

# A CASE-CONTROL STUDY OF RISK FACTORS FOR INFANT MORTALITY IN A BRAZILIAN MUNICIPALITY

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## ABSTRACT

**Introduction:** Reducing infant deaths is a key objective of various national and international initiatives. Pato Branco is a Brazilian municipality located in the southwest of Paraná State. The city has had higher infant mortality rates than the State. In 2019, it had the worst rate in recent years (16.07/1000 live births). The study aimed to identify risk factors associated with infant mortality in Pato Branco/PR/BR from January/2013 to December/2019.

**Methods:** We conducted a case-control study with data obtained from the Information System on Live Births (SINASC), the Mortality Information System (SIM), the Primary Health Care Information System (e-SUS APS), and a review of electronic medical records. The cases involved children who died between 2013 and 2019 before completing one year. Controls were selected among children born in the same hospital and on the same date, matched by sex, and who completed one year of life.

**Results:** We included 103 cases and 206 controls. In a hierarchical conditional logistic regression model, absence of a steady partner (OR: 2.8), prenatal or childbirth complications (OR: 23.8), <7 prenatal visits (OR: 11.69), congenital anomalies (OR: 32.5), gestational age <37 weeks (OR: 7.4), Apgar <4 (OR: 17.6) and not having been breastfed (OR: 8.12) were risk factors for mortality, in the municipality. Lower education was a protective factor (up to elementary II - OR: 0.12; up to high school - OR: 0.26).

**Conclusion:** Congenital anomalies, prematurity, and unfavorable perinatal conditions were associated with higher mortality, not differing from previous studies. The direct association between maternal education and the high rate of congenital anomalies deserves detailed investigation. This data suggests that social determinants of health may be context-specific, emphasizing the importance of conducting local studies.

**Keywords:** *Infant mortality; Infant death; Cause of death; Risk factors; Congenital abnormalities; Social determinants*

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## BACKGROUND

The reduction of infant deaths is a key objective of various national and international initiatives due to its significant global impact. In 2016, according to data from the World Health Organization<sup>1</sup>, 2.6 million newborns died, most before completing one week of life. In Brazil<sup>2</sup>, infant mortality declined from 1990 to 2015, reducing from 52.4 to 14.1 per 1000 live births and thus reaching one of the millennium goals.

In 2019, Paraná State (BR) recorded the lowest infant mortality rate in the history of public health in the State before the COVID-19 pandemic. With 10.3 deaths of children up to one incomplete year of life per thousand live births, in recent years, the State has reduced infant mortality by 14% and maternal mortality by 29% compared to 2010 rates<sup>3</sup>. Pato Branco is a Brazilian municipality located in the southwest of Paraná. According to the 2010 IBGE census<sup>4</sup>, its population was 72,370 people with a human development index (HDI) of 0.782, reaching 84,779 in 2021. It ranks as the third best city regarding quality of life in Paraná and the 113th in Brazil. The city stands out in the micro-region

as a service center emphasizing the health and education sectors. However, Pato Branco has had higher infant mortality rates than the State. In 2019, it had the worst rate in recent years (16.07/1000 live births)<sup>5</sup>. Every year, the municipality seeks strategies to minimize the impact of these numbers and reach the single-digit mark in the rate, achieved only in 2015. Therefore, we conducted a case-control study aiming to identify the risk factors associated with infant mortality in Pato Branco/PR/BR from January 2013 to December 2019.

## METHODS

We conducted a case-control study with data collected from May 20, 2019, to January 30, 2020 retrospectively from the Information System on Live Births (SINASC), the Mortality Information System (SIM), and the Primary Care Information System in Health (e-SUS APS). In addition, we reviewed electronic medical records to complement the information from the SIM and the Primary Care Information System (SIAB) and collected prenatal, sociodemographic, and lifestyle data. The study was approved by the Ethics and Research Committee of the Hospital de Clínicas de Porto Alegre (CAAE 11637319.8.0000.5327).

The cases involved children who died between 2013 and 2019 before completing one year. Controls were children born in the same hospital and date and who completed the first year of life, matched by sex.

The sample size calculation considered a statistical power of 80%, an alpha error of 0.5, an odds ratio of 1.5, the proportion of 2 controls for each case, and a prevalence of exposure in controls of 30%. It would be necessary to include 93 cases and 186 controls. Considering possible losses, a total of 309 participants was reached, with 103 cases and 206 controls.

