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# Congenital anomalies in Rio Grande do Sul State: a time series analysis

## *Anomalias congênitas no estado do Rio Grande do Sul: análise de série temporal*

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**ABSTRACT:** ***Introduction:*** In Rio Grande do Sul Sate (Brazil), the incidence of congenital anomalies ranges from 10 to 15/1,000 live births. Identifying risk factors can change congenital anomalies frequency and neonatal mortality. This paper intends to analyze temporal variation of congenital anomalies in the State of Rio Grande do Sul, from 2005 to 2014, and to identify the factors associated with its occurrence. ***Method:*** This is a descriptive, time series study based on secondary data on congenital anomalies and sociodemographic and health variables of mothers and newborns living in Rio Grande do Sul, from 2005 to 2014. ***Results:*** In the period surveyed, there were 1,386,803 births of mothers living in Rio Grande do Sul, and the cases diagnosed with congenital anomalies corresponded to a general average rate of 9.2 per thousand cases, with a greater rate in the group of mothers of newborns whose Apgar score was lower than seven; who had a weight equal to or lower than 1,500 grams; with a gestational age equal to or lower than 31 weeks and living in the metropolitan region. The most frequent types of congenital anomalies were those located in the musculoskeletal system, the nervous system and the circulatory system. ***Conclusion:*** These data warn us about the change in the epidemiological profile of mothers of children with congenital anomalies, thereby indicating the groups at greatest risk.

***Keywords:*** Perinatology. Congenital anomalies. Epidemiology.

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**RESUMO:** ***Introdução:*** No estado do Rio Grande do Sul, a incidência de anomalias congênitas varia de 10 a 15/1.000 recém-nascidos vivos. Reconhecer os fatores de risco pode modificar a frequência das anomalias congênitas e a mortalidade neonatal. Este artigo teve o objetivo de analisar a variação temporal de anomalias congênitas no Rio Grande do Sul, de 2005 a 2014, e identificar os fatores associados à sua ocorrência. ***Método:*** Trata-se de um estudo descritivo de série temporal, baseado em dados secundários, sobre anomalias congênitas e as variáveis sociodemográficas e de saúde das mães e dos recém-nascidos residentes no Rio Grande do Sul, no período de 2005 a 2014. ***Resultados:*** No período investigado, ocorreram 1.386.803 nascimentos oriundos de mães residentes no Rio Grande do Sul, e os casos diagnosticados com anomalias congênitas corresponderam a uma taxa média geral de 9,2 por mil casos, com maior taxa no grupo de mães de recém-nascidos cujo índice de Apgar foi menor que 7; com peso igual ou menor que 1.500 g; com idade gestacional igual ou menor que 31 semanas e residentes na região metropolitana. As anomalias congênitas mais frequentes foram as do sistema osteomuscular, sistema nervoso e aparelho circulatório. ***Conclusão:*** Esses dados alertam sobre a mudança no perfil epidemiológico das mães de crianças com anomalias congênitas, mostrando os grupos de maior risco.

***Palavras-chave:*** Perinatologia. Anomalias congênitas. Epidemiologia.

## INTRODUCTION

Congenital anomalies (CA) are functional and / or morphological anomalies (malformations, deformations and disruptions) of genetic, environmental or unknown causes that occur in intrauterine life and which can be detected during or after pregnancy[1]. In general, around 5% of newborns (NB) have at least one CA[2], putting them among the top five causes of morbidity in children under one year of age (the first in developed countries). Official data for Brazil show a frequency of 0.7% in 2014, which shows a high underreporting of cases[4]. For more than 40 years, the Latin American Collaborative Study of Congenital Malformations (ECLAMC) has observed heterogeneous CA rates among different countries in the region[3]. In 2011, the overall rate of CAs, according to ECLAMC, was 2.7%, varying from 1.4% in Ecuador to 4.2% in Brazil[5]. Studies in several regions of Brazil showed varied rates, such as: 0.48% in the interior of Paraíba[6]; 1.2% in the city of São Paulo[7]; 1.4%, in the city of Pelotas (RS)[8]; and 1.7% in Rio de Janeiro[9]. Underreporting, however, is a serious epidemiological problem in South America, negatively influencing the reliable comparison of data[3,10].

