27	0.155
Region 3	25	15.6	16	10.0			
Wind direction**							
Region A	12	7.5	6	3.7	1.28	0.35-4.81	0.677
Region B	122	76.2	136	85.0	0.57	0.28-1.18	0.103

*Residence of the mother during pregnancy according Figure 1A; and **according Figure 1B
OR: odds ratio; CI: 95% confidence interval

nal age, chronic disease, and smoking.

For stillbirths, statistically significant odds ratios were observed for advanced maternal age and chronic diseases. A lower than expected proportion of mothers of cases, compared to mothers of controls, lived in Region 2 (Region 3 used as reference). For malformed infants, the odds ratio were significantly higher for advanced maternal age.

Table 4 - Conditional multiple regression analysis: maternal residence distance from petrochemical plant.*

	OR	CI	p-value
Low birth weight (N=990)			
Maternal age (years)			
≤18	1.35	1.02-1.79	0.038
≥35	1.26	0.92-1.72	0.155
Chronic disease	2.22	1.21-4.07	0.009
Smoking	2.12	1.71-2.63	0.000
Geographic distance			
Region 1	1.50	0.90-2.50	0.117
Region 2	1.02	0.74-1.41	0.889
Stillbirths (N=230)			
Maternal age (years)			
≤18	1.26	0.65-2.46	0.489
≥35	1.89	1.02-3.50	0.042
Chronic disease	7.30	2.13-25.03	0.002
Smoking	1.47	0.91-2.38	0.118
Geographic distance			
Region 1	0.71	0.20-2.56	0.602
Region 2	0.52	0.29-0.94	0.032
Malformations (N=160)			
Maternal age (years)			
≤18	1.23	0.56-2.71	0.603
≥35	2.96	1.41-6.23	0.004
Smoking	1.33	0.79-2.22	0.284
Geographic distance			
Region 1	0.30	0.70-1.27	0.103
Region 2	0.52	0.24-1.13	0.099

OR: odds ratio; CI: 95% confidence interval
*According Figure 1A

Table 5 - Conditional multiple regression analysis: maternal residence according to preferential wind direction.

	OR	CI	p-value
Low birth weight (N=990)			
Maternal age (years)			
≤18	1.34	1.01-1.78	0.040
≥35	1.27	0.92-1.74	0.142
Chronic disease	2.15	1.17-3.93	0.013
Smoking	2.11	1.70-2.61	0.000
Wind direction*			
Region A	1.42	0.87-2.31	0.158
Region B	1.03	0.75-1.42	0.857
Stillbirths (N=230)			
Maternal age (years)			
≤18	1.07	0.70-1.64	0.752
≥35	1.24	0.88-1.77	0.221
Chronic disease	1.89	1.22-2.93	0.005
Smoking	1.19	0.87-1.62	0.267
Wind direction*			
Region A	0.88	0.50-1.55	0.666
Region B	0.71	0.50-1.03	0.069
Malformations (N=160)			
Maternal age (years)			
≤18	1.24	0.56-2.74	0.594
≥35	2.94	1.39-6.22	0.005
Smoking	1.25	0.74-2.12	0.394
Wind direction*			
Region A	1.08	0.30-3.88	0.907
Region B	0.48	0.22-1.05	0.068

OR: odds ratio; CI: 95% confidence interval
*According Figure 1B

When all risk factors were analyzed together using conditional regression analysis (Table 4 and 5), geographic impact for low birth weight didn't show any statistical significance. Maternal age (young), smoking and chronic diseases were still significant. For stillbirths, a lower than expected proportion of mothers of cases living in Region 2 and B was still significant. Chronic diseases and advanced maternal age are important risk factors. For malformed infants, advanced maternal age was the only risk factor identified.

DISCUSSION

In the present case-control study, in the unadjusted analysis, it was found an association between low-birth weight and maternal residence during pregnancy in the vicinity of the petrochemical plant as well as having residence in the region of preferential wind direction. However there was no association when other potential risk factors were included in the analysis. Smoking is one of the best known risk factors for low birth weight. Chronic disease and young maternal age are also reasonable explanation for this outcome.[6] Uneven distribution of these confounders in the study regions could explain the fact that no association between low birth weight and mother's residence was seen in the conditional logistic regression. Advanced maternal age is well recognized as a risk factor for malformation and stillbirth and chronic disease is a known risk factor for stillbirths.[6] Other potential risk factors such as alcohol consumption, parental occupation and parental socioeconomic status were not studied because they were not available in the medical records.

It was found a lower than expected proportion of mothers of cases with residence in Region 2 than controls, compared to Region 3. A possible explanation is that Montenegro, the main city of the study area, is located in Region 2 and has a better healthcare system including a better equipped hospital, which could contribute to reduce stillbirth rates.