The primary outcome was infant mortality. Variables analyzed as potential risk factors included sociodemographic data collected from e-SUS APS: residence (neighborhood and city), basic sanitation conditions, type of construction, skin color, schooling, partner, and family income); parents' lifestyle information collected from e-SUS APS and medical records (smoking, alcohol consumption, illicit drug use); the pregnancy and delivery information collected from SINASC and medical records (maternal age, number of pregnancies, number of abortions, number of prenatal consultations, link to the reference maternity, type of delivery, prenatal risk classification, maternal comorbidities pre-existing conditions, prenatal or childbirth complications, gestational age); SINASC, SIM, and medical records provided newborn data (birth weight, presence of congenital anomalies, Apgar score at 5th minute,

place of birth, length of hospital stay after birth, cause of death). We included only complete forms that made complete data analysis possible.

## Data collection and statistical analysis

To formulate the collection instrument and the database, we used the REDCap (Research Electronic Data Capture) platform to construct and manage surveys<sup>6,7</sup>. After collection and tabulation, the data were exported in Excel format to the PASW Statistics 18 software. Initially, a descriptive analysis of the data was carried out, with absolute frequencies and percentages, mean or median, and standard deviation or interquartile range. Afterward, statistical tests of normality (Kolmogorov-Smirnov and Shapiro-Wilk) were performed. In the case of non-normality, we chose to categorize the variable. The chi-square test was applied to compare the variables between cases and controls. We used conditional logistic regression to identify independent risk factors, including variables with  $p < 0.20$  obtained in the univariable analysis. A significance level of 5% was considered. Hierarchical analysis started with the variables most distant from the outcome. The variables that maintained statistical significance with  $p < 0.10$  remained in the following model. The first model considered sociodemographic variables, the second was related to the period of pregnancy and delivery, and the third was related to the newborn. Collinearity between variables was avoided and each model was adjusted for confounders according to the results of the previous one, keeping variables with  $p \leq 0.10$ . There was no missing data.

## RESULTS

Pato Branco registered 8,912 births during the study period, of which 103 (1.16%) deaths occurred, and 206 controls were analyzed. We excluded 32 potential controls due to insufficient data. About half of the sample was male, and most of the newborns were white, lived in homes made of bricks, used the general sewage system, received water from the general network, and had an income of three or more minimum wages. There was a statistically significant difference regarding the presence of a steady partner, which was less frequent in cases ( $p=0.026$ ). At the same time, treatment of water received from the general network with the addition of chlorine or filtration ( $p=0.028$ ), higher education ( $p<0.001$ ), and white skin color ( $p=0.014$ ) were more frequent. Mother's age was similar between cases and controls, ranging from 15 to 47 years. Sociodemographic characteristics are detailed in Table 1.