In the State of Rio Grande do Sul, the incidence of CAs varies from 10 to 15 / 1,000 live newborns[11]. The Birth Defect Monitoring Program (PMDC), linked to ECLAMC and conducted at the *Hospital de Clínicas* of Porto Alegre (HCPA), has evaluated approximately 60 thousand newborns since 1983[1,12]. Between 2001 and 2005, 765,230 newborns were registered, with annual average of 153,046 children and occurrence of 0.81% diagnosed CAs[11]. For each diagnosed case of heart disease at birth, trisomy 13 and 18, diaphragmatic hernia and central nervous system (CNS) anomalies[11], about three others were not noticed, with the newborns dying in the first year of life.

It is estimated that 276 thousand newborns with CAs die during the first month of life per year worldwide[13]. In Latin American and Caribbean countries, CAs account for 17% of deaths in children younger than one year[14]. Brazilian studies highlight mortality rates of 14-32% for fetuses with some type of severe CA, such as CAs of the CNS or multiple malformations[15, 16].

Continuous monitoring helps to implement prevention measures, reducing the frequency and mortality of CAs in the population[14], since 50% of them are preventable[17]. Early diagnosis in the prenatal period may indicate a high-risk pregnancy and thus result in the birth occurring in a referral hospital that can adequately care for the child with CAs, thereby improving survival[17]. Another possibility is genetic counselling which makes possible to avoid the gestation of a child with a CA. Recognizing maternal and neonatal risk factors can help to change the frequency and mortality of CAs[13].

Given the context, a time-series study can help to understand future trends of CA occurrences by macro-region of RS and by maternal and neonatal characteristics. Therefore, the objectives of the present study are to analyze the temporal variation of CAs in Rio Grande do Sul, from 2005 to 2014, and to identify the factors associated with its occurrence.

## METHOD

A descriptive, time-series study based on secondary data. The data were collected by means of a study on CAs and the sociodemographic and health variables of mothers and newborns living in RS, from 2005 to 2014. The records related to CAs are completed in the Declaration of Live Births (DNV), a document consisting of 41 domains distributed in seven blocks of variables: registry office; place of occurrence; mother; gestation and delivery; newborn; identification; and signature of the responsible professionals. Domain 34 related to CAs was included in the DNV in 1999 and composes the "newborn" section. The data collected are gathered in the Municipal Health Secretariats, sent to the State Secretariats and, after being revised, sent to the Ministry of Health (MS), which publishes them through the Department of Informatics of the Unified Health System/Live Birth Information System (DATASUS/SINASC)[18]. SINASC was implemented in 1990 and aims to collect, organize, produce and provide information on births in the national territory[18].

The variables selected for analysis were: type of CA, according to the International Classification of Diseases (ICD 10) (congenital malformations of the nervous system (Q00-Q07); congenital malformations of the circulatory system (Q20-Q28); cleft lip and cleft palate (Q35-Q37); absence of atresia and stenosis of the small intestine (Q38-Q41.8); congenital malformations of the digestive system (Q48-Q45) or undescended testes (Q50-Q53); malformations of the genitourinary tract (Q60–Q64); congenital deformities of the hip (Q65-Q65.8); congenital deformities of the feet (Q65-Q66.9); other malformations and congenital deformities of the musculoskeletal system (Q65-Q79); other congenital malformations, chromosomal anomalies – unclassified in other parts (Q90–Q99) hemangioma (D18.0) and lymphangioma (D18.1); maternal data – marital status (single, married, widow, legally

separated or in consensual civil union), age (10 to 14, 15 to 19, 20 to 24 ... 55 to 59 years), skin color (white, black, yellow, brown or indigenous), schooling (0 to 12 years or more), macro-region of residence (Midwest, Metropolitan, *Missioneira,* North, Highlands, South or Valleys, gestation time (less than 22 weeks, 22 to 27, 28 to 31, 32 to 36, 37 to 41, 40 weeks or more) and type of gestation (single, double or triple and more), type of delivery ( vaginal or caesarean section) and number of prenatal appointments (0, 1 to 3, 4 to 6, 7 or more).

The selected variables of the NB were: gender (male or female), weight (less than 500 g, 500 to 900 g, 1,000 g to 1,499 g ... to more than 4,000 g) and Apgar score (0 to 2, 3 to 5, 6 to 7, 8 to 10). From these data, the total annual occurrence of CAs for the period studied and the specific occurrences according to maternal variables, the NB and the affected area or systems were calculated. The overall mean rate of CA cases per year was calculated by the number of CA cases divided by the number of live births in RS, multiplied by one thousand.