There was no deviation from the expected for most selected malformations. Lower than expected frequencies were observed for newborns with Down syndrome, anencephaly and nonsyndromal multiple congenital anomalies patterns. Underreporting in this hospital could have contributed to this observation. Exposure misclassification is a potential weakness of the present study and it is a common problem in most environmental epidemiological studies. The actual maternal exposure during pregnancy to chemicals from the petrochemical plant is not known. Geographic regions were arbitrarily defined based on their

proximity and wind direction, surrogate measures for potential exposures. FEPAM is currently conducting studies to identify presence of volatile organic compounds in the air and water. It is possible that the petrochemical plant's pollution control measures are effective enough to avoid exposing the neighboring population to dangerous pollutants. Other studies on human health effects (cancer, lung diseases) are also being conducted by FEPAM in this area.

The sample size is another potential limitation of the study, especially to what concerns congenital malformations and stillbirths, seen in lower numbers. For example, for stillbirths in the unadjusted analysis (sample size = 287; 3.1% of controls born to mothers living in Region 1 and 5.6% in Region A), there is an 80% power with 95% confidence interval to detect an OR of approximately 3.0 for geographic proximity (Region 1) and an OR of 2.5 for wind direction (Region A). The same calculation for malformed infants (sample size = 188; 4.4% of controls born to mothers living in Region 1 and 3.7% in Region A) would permit to detect an OR of 3.5 for geographic proximity (Region 1) and an OR of 3.8 for wind direction (Region A).

Several studies have already demonstrated an association between potential environmental contamination and low-birth weight. In one study a statistically significant excess of low birth weight was found among white live-born infants in the Love Canal neighborhood, a disposal site for various chemicals.[10] In studies of drinking water contaminated with trialomethane and carbon tetrachloride[5], exposed mothers gave birth to a higher proportion of small for gestational age newborns than unexposed mothers. In a study conducted in Sweden, a decline in average birth weight in a community potentially exposed to arsenic was found.[17] A study of water pollution caused by benzene in a Michigan area showed an association with low birth weight.[22] Another study examined the relationship between birth weight and mother's residence near a hazardous waste landfill in Lipari, New Jersey. A significant reduction in birth weight in the population living in an area immediately adjacent to the landfill was observed.[4]

However, there are also negative studies. A case controlled study from Denver did not show any association between higher neighborhood carbon monoxide levels and higher odds of low birth weight.[1] Investigations of communities living near a lead smelter,[14] dioxin-contaminated soil[20] and a toxic waste landfill did not find significant declines in the average birth weight infants or elevated prevalence of low birth weight infants.[12] Two studies in communities exposed to environmental industrial pollution (New York and San Francisco Bay area, respectively) also failed to correlate with low birth weights.[3,19]

Birth defects are outcomes frequently investigated for environmental contamination. For organic solvents, there are studies showing association of contamination of public drinking water with neural tube defects, major cardiac malformations, oral clefts, and central nervous system defects.[5,13] In South America, the ECLAMC[7] analyzed the association between industrial activity and occurrence of 34 congenital anomalies in 21 counties in Argentina during the 1982–1994 period. Significant associations ($p<0.01$) between textile industry and anencephaly, and between engine manufactures and microcephaly were found. Most of the studies, however, show negative associations between environment and birth defects.[16]

In one study on potential contamination caused by petrochemical plants, it was observed[8] that most children with orofacial defects in Pourt Harcout came from regions of high number of petrochemical refineries. A relationship between contamination from petrochemical industries and adverse pregnancy outcomes was not observed in Stegnungsum, Sweden,[2] a locality close to 5 petrochemical industries.

There were fewer studies associating stillbirths and environmental contamination. One study found a negative association between PCB-contaminated fish consumption and spontaneous fetal death.[15] Positive association was seen between spontaneous abortions when analyzed in an industrialized Finnish community according to the occupation and workplace of both women and their husbands.[11] An epidemiological study was conducted to investigate adverse outcomes of pregnancies among women who resided in a census tract are in Santa Clara county, California, that was thought to be exposed to drinking water from a well contaminated with organic solvent trichloroethane. Spontaneous abortion rate was more than twice higher than that observed in a comparable control community, and the difference persisted when rates were adjusted for maternal risk factors.[9]

Spontaneous abortion is frequently linked to environment chemical contamination.[18] In the present study, however, spontaneous abortions could not be ascertained. First because this information was not available in the Montenegro hospital registries. Second, abortion is illegal in Brazil and induced abortion is often misreported as spontaneous abortion for the mother's legal safeguard.

In Brazil, there are few specific studies designed to

investigate reproductive effects of environmental contamination. In the highly polluted town of Cubatão, a cluster of anencephaly was suspected. After prospectively surveying 10,000 births, no increase in major malformations was possible to attribute to environmental conditions.[16]

In conclusion, the 15-year birth data analysis of congenital malformations, low birth weight and stillbirths in the municipalities of Montenegro and Triunfo did not reveal the presence of a major environmental hazard in the study area. However, low birth weight could be a useful parameter for evaluating possible environmental contamination and should be closely monitored in the area. Further analysis of the actual population exposure could help interpreting the data collected in the study.

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