**Table 1:** Socio-demographic characteristics of the sample of newborns in Pato Branco, BR, from 2013 to 2019.

| Variables               | Cases |      | Controls |      | OR (95% CI)        | p      |
|-------------------------|-------|------|----------|------|--------------------|--------|
|                         | n     | %    | n        | %    |                    |        |
| Type of construction    |       |      |          |      |                    | 0.898  |
| Wood/reclaimed          | 19    | 18.6 | 40       | 19.3 | 0.96 (0.53 – 1.76) |        |
| Masonry/brick           | 83    | 81.4 | 167      | 80.7 | 1                  |        |
| Water treatment         |       |      |          |      |                    | 0.028  |
| No additional treatment | 90    | 88.2 | 198      | 95.7 | 0.36 (0.15 – 0.90) |        |
| Filtered/Chlorinated    | 12    | 4.9  | 9        | 2.4  | 1                  |        |
| Sewage                  |       |      |          |      |                    | 0.071  |
| Trench/Open sky         | 16    | 15.7 | 51       | 24.6 | 0.57 (0.31-1.05)   |        |
| General sewage network  | 86    | 84.3 | 156      | 75.4 | 1                  |        |
| Water Source            |       |      |          |      |                    | 0.596  |
| Well or spring water    | 2     | 1.96 | 6        | 2.90 | 0.63 (0.11- 3.44)  |        |
| General water supply    | 101   | 98.0 | 200      | 97.1 | 1                  |        |
| Schooling               |       |      |          |      |                    |        |
| < high school           | 13    | 12.7 | 64       | 30.9 | 0.09 (0.03 – 0.25) | <0.001 |
| High school             | 64    | 62.7 | 125      | 60.4 | 0.26 (0.12 – 0.55) | 0.001  |
| College                 | 25    | 24.5 | 18       | 8.7  | 1                  |        |
| Skin color              |       |      |          |      |                    | 0.014  |
| Brown / Black           | 29    | 28.4 | 86       | 41.5 | 0.49 (0.26 – 0.86) |        |
| White                   | 73    | 71.6 | 121      | 58.5 | 1                  |        |
| Income <3 wages         | 5     | 4.9  | 18       | 8.7  | 0.53 (0.19 -1.48)  | 0.224  |
| < 5 rooms in the house  | 19    | 18.6 | 56       | 27.1 | 0.60 (0.33 -1.10)  | 0.101  |
| Non steady partner      | 22    | 21.4 | 25       | 12.1 | 2.16 (1.09 – 4.25) | 0.026  |
| Smoking                 | 12    | 11.8 | 27       | 13.0 | 0.88 (0.43 -1.83)  | 0.738  |
| Alcohol abuse           | 2     | 1.96 | 1        | 0.48 | 4.0 (0.36 – 44.12) | 0.258  |
| Use of illicit drugs    | 3     | 2.9  | 4        | 1.9  | 1.50 (0.33 – 6.70) | 0.596  |
| ≥ 35 years old          | 20    | 19.6 | 38       | 18.5 | 1.04 (0.55 -1.97)  | 0.913  |

The variables related to obstetric history and childbirth are described in Table 2. The classification of high gestational risk was more frequent among the cases than controls, while usual gestational risk was more frequent in controls ( $p<0.001$ ). Prenatal consultations occurred in more significant numbers

among controls ( $p<0.001$ ), while maternal comorbidities ( $p=0.06$ ) and prenatal or childbirth complications were less frequent in this group ( $p<0.001$ ). Most of the cases and controls were linked to the reference maternity; the pregnancy was with a single fetus, and the delivery was a cesarean section.

**Table 2:** Maternal and prenatal obstetric history in the sample of newborns in Pato Branco, BR, from 2013 to 2019.

| Variables                             | Cases |      | Controls |      | OR (95% CI)          | p      |
|---------------------------------------|-------|------|----------|------|----------------------|--------|
|                                       | n     | %    | n        | %    |                      |        |
| Previous abortion                     | 8     | 7.9  | 27       | 13.0 | 0.60 (0.26 -1.36)    | 0.219  |
| Delivery                              |       |      |          |      |                      | 0.335  |
| Cesarian section                      | 55    | 53.9 | 124      | 59.9 | 0.77 (0.46 -1.31)    |        |
| Vaginal                               | 47    | 46.1 | 83       | 40.1 | 1                    |        |
| Gestational risk                      |       |      |          |      |                      | <0.001 |
| High                                  | 77    | 75.5 | 92       | 44.4 | 3.66 (2.14 - 6.23)   | <0.001 |
| Intermediate                          | 3     | 2.9  | 5        | 2.4  | 2.64 (0.58 -11.78)   | 0.206  |
| Habitual                              | 22    | 21.6 | 110      | 53.1 | 1                    |        |
| Comorbidities                         | 27    | 26.5 | 35       | 16.9 | 1.74 (0.98 - 3.10)   | 0.060  |
| Prenatal and childbirth complications | 91    | 89.2 | 78       | 37.7 | 10.73 (5.33 - 21.63) | <0.001 |
| < 7 prenatal visits                   | 53    | 51.5 | 16       | 7.8  | 11.69 (5.53 - 24.70) | <0.001 |

Table 3 describes the variables related to the newborn. Of the total deaths, 97 (95.1%) occurred in hospitals, three in another health facility and two at home. The presence of congenital anomalies was more frequent in the cases ( $p<0.001$ ), as well

as birth asphyxia ( $p<0.001$ ), twin pregnancy ( $p<0.001$ ), and lack of breastfeeding ( $p<0.001$ ). Gestational age at birth ranged from 29 to 41 weeks among controls and 18 to 41 weeks among cases ( $p<0.001$ ). Birth weight was  $1,642 \pm 1,010$  grams,

with a minimum of 300 g and a maximum of 2,570 g for cases, and 3,139  $\pm$ 588 g, with a minimum of 365 g and a maximum of 3,558 g for controls.