For this calculation, the total number of cases of tuberculosis in each period divided by five was entered into the numerator and, the population of each sector in the center of the period was entered in the denominator. The number of ignored cases were quantified but then excluded from the analyses, as they corresponded to a small N and no statistically significant result was found for this group.

The types of CAs were categorized into seven groups: musculoskeletal system; nervous system; circulatory system; genitourinary system; cleft lip and palate; digestive tract and other anomalies – chromosomal abnormalities, hemangiomas, lymphangiomas, congenital ichthyosis, epidermolysis bullosa and hereditary lymphedema.

To test whether CA trends and maternal and infant variables were decreasing, increasing or stationary between 2005 and 2014, the Prais-Winsten regression method was used, with a residual minimization adjustment. This test corrects the first-order autocorrelation effect and quantifies the annual variation of proportions[19]. The trend whose regression coefficient was not different from zero ($p > 0.05$) was considered stationary, and the confidence intervals (95%CI) were also calculated. The Stata 14.0 package was used for statistical analysis. There was no need for approval by the Research Ethics Committee, since public data were available in DATASUS / SINASC.

## RESULTS

From 2005 to 2014, there were 1,386,803 births from mothers residing in RS, of whom 12,818 (0.92%) had CAs, which corresponds to a general average rate of 9.2 per thousand cases (95%CI 8.4 to 10.3).

The highest occurrences of CAs were in the NB group with Apgar score less than 7; weight equal to or less than 1,500 g; and gestational age (GA) equal to or less than 31 weeks. The lowest rates occurred in the groups of mothers between 20 and 34 years of age, of white skin color, from the Midwest, South, *Missioneira*, North, Highlands and Valley regions, with a GA of 37 weeks or more, 7 or more prenatal appointments and whose newborns had a birth weight between 3,000 and 3,999 g, Apgar score between 8 and 10 and were female (Table 1).

Table 1. Mean rate (per thousand) of congenital anomalies according to maternal and NB characteristics, Rio Grande do Sul, Brazil, 2005 to 2014 (n = 1,386,803).

| Characteristics | N | Median rate (per thousand) | 95%CI |
|---|---|---|---|
| Maternal age (years) | | | |
| 10 - 19 | 235.193 | 9.7 | 8.4 – 11.8 |
| 20 - 34 | 952.634 | 8.5 | 7.4 – 9.5 |
| 35 - 39 | 153.616 | 10.8 | 9.9 – 11.8 |
| ≥ 40 | 45.352 | 17.2 | 14.1 – 19.7 |
| Marital status | | | |
| Single | 775.010 | 9.7 | 8.9 – 10.6 |
| Married or civil union | 577.917 | 8.5 | 7.3 – 10.0 |
| Widowed or separated | 25.678 | 10.7 | 8.3 – 14.2 |
| Color of skin | | | |
| White | 1.197.311 | 8.9 | 8.1 – 10.0 |
| Black or brown | 175.920 | 11.8 | 10.0 – 13.8 |
| Yellow or indigenous | 6.756 | 7.7 | 1.3 – 15.3 |
| Region | | | |
| Midwest and South | 257.365 | 8.3 | 6.4 – 9.5 |
| Metropolitan | 645.591 | 11.9 | 10.2 – 13.8 |
| *Missioneira* and North | 249.589 | 6.2 | 5.3 – 7.4 |
| Highlands and Valleys | 234.385 | 6.2 | 4.9 – 7.6 |
| Schooling (years completed) | | | |
| 1 - 7 | 464.825 | 9.9 | 8.5 – 11.2 |
| 8 - 11 | 645.113 | 9.2 | 8.0 – 10.5 |
| ≥ 12 | 268.018 | 8.3 | 7.7 – 9.1 |
| Gestational age (weeks) | | | |
| 22 - 31 | 19.979 | 32.1 | 26.4 – 37.5 |
| 32 - 36 | 120.720 | 20.2 | 17.4 – 22.6 |
| ≥ 37 | 1.235.404 | 7.8 | 7.1 – 8.7 |
| Pregnancy | | | |
| Single | 1.355.607 | 9.2 | 8.4 – 10.3 |
| Multiple | 30.661 | 11.8 | 6.9 – 16.6 |

Continue...

