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Artigo original

Maternal and neonatal factors associated with congenital anomalies*

Fatores maternos e neonatais associados às anomalias congênitas

Factores maternos y neonatales asociados a anomalías congénitas

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Abstract

Objective: to analyze maternal and neonatal factors associated with congenital anomalies in the state of Rio Grande do Sul. **Method**: cross-sectional study with secondary data. The sample consisted of 5,830 live births between 2012 and 2015. Maternal and neonatal variables that described demographic and health aspects were analyzed. Descriptive and inferential statistics were applied. **Results**: the occurrence of congenital anomalies was present in 0.8% of live births and the most frequent were related to the musculoskeletal, circulatory and genitourinary systems. There was a significant statistical association between mothers with children with a history of previous stillbirth, prematurity and a lower Apgar score in the 5th minute with the occurrence of anomalies. **Conclusion**: the study analyzed maternal and neonatal factors associated with congenital anomalies, demonstrating the groups at highest risk for congenital anomalies. The importance of providing access to prenatal care is highlighted, considering the living and working conditions of the pregnant woman.

Descriptors: Congenital Abnormalities; Congenital, Hereditary, and Neonatal Diseases and Abnormalities; Maternal and Child Health; Infant Mortality; Risk Factors

Resumo

Objetivo: analisar os fatores maternos e neonatais associados às anomalias congênitas no estado do Rio Grande do Sul. **Método**: estudo transversal com dados secundários. A amostra foi composta por 5.830 nascidos vivos entre 2012 a 2015. Foram analisadas variáveis maternas e neonatais que descreviam aspectos demográficos e de saúde. Aplicou-se estatística descritiva e inferencial. **Resultados**: a ocorrência de anomalias congênitas esteve presente em 0,8% dos nascidos vivos e as mais frequentes foram relacionadas ao sistema osteomuscular, circulatório e geniturinário. Houve associação estatística

significativa entre mães com filhos com histórico de natimortalidade prévia, prematuridade e menor índice de Apgar no 5º minuto com a ocorrência de anomalias. **Conclusão**: o estudo analisou os fatores maternos e neonatais associados às anomalias congênitas, demonstrando os grupos com maior risco para as anomalias congênitas. Ressalta-se a importância de proporcionar acesso aos cuidados pré-natais, considerando as condições de vida e trabalho da gestante.
Descritores: Anormalidades Congênitas; Doenças e Anormalidades Congênitas, Hereditárias e Neonatais; Saúde Materno-Infantil; Mortalidade Infantil; Fatores de risco

Resumen

Objetivo: analizar factores maternos y neonatales asociados a anomalías congénitas en el estado de Rio Grande do Sul. **Método**: estudio transversal con datos secundarios. La muestra estuvo compuesta por 5.830 nacidos vivos entre 2012 y 2015. Se analizaron variables maternas y neonatales que describieron aspectos demográficos y de salud. Se aplicó estadística descriptiva e inferencial. **Resultados**: la aparición de anomalías congénitas estuvo presente en el 0,8% de los nacidos vivos y las más frecuentes estuvieron relacionadas con los sistemas musculoesquelético, circulatorio y genitourinario. Hubo asociación estadística significativa entre madres con hijos con antecedentes de muerte fetal previa, prematuridad y menor puntaje de Apgar en el 5.° minuto con la aparición de anomalías. **Conclusión**: el estudio analizó factores maternos y neonatales asociados a anomalías congénitas, demostrando los grupos de mayor riesgo para anomalías congénitas. Se destaca la importancia de brindar acceso a la atención prenatal, considerando las condiciones de vida y trabajo de la gestante.
Descriptores: Anomalías Congénitas; Enfermedades y Anomalías Neonatales Congénitas y Hereditarias; Salud Materno-Infantil; Mortalidad Infantil; Factores de Riesgo

Introduction

Congenital anomalies (CA) are an important factor in the global increase in infant mortality,[1] being the second leading cause of death of newborns and children in the Americas.[2] In Brazil, between 2010 and 2021, the prevalence of CA was 0,8%.[3] This data may demonstrate underreporting of condition due to failures in filling out the form of underdiagnosis.[4]