The mean age at death was 29 days ( $\pm$ 58.24), ranging from 0 to 300 days, 50% of which occurred in the neonatal period.

**Table 3:** Newborn variables in the sample (Pato Branco, BR, from 2013 to 2019).

| Variables                  | Cases |      | Controls |      | OR (95% CI)         | p      |
|----------------------------|-------|------|----------|------|---------------------|--------|
|                            | n     | %    | n        | %    |                     |        |
| Apgar score <4             | 45    | 44.1 | 6        | 2.9  | 43.75(10.61-80.49)  | <0.001 |
| Multiple pregnancy         | 15    | 14.6 | 6        | 2.9  | 116.4(1.19-1354.5)  | 0.042  |
| Congenital anomalies       | 25    | 24.5 | 6        | 2.9  | 25.27(5.99-106.56)  | <0.001 |
| Not breastfeeding          | 56    | 84.8 | 189      | 91.3 | 8.12 (4.07-16.17)   | <0.001 |
| Weight $\leq$ 2500g        | 73    | 70.9 | 25       | 12.1 | 37.65(11.82-19.98)  | <0.001 |
| Gestacional age < 37 weeks | 73    | 70.9 | 23       | 11.2 | 29.62(10.8 - 81.36) | <0.001 |

Table 4 presents the multivariable analysis. The independent risk factors that most contributed to newborn mortality before one year of life were identified as the presence of congenital anomaly, prenatal or delivery complications, Apgar < 4

(OR greater than 15). Not having been breastfed, prenatal consultations < 7, GA < 37 weeks showed an OR close to 10. Among the sociodemographic variables, the absence of a steady partner and higher education remained risk factors.

**Table 4:** Risk factors for infant mortality in the first year of life (Pato Branco, BR, from 2013 to 2019).

| Variable                                         | OR crude | OR adjusted | 95% CI          | p     |
|--------------------------------------------------|----------|-------------|-----------------|-------|
| Model 1 - sociodemographic                       |          |             |                 |       |
| No stable partner                                | 2.16     | 2.80        | (1.30 - 6.01)   | 0.008 |
| Deficient basic sanitation                       | 0.57     | 0.86        | (0.44 - 1.70)   | 0.673 |
| Brown/Black skin color                           | 0.48     | 1.63        | (0.84 - 3.14)   | 0.144 |
| No-chlorinated water                             | 0.36     | 0.43        | (0.16 - 1.15)   | 0.091 |
| Schooling                                        |          |             |                 |       |
| < high school                                    | 0.09     | 0.12        |                 |       |
| High school                                      | 0.26     | 0.26        | (0.04 - 0.32)   | <0001 |
| College                                          | 1        | 1           | (0.11- 0.59)    | <0001 |
| <5 rooms                                         | 0.60     | 1.32        | (90.65 - 2.65)  | 0.448 |
| Model 2 – maternal and gestational risk factors* |          |             |                 |       |
| Maternal comorbidity                             | 1.74     | 1.21        | (0.42 - 3.55)   | 0.718 |
| Prenatal and delivery complications              | 10.73    | 23.77       | (7.45 - 75.83)  | <0001 |
| < 7 prenatal visits                              | 11.6     | 9.11        | (3.48 - 23.85)  | <0001 |
| Model 3 – Newborn risk factors**                 |          |             |                 |       |
| Gestacional age <37 weeks                        | 29.61    | 7.39        | (1.18 - 46.02)  | 0.032 |
| Apgar score < 4                                  | 43.75    | 17.56       | (2.10 - 146.85) | 0.008 |
| Non breastfeeding                                | 8.12     | 9.28        | (1.59 - 53.93)  | 0.013 |
| Congenital anomaly                               | 25.27    | 32.50       | (2.27- 466.40)  | 0.010 |

\*Adjusted for the partner, skin color, chlorinated water, basic sanitation, room number, and maternal schooling.

\*\*Adjusted for partner, skin color, chlorinated water, basic sanitation, room number, maternal schooling, maternal comorbidity, prenatal and delivery complications, and number of prenatal visits.