Table 1. Continuation.

| Characteristics | N | Median rate (per thousand) | 95%CI |
|---|---|---|---|
| Pre-natal appointments | | | |
| 0 - 3 | 109.631 | 13.4 | 9.6 – 17.3 |
| 4 - 6 | 289.254 | 10.7 | 9.2 – 11.6 |
| ≥ 7 | 979.294 | 8.4 | 7.7 – 9.3 |
| Type of delivery | | | |
| Vaginal | 600.402 | 8.2 | 6.9 – 9.5 |
| C-section | 786.018 | 10.0 | 9.1 – 11.0 |
| Birth weight (grams) | | | |
| < 1.500 | 19.275 | 39.0 | 29.9 – 43.6 |
| 1.500 - 2.499 | 109.688 | 22.8 | 21.2 – 24.3 |
| 2.500 - 2.999 | 326.742 | 10.1 | 9.0 – 11.3 |
| 3.000 - 3.999 | 861.856 | 6.7 | 6.0 – 7.7 |
| ≥ 4.000 | 68.965 | 7.7 | 6.5 – 9.9 |
| 5-minute Apgar | | | |
| 1 - 7 | 31.650 | 58.6 | 52.6 – 64.7 |
| 8 - 10 | 1.331.929 | 8.1 | 7.3 – 9.0 |
| Gender | | | |
| Male | 710.033 | 10.3 | 9.0 – 11.5 |
| Female | 676.749 | 8.0 | 7.2 – 9.0 |
| Total | 1.386.803 | 9.2 | 8.4 – 10.3 |

95% CI: 95% confidence interval.

Mothers aged 40 or older had a higher occurrence of CAs than those between 35-39 and 20-34 years. The average rate of black or brown mothers prevailed over that of white mothers. The Metropolitan region had the highest rate with 11.9 cases per thousand in relation to the Midwest and Southern macro regions, *Missioneira,* North, Highlands and Valleys. Mothers who performed less than three prenatal appointments had a higher average rate than those who had seven or more. The group of mothers with male NBs obtained a higher rate than those with female NBs. The lower the GA, the Apgar score and the newborn weight, the higher the CA rates were in the study population. There was no difference in the mean rates for the variables "marital status", "schooling", "type of pregnancy" and "type of delivery" (Table 1).

Table 2 shows the temporal trend of CAs for maternal and NB characteristics. The analysis by Prais-Winsten revealed a trend of CAs in married or women in a civil union, with a mean

Table 2. Temporal trend of congenital anomalies according to maternal and NBcharacteristics, Rio Grande do Sul, Brazil, 2005 to 2014 (n = 1,386,803).

| Characteristics | Annual variation rate (per thousand) | 95%CI | p-value* |
|---|---|---|---|
| Maternal age (years) | | | |
| 10 - 19 | 0.14 | -0.14 – 0.42 | 0.28 |
| 20 - 34 | 0.13 | 0.00 – 0.26 | 0.05 |
| 35 - 39 | 0.07 | -0.04 – 0.18 | 0.20 |
| ≥ 40 | -0.29 | -0.54 – -0.04 | 0.03 |
| Ignored | 16.4 | -1.19 – 34.0 | 0.06 |
| Marital status | | | |
| Single | 0.07 | -0.06 – 0.19 | 0.25 |
| Married or civil union | 0.19 | 0.01 – 0.37 | 0.04 |
| Widowed or separated | 0.10 | -0.08 – 0.27 | 0.25 |
| Ignored | -0.30 | -1.22 – 0.63 | 0.48 |
| Skin color | | | |
| White | 0.12 | -0.01 – 0.24 | 0.06 |
| Black or brown | -0.08 | -0.31 – 0.14 | 0.43 |
| Yellow or indigenous | 0.63 | -0.60 – 1.86 | 0.27 |
| Ignored | -0.48 | -2.05 – 1.09 | 0.50 |
| Region | | | |
| Midwest or South | -0.12 | -0.46 – 0.22 | 0.47 |
| Metropolitan | 0.24 | 0.09 – 0.39 | 0.01 |
| *Missioneira* or North | 0.14 | 0.01 – 0.28 | 0.04 |
| Highlands or Valleys | -0.09 | -0.23 – 0.05 | 0.18 |
| Schooling (completed years) | | | |
| 1 - 7 | 0.19 | 0.02 – 0.37 | 0.04 |
| 8 - 11 | 0.16 | 0.04 – 0.28 | 0.02 |
| ≥ 12 | -0.08 | -0.14 – -0.02 | 0.02 |
| Ignored | 0.29 | -1.04 – 1.61 | 0.63 |
| Gestational age (weeks) | | | |
| 22 - 31 | 0.03 | -0.65 – 0.70 | 0.92 |
| 32 - 36 | -0.22 | -0.70 – 0.25 | 0.31 |
| ≥ 37 | 0.08 | -004 – 0.20 | 0.16 |

Continue...