CAs are structural or functional alterations that originate in uterine life and can be classified as malformations, dysplasias, deformations and disruptions. They occur through sequences, association or as a syndrome.[4] The development of CA during pregnancy has a multifactorial origin, including viral infections, genectic alterations, environmental and teratogenic factores,[5] and are visible at birth or manifest afterwards.[6]

Brazil has an uneven distribution of CA rates in each Federation Unit. The priority types of anomalies for surveillance at birth are neural tube defects, microcephaly, congenital heart defects, oral clefts, genital organ defects, limb defects, abdominal wall defects and Down

syndrome.[3] Rio Grande do Sul (RS), in turn, has the second highest prevalence of CA related to the circulatory system.[4]

Regarding maternal factors associated with CA, a history of miscarriages and stillbirths may represent conditions that causing the occurrence of anomalies.[7] A study carried out in a rural community in India[8] described that women who had suffered previous miscarriages were four times more likely to have children with CA. Despite its importance for clinical practice, the relationship between previous stillbirths is a poorly documented alarm factor.

Other associated factors described in the literature are: history of congenital malformations,[8-9] age,[9] skin color, folic acid supplementation and tobacco use.[5] Neonatal factors associated with CA include: prematurity, male gender and Apgar score below 7.[10-11] Studies indicate that exposure to pesticides in the preconception period or during pregnancy may also be associated with the appearance of anomalies.[12-13]

Given this, Brazilian and global public policies should prioritize scientific evidence on CA and its associated factors, in order to offer guidance to health professionals, with a view to possible interventions in the gestational and preconception period. This way, the health team can also be able to welcome and understand the family in cases of CA, situations that generate fear and impact those who receive the news.[14]

Thus, considering the high infant mortality rate caused by CA and the impact on the family's life course, the aim of this study was to analyze maternal and neonatal factors associated with congenital anomalies in the state of RS.

Método

This is a cross-sectional study[15] based on secondary data available from the Live Birth Certificate (DNV). The population was made up of mothers and live births from 2012 to 2015 (Table 1) in the state of Rio Grande do Sul. This time period was delimited from 2012 because in 2011 there was a change in the DNV regarding the CA field.[16]

Table 1 - Incidence of congenital anomalies in the state of Rio Grande do Sul between 2012 and 2015.

Year	Total Births RS	Congenital anomaly	
		N	%

2012	138.941	1.413	1,01
2013	141.350	1.382	0,97
2014	143.315	1.234	0,86
2015	148.359	1.262	0,85
Total	571.965	5.291	

Source: DATASUS, 2020.

The sample size was based on data from DATASUS, considering a 95% confidence level, an estimated CA incidence of 1% and a margin of error of 0.3%, obtaining a minimum of 5,830 live births, out of a total of 571,965 births. The DNVs from 2012 to 2015 were included, which is justified due to the period used by the service to qualify and release the data, and 67,565 DNVs were excluded if they contained any unfilled fields relating to the variables studied, with the occupation variable being highlighted for being unfilled.

Data was collected from the DNVs requested from SINASC, in a previously constructed database. The following maternal variables were considered: education, occupation, age, race/color, gestational trimester when prenatal care began, number of prenatal care visits, type of pregnancy, gestational age, type of delivery, number of previous pregnancies, number of children and number of dead/aborted children. The neonatal variables were: gender, type of congenital anomaly and Apgar score in the 1st and 5th minutes of life.

The data of interest was entered and stored in an Excel® spreadsheet, validated and then transferred to the Statistical Package for the Social Sciences (SPSS) for Windows version 21.0 for statistical analysis.

Quantitative variables were described by mean and standard deviation or median and interquartile range and categorical variables by absolute and relative frequencies. Pearson's chi-square or Fisher's exact tests were used to assess the association between categorical variables. In the case of polytomous variables, the analysis of adjusted residuals was used to locate significant associations. The Student's t-test was used to compare means. In the event of asymmetry, the Mann-Whitney test was applied. To control for confounding factors, the multivariate Poisson regression model was used. The criterion for entering the variable in the multivariate model was that it had a p-value of <0.20 in the bivariate analysis and for remaining

in the final model was that the variable had a p-value of <0.10. A significance level of 5% (p<0.05) was adopted. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist was used.