## DISCUSSION

In the present case-control study, which aimed to identify risk factors for mortality before one year of life in the city of Pato Branco-PR-BR, sociodemographic factors independently associated with an increase in the chance of infant death were the absence of a steady partner and higher schooling. Complications during pregnancy or childbirth, less than seven prenatal consultations, gestational age below 37

weeks, and lack of breastfeeding led to a high risk of death. In addition, very high-risk factors for death were severe hypoxemia at birth and fetal anomaly.

The same risk factors were identified in previous Brazilian studies<sup>8-10</sup>. Migoto et al.<sup>8</sup> analyzed the risk factors for early neonatal mortality in the State of Paraná-BR in the year 2014, according to the risk stratification criteria of the Care Line of the Rede Mãe Paranaense Program. The main risk factors were related mainly to the characteristics of the newborn,

such as male gender, low birth weight, prematurity, Apgar score lower than seven in the fifth minute of life, and the presence of a congenital anomaly. Similar results were found in studies by Doldan et al.<sup>9</sup> and Kropiwek et al.<sup>10</sup> In the first, 69 cases of neonatal death occurred in 2007, and 138 controls matched by sex were analyzed. The second study analyzed about 8,000 live births in 2012. Unlike the study by Migoto et al.<sup>8</sup>, in the first, there was pairing by gender – as in the present study. In the second, the authors did not analyze gender as a potential risk factor. The difference in results concerning gender may be due to differences in sample characteristics and the statistical analysis model.

Congenital anomalies are the second leading cause of death in newborns and children under five in Brazil<sup>11</sup>. In 2019, the congenital anomaly was the first cause of death of children up to one year old, corresponding to 21% of the 20,927 deaths recorded in North America by the National Vital Statistics Reports<sup>12</sup>. The congenital anomaly also conferred a higher risk of mortality in the first year of life in the present study. In a study<sup>13</sup> whose population consisted of children under one year of age who died after discharge from the maternity hospital between 2000 and 2013, in a municipality located in the northern region of the State of Paraná-BR, congenital malformations as the underlying cause of death led to the occurrence of death in a higher percentage in the post-neonatal period. In the studies of Migoto et al.<sup>8</sup>, Doldan et al.<sup>9</sup>, and Kropiwek et al.<sup>10</sup> that evaluated the neonatal period, congenital malformations were also the highest risk factor, with a lower adjusted OR compared to our study. Comparing the rates of malformations in cases and controls in those studies, we observed that they were higher in Pato Branco. Concerning a city located in the north of the State<sup>9</sup>, they were very close. However, with a higher adjusted OR in Pato Branco (32.5 vs. 10.1). These data suggest that the causes of congenital malformations should be further studied in Pato Branco and that they could contribute to the higher infant mortality rate compared to the State. In the four studies, therefore, the common factor that conferred greater risk was the presence of congenital anomalies. A study<sup>14</sup> carried out with data from the MS Information System on Live Births (SINASC) for the city of São Paulo (Brazil) in the period 2010-2014 found a prevalence of congenital malformations of 17.9 cases /1,000 live births. Factors associated with congenital anomaly were prematurity, multiple gestation, maternal age > 40 years and < 19 years, birth weight between 500 and 2,500g or > 3,550g, black and yellow mother, and male gender. Prematurity was an independent risk factor for death in our study. However, the association of prematurity with congenital malformation found by Cosme et al.<sup>14</sup> may reflect reverse causality since it is a cross-sectional study.

The EUROCAT (European Surveillance of Congenital Anomalies)<sup>15</sup> recorded a prevalence of major congenital malformations of 23.9 per thousand births from 2003 to 2007. Eighty percent of cases were live births, 2.5% died in the first week of life, and 2.0% corresponded to stillbirths or fetal death from 20 weeks of gestation. In 17.6%, the pregnancy was terminated after prenatal diagnosis. Although not all malformations are fatal, children who survive the neonatal period are at greater risk of long-term disability and require health and other support services to improve their quality of life. Despite the advancement of technology, which has increased the survival time related to malformation, most deaths from malformations are challenging to reduce due to individual peculiarities and complications of chronicity, such as infectious and respiratory diseases<sup>13</sup>. Additionally, identification of the cause of the malformation does not reach 50% of cases<sup>16</sup>.