Table 2. Continuation.

| Characteristics | Annual variation rate (per thousand) | 95%CI | p-value* |
|---|---|---|---|
| Ignored | -0.31 | -3.79 – 3.18 | 0.84 |
| Pregnancy | | | |
| Single | 0.11 | -0.02 – 0.24 | 0.09 |
| Multiple | -030 | -0.78 – 0.18 | 0.18 |
| Ignored | 1.17 | -0.44 – 2.78 | 0.13 |
| Pre-natal appointments | | | |
| 0 - 3 | 0.55 | 0.09 – 1.02 | 0.03 |
| 4 - 6 | 0.00 | -0.16 – 0.16 | 1.00 |
| ≥ 7 | 0.12 | 0.00 – 0.24 | 0.05 |
| Ignored | 0.81 | -2.30 – 3.92 | 0.57 |
| Type of delivery | | | |
| Vaginal | 0.08 | -0.08 – 0.23 | 0.30 |
| Caesarean | 0.08 | -0.05 – 0.21 | 0.20 |
| Ignored | 1.17 | -0.44 – 2.78 | 0.13 |
| Birth weight (grams) | | | |
| < 1.500 | 0.66 | -0.24 – 1.55 | 0.13 |
| 1.500 - 2.499 | 0.13 | -0.08 – 0.33 | 0.20 |
| 2.500 - 2.999 | 0.08 | -0.09 – 0.26 | 0.30 |
| 3.000 - 3.999 | 0.09 | -0.03 – 0.20 | 0.11 |
| ≥ 4.000 | 0.13 | -0.21 – 0.46 | 0.42 |
| Ignored | 3.62 | -1.42 – 8.66 | 0.14 |
| 5-minute Apgar | | | |
| 1 - 7 | 1.01 | 0.67 – 1.35 | < 0.01 |
| 8 - 10 | 0.09 | -0.03 – 0.21 | 0.12 |
| Ignored | -0.26 | -1.14 – 0.62 | 0.51 |
| Gender | | | |
| Male | 0.18 | 0.05 – 0.30 | 0.01 |
| Female | 0.03 | -0.13 – 0.18 | 0.71 |
| Ignored | -0.30 | -1.22 – 0.63 | 0.48 |
| Total | 0.11 | -0.01 – 0.23 | 0.07 |

95% CI: 95% confidence interval; * Prais-Winsten regression.

annual variation of 0.19 cases per thousand (95%CI 0.01–0.37). There was a growth trend in two macroregions: Metropolitan, with a mean annual variation of 0.24 cases per thousand (95%CI 0.09–0.39), and *Missioneira* and North, with an average variation of 0.14 cases per thousand (95%CI 0.01–0.28). There was an increasing trend of mothers with up to 11 years of schooling, divided into two groups: 0.19 cases per thousand (95%CI 0.02–0.37) among those who had up to 7 years and 0.16 cases per thousand (95%CI 0.04–0.28) among those who had between 8 to 11 years. This increase was also indicated in the group of women who had up to three prenatal appointments (0.55 per thousand and 95%CI 0.09–1.02) and whose NB had an Apgar score between 1 and 7 (1.01 per thousand, 95%CI 0.65–1.35) and were male (0.18 per thousand, 95%CI 0.05–0.30).

Table 2 also shows a decreasing trend among mothers aged 40 years or older, with -0.29 cases per thousand (95%CI -0.54; -0.04), and schooling equal to or greater than 12 years of study, with a rate of -0.08 cases per thousand (95%CI -0.14; -0.02). There was a borderline statistical significance ($p = 0.05$) for women aged between 20 and 34 years and for those who had 7 or more prenatal appointments.