Developed during 2020, the research follows the ethical standards required by Resolutions 466/2012, 510/2016 and 580/2018 of the Ministry of Health. The study is part of the larger project entitled "Exposure to Pesticides and Perinatal Outcomes in the State of Rio Grande do Sul", awarded by MCTIC-CNPq Universal Call No. 28/2018, approved by the Research Ethics Committee of the Federal University of Rio Grande do Sul, on July 5, 2018, under the number 84275318.4.0000.5347, and of the School of Public Health of Rio Grande do Sul, on August 8, 2018, under the number 84275318.4.3001.5312.

Resultados

From the sample of n=5830 live births, the incidence of CA was 0.8% (n=49), 61.2% (n=30) were male and 38.8% (n=19) were premature. With regard to maternal variables in cases of CA, the average age was 26.8 years and 57.1% (n=28) reported having between 8 and 11 years of schooling. In addition, 77.6% (n=38) had a caesarean section as their mode of birth. As for maternal occupation, there was no statistical association with CA (p>0.05). The maternal and neonatal variables are described in Tables 2 and 3.

Table 2 – Characterization of the sample according to maternal variables. Porto Alegre, RS, 2020. N=5830.

Variables	Total sample (n=5830; 100%)	With congenital anomaly (n=49; 0,8%)	No congenital anomaly (n=5781; 99,2%)	p
Mother's age (years) - mean ± SD	26,8 ± 6,7	26,4 ± 6,5	26,8 ± 6,7	0,709
Mother's race/color - n (%)				0,140
White	4679 (81,9)	39 (79,6)	4640 (81,9)	
Black	436 (7,6)	8 (16,3)	428 (7,6)	
Yellow	10 (0,2)	0 (0,0)	10 (0,2)	
Brown	559 (9,8)	2 (4,1)	557 (9,8)	
Indigenous	30 (0,5)	0 (0,0)	30 (0,5)	
Mother's occupation - n				1,000

(%)				
Agriculture	324 (5,6)	2 (4,1)	322 (5,6)	
Non-agriculture	5506 (94,4)	47 (95,9)	5459 (94,4)	
Number of children– median (P25-P75)	1 (0 – 1)	1 (0 – 1)	1 (0 – 1)	0,683
Stillbirths – n(%)				0,034
Yes	922 (16,4)	14 (28,6)	908 (16,3)	
No	4702 (83,6)	35 (71,4)	4667 (83,7)	
Mother's schooling - n(%)				0,475
None	14 (0,2)	0 (0,0)	14 (0,2)	
1 to 3 years	140 (2,4)	3 (6,1)	137 (2,4)	
4 to 7 years	1392 (24,0)	10 (20,4)	1382 (24,0)	
8 to 11 years	3145 (54,1)	28 (57,1)	3117 (54,1)	
12 and more	1120 (19,3)	8 (16,3)	1112 (19,3)	
Pregnancy – n(%)				0,006
Unique	5692 (97,6)	44 (89,8)	5648 (97,7)	
Double/Triple or more	138 (2,4)	5 (10,2)	133 (2,3)	
Trimester of pregnancy when prenatal care began - n (%)				0,906
1º	4483 (79,9)	38 (79,2)	4445 (78,9)	
2º	1019 (17,9)	8 (18,8)	1010 (17,9)	
3º	180 (3,2)	1 (2,1)	179 (3,2)	
Route of birth – n(%)				0,019
Vaginal	2322 (39,8)	11 (22,4)	2311 (40,0)	
Cesarean section	3507 (60,2)	38 (77,6)	3469 (60,0)	
Number of prenatal consultations - n(%)				0,118
None	116 (2,0)	1 (2,1)	115 (2,0)	
1 to 3	353 (6,1)	2 (4,2)	351 (6,1)	
4 to 6	1140 (19,6)	16 (33,3)	1124 (19,5)	
7 and more	4198 (72,3)	29 (60,4)	4169 (72,4)	
Gestational age at birth - n(%)				<0,001
<22 weeks	2 (0,0)	0 (0,0)	2 (0,0)	
22 to 27 weeks	20 (0,3)	1 (2,0)*	19 (0,3)	
28 to 31 weeks	64 (1,1)	2 (4,1)*	62 (1,1)	
32 to 36 weeks	629 (10,9)	16 (32,7)*	613 (10,7)	
37 to 41 weeks	4944 (85,8)	28 (57,1)	4916 (86,1)*	
Sex of baby - n(%)				0,246
Male	3029 (52,0)	30 (61,2)	2999 (51,9)	

Female	2801 (48,0)	19 (38,8)	2782 (48,1)	
Number of previous pregnancies - median (P25-P75)	1 (0 – 2)	1 (0 – 2)	1 (0 – 2)	0,240
Number of vaginal deliveries - median (P25-P75)	0 (0 – 1)	0 (0 – 1)	0 (0 – 1)	0,969
Number of cesarean deliveries - median (P25-P75)	0 (0 – 1)	0 (0 – 1)	0 (0 – 1)	0,373

*statistically significant association by the adjusted residuals test at 5% significance level.