In different studies, prematurity was strongly associated with the outcome of infant death in addition to congenital anomalies. In the case of congenital anomalies, the quality of prenatal care could interfere with reducing these rates if there were greater access and investment in technologies that provide early diagnosis, such as through the offer of genetic screening tests<sup>17</sup>. Furthermore, maternal comorbidity leads to complications during pregnancy and childbirth, and cases were 23 times more likely to have been exposed to such complications. This fact also reinforces the importance of more significant investments in technologies, skilled labor, and qualification of health network services, from primary care to high complexity.

When addressing pregnant women's access to health services, a study<sup>18</sup> identified that the mother not having performed prenatal care or had inadequate prenatal care and not being linked to maternity during prenatal care are factors significantly associated with infant death. Doldan et al.<sup>9</sup> concluded that newborns whose mothers had less than four consultations during prenatal care had a higher risk of death and that, excluding congenital anomalies, the other variables are intrinsically related to providing quality health services, mainly through the prenatal and childbirth care program. In the present study, complications during pregnancy or childbirth and fewer than seven prenatal consultations were also factors that gave a high chance of infant mortality, reinforcing the importance of strengthening care networks for pregnant women and newborns at all levels.

Breastfeeding protects against mortality from respiratory infections and diarrhea<sup>19</sup>. In the present study, newborns who did not have enough time to breastfeed were not excluded from the analysis. Although adjusted for factors that would prevent breastfeeding, the OR for non-breastfeeding may be



overestimated. In the population-based case-control study by Victora et al.<sup>19</sup> carried out in the metropolitan region of Porto Alegre and Pelotas (RS-BR), intending to evaluate mortality due to diarrhea, respiratory infection, and other infections, the adjusted relative risk of offering cow's milk exclusively was 11.6 (95% CI 4.5-29.8) and formula exclusively was 16.3 (95% CI 6.4-41.3) for infant mortality due to diarrhea and 3.3 (95% CI 1.4-7.8) and 3.9 (95% CI 1.8-8.7), respectively, for mortality due to respiratory infection. The OR of not having been breastfed in the present study is close to the RR for mortality from diarrhea and above that from childhood pneumonia. The absence of deaths from diarrhea reinforces the possibility that it was overestimated but does not invalidate the conclusion that not having been breastfed is an independent risk factor for infant mortality in Pato Branco. The absence of diarrhea as a cause of death may be because practically everyone lived in homes with good sanitary facilities, and the majority had an income greater than three minimum wages.

Regarding socioeconomic factors, the absence of a steady partner and higher education (bachelor's degrees) were identified as risk factors. In the study by Migoto et al.<sup>8</sup>, only the absence of a partner was a risk factor among the socioeconomic variables, and lower education lost significance when adjusted for confounders. The studies conducted in Foz do Iguaçu-BR<sup>9</sup> and Joinville-BR<sup>10</sup> did not show a statistically significant association. In our study, the protection conferred by lower education may be related to the socioeconomic characteristics of the municipality with a high HDI, where women with higher education possibly work outside the home. Working outside the home may also contribute to fewer prenatal consultations. The characteristics of the population can also explain the lack of association with age since only four pregnant women were between 15 and 18 years of

age. A retrospective study<sup>20</sup> with data from the Birth Statistical Master files in California (2007 to 2015) found significant disparities in infant mortality rates in different population groups according to maternal sociodemographic and economic characteristics and maternal characteristics during pregnancy. In general, the results agree with our study. However, it shows that infants of women with bachelor's degrees or higher were less likely to die (OR 1.89; 95% CI, 1.76–2.04) compared to infants of women with less education than in high school. This data suggests that social determinants of health may be context-specific, emphasizing the importance of conducting local studies.

The study's main limitation is the retrospective data collection based on secondary data. Even complementing the data through reviewing the children's medical records, the lack of adequate registration precluded the analysis of other potential risk factors, such as the number of children and adults in the house at the time of pregnancy and birth and the number of previous infant deaths.

## CONCLUSION

Congenital anomalies, prematurity, and unfavorable perinatal conditions were associated with higher mortality before one year of life in Pato Branco-PR-BR, not differing from previous studies. However, the direct association between maternal education and the high rate of congenital anomalies deserves a more detailed investigation in the search for local factors.

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