Regarding the occurrence of different types of CAs in the study period, musculoskeletal, nervous and circulatory system CAs were most frequent. Table 3 shows a statistically significant increase in the occurrence of circulatory system malformations with an annual rate of change of 0.74 percentage points (95%CI 0.41–1.47); genitourinary systems, with 0.17 percentage points (95%CI 0.10–0.24); and digestive systems, with 0.11 percentage points (95%CI 0.02–0.20). In the same period, a decrease of 0.37 percentage points (95%CI -0.64; -0.10) was observed in CAs classified as other types (chromosomal abnormalities, hemangiomas, lymphangiomas, congenital ichthyosis, epidermolysis bullosa and lymphedema hereditary, among others); 0.33 percentage points in the musculoskeletal system (95%CI -0.62; -0.04); and 0.13 percentage points (95%CI -0.23; -0.03) in the cleft lip and palate (Table 3). There was no change in the mean rate for CAs of the nervous system (-0.21 percentage points, 95%CI -0.65–0.24).

Table 3. Annual variation rate for types of congenital anomalies, Rio Grande do Sul, Brazil, 2005 to 2014 (n = 1,386,803).

| Cause of congenital anomaly | Annual rate of change (in percentage points) | 95%CI | p-value |
|---|---|---|---|
| Musculoskeletal system | -0.33 | -0.62 – -0.04 | 0.03 |
| Nervous system | -0.21 | -0.65 – -0.24 | 0.31 |
| Circulatory system | 0.74 | 0.41 – 1.47 | < 0.01 |
| Genitourinary system | 0.17 | 0.10 – 0.24 | < 0.01 |
| Cleft palate | -0.13 | -0.23 – -0.03 | 0.02 |
| Digestive system | 0.11 | 002 – 0.20 | 0.02 |
| Others* | -0.37 | -0.64 – -0.10 | 0.01 |

95% CI: 95% confidence interval; *chromosomal abnormalities, hemangiomas and lymphangioma, congenital ichthyosis, epidermolysis bullosa, hereditary lymphedema, among others.

## DISCUSSION

This study analyzed the temporal variation of CAs in Rio Grande do Sul and identified its associated factors. In the period from 2005 to 2014, the average CA rate was 0.92% (12,818 NB), which represented an increase from the rate of 0.81% (6,236 NB) observed between 2001 and 2005 by another study performed in the same state[11].

The data from the present study show higher CA rates among mothers aged 40 and over, with black or brown skin color, and who performed less than three prenatal appointments. Among these risk factors, advanced age stands out because of its recognized importance in the context of CA, particularly Down syndrome[14].

A study carried out in Chile, between 1970 and 2005, showed similar data to that found in the State of RS. There were higher rates of CAs[20] in the maternal age groups between 40 and 44 years (11.9%) and over 45 years (20.0%). In Portugal, the National Registry of Congenital Anomalies reported 11,502 cases of CAs between 2000 and 2010, with the highest occurrence in the 40+ age group: rates of 228.52 per 10,000 live births in the group of mothers above 40, and 366.13 per 10,000 live births in the group of mothers between 45 and 49 years of age[21.]

In this study, the number of prenatal appointments and schooling levels were associated with higher incidence of CAs. The Prais-Winsten analysis showed a growing annual trend in the CA rate of the group of mothers with no schooling until that of those with 11 years of schooling.

This rate is similar to a study in São Paulo, in which the group of mothers with 8 to 11 years of schooling had a higher incidence of CAs (53%)[7]. Another study, conducted in the city of Maringá (PR), with the objective of characterizing CA patients between 2000 and 2007, related to maternal age, showed that risk groups (adolescent mothers and older mothers) had insufficient prenatal appointments (less than seven)[22]. It is understood that a woman empowered by her condition, through her frequent participation in prenatal appointments and/or with a higher level of schooling, may help in the prevention process or favor early diagnosis[14].

The occurrence of CAs in male NBs was also high in a study conducted in Rio de Janeiro with 487,953 live births in the period from 1990 to 2002, with a significant CA rate among male NBs (90.6 / 10 thousand live births). In this study, CA rates were similar in the variables "lower GA" (<37 weeks) and "birth weight" (<2,500 g) [23]. Another study, performed in Paraíba Paulista (SP), identified statistical association (p = <0.001) between gestation duration (<37 weeks), lower Apgar score <7 and low birth weight (<2,500 g)[24].

This study showed a higher incidence of CAs in the Metropolitan Region (11.4 cases per thousand) and an increasing trend with an average annual variation of 0.24 cases per thousand for the same region. These data suggest that there is a concentration of records in regions with more prepared and qualified services, such as the capital, Porto Alegre, and its neighboring areas. Since 2014, the National Policy for the Care of Persons with Rare

Diseases has highlighted the need for at least one reference center in per State, whether it be a medical genetics service in university hospitals or research centers in universities[25].

The low CA rates in regions such as *Missioneira*, North, Highlands and Valley may suggest underreporting and reinforces the need to improve the DNVs for better estimates, as well as the establishment of public policies that promote comprehensive care for these users. A Canadian study conducted between 1998 and 2009 reported a decrease from 541 to 385 CAs per 10,000 newborns, probably due to a number of factors that involved:

- increased prenatal diagnosis and subsequent termination of pregnancy;
- implementation of measures such as mandatory folic acid fortification;
- behavioral changes and health practices to reduce the risk of CAs, such as smoking cessation and alcohol abstinence[2].

Since 2005, prophylactic supplementation with folic acid for pregnant women, through the National Iron Supplementation Program[26] has obtained significant results regarding the reduction of CA rates, as reported by a study conducted in the State of São Paulo, which analyzed SINASC data before and after folic acid fortification. There was a 35% (0.57 to 0.37 per thousand live births) reduction in the prevalence of neural tube defects after fortification[27].

In other Latin American countries, similar studies have shown a reduction in CA rates as a result of fortification. In Chile (1999-2000), there was a 50% decrease in the rates of all CAs: 17.1 / 10 thousand births (total of 120,566 NBs) to 8.5 / 10 thousand births (total of 489,915 NBs)[28]. Another study in Argentina showed a reduction in anencephaly mortality rates from 53.1 / 100 thousand (period 2000-2003) to 23.3 / 100 thousand (2005-2006)[29].

In this study, the most frequent types of CAs were those of the musculoskeletal and nervous systems. These data were similar to those of a study carried out in the city of Souza (PB) between 2012-2014, in which the musculoskeletal system (35.7%), mainly crooked feet, and the nervous system (28.6%), especially anencephaly, were the groups with the highest incidences[6]. The study, however, showed a decreasing annual trend in the occurrence of musculoskeletal CAs (rate of 0.33 percentage points), and no statistical significance ($p = 0.31$) for CAs of the nervous system,

Since 2016, studies related to CAs of the nervous system have begun to take a new direction with regard to the association between Zika virus infections and microcephaly. Of the 462 confirmed cases in Brazil, 98% of cases were concentrated in the Northeast region and only one was registered in RS. The data show that the case of microcephaly in RS had no epidemiological relevance in the health of the child[30].

The present study highlights the probable failure of DNV information, a primary source of statistical studies, as a limitation, which did not allow a reliable analysis of the observed reality, since the number of ignored cases, although analyzed, did not differ from the others. The underreporting (0.92%) of the CA cases in RS was verified, according to the established worldwide standard (2 to 5%)[1].

Another study carried out in RS reported that, in 2002, less than 30% of newborns from the total number of performed obstetric ultrasonography (47,095) had undergone the

examination by the end of gestation[11]. This finding highlights the need for future studies that evaluate SINASC in order to contribute to epidemiological surveillance in perinatal health.

The strengths of the study include the use of the Prais-Winsten analysis, which made it possible to verify the time series of the annual CA rates as well as the groups at greater risk. In terms of external validity, the socioeconomic characteristics of RS can represent the reality of the South and Southeast regions of Brazil.

A study with the objective of studying the prevalence of newborns in maternity hospitals in São Paulo from 2010 to 2014, identified a strong association of CA with maternal age over 40 years, multiple gestations, low birth weight (between 500 and 2,500 g), weight greater than 3,550 g and black or yellow skin color. With regard to gender, there was a lower prevalence in the females [31].

## CONCLUSION

The study reinforces the importance of CA prevention since they are frequent, debilitating and cause sequelae[14]. The risk factors associated with its occurrence were observed in the group of NB with Apgar score less than 7, weight equal to or less than 1,500 g and GA equal to or less than 31 weeks.

This research also showed the transition of CA rates in the period evaluated according to important maternal characteristics, such as: increasing temporal trend in the group of mothers between 20 and 34 years and among those who perform more than 7 prenatal appointments. Such data suggest a change in the epidemiological profile of mothers of children with CAs. Alerting the professionals who accompany maternal and child health is fundamental for the reduction of infant mortality in the country, with possible implication in the development of individuals with a better life quality.

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