Table 3 – Characterization of the sample according to neonatal variables. Porto Alegre, RS, 2020. N=5830.

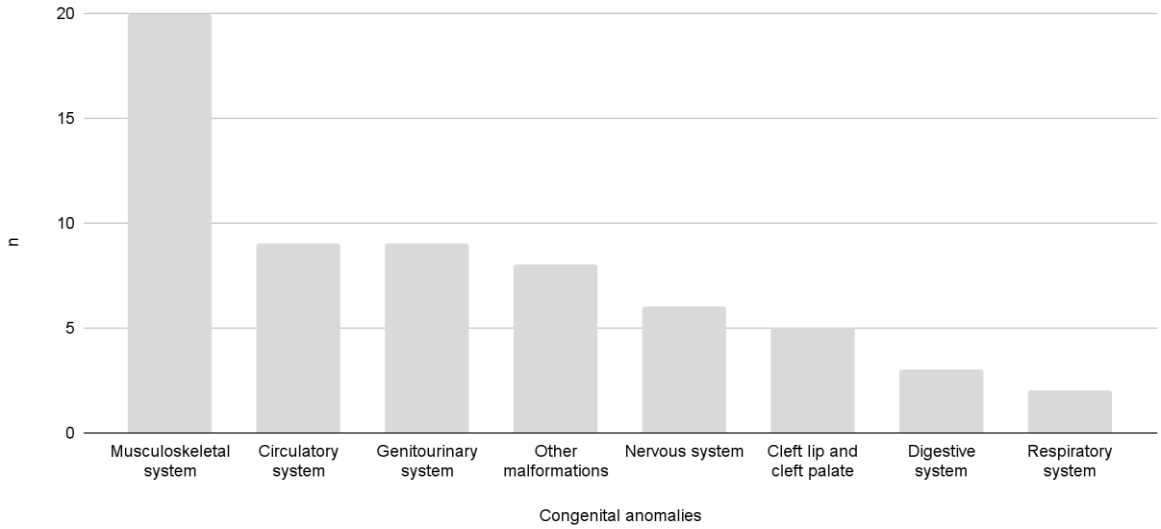
Variables	Total sample (n=5830; 100%)	With congenital anomaly (n=49; 0,8%)	No congenital anomaly (n=5781; 99,2%)	p
Sex of baby – n(%)				0,246
Male	3029 (52,0)	30 (61,2)	2999 (51,9)	
Female	2801 (48,0)	19 (38,8)	2782 (48,1)	
Apgar score at 1st minute - mean and standard deviation	9 ± 4	8 ± 2,3	9 ± 4	0,016
Apgar score at the 5th minute - mean and standard deviation	10 ± 4	9 ± 2	10 ± 4	0,001

*statistically significant association by the adjusted residuals test at 5% significance level.

With regard to gestational age, 38.8% (n=19) of CA cases were considered preterm, compared to 12.1% (n=694) of births without CA. In addition, 28.6% (n=14) of the mothers of newborns with CA reported having already had a stillbirth or miscarriage.

Of the 49 cases of CA in the sample, the most frequent types were of the musculoskeletal system with an incidence of 32.3% (n=20), the circulatory system with 14.5% (n=9) and the genitourinary system with 14.4 (n=9) (Figure 1).

Figure 1 - Characterization of congenital anomalies in live births. Porto Alegre, RS, 2020. N=49.



After the regression analyses (Table 4), the chances of CA were higher in premature newborns (95% CI 2.79; 1.53 - 5.10; p 0.001) and in mothers who had already had stillbirths (95% CI 1.94; 1.07 - 3.53; p 0029) and, for each point higher in APGAR at the 5th minute, there was a reduction in the chances of CA occurring (95% CI 0.72; 0.64 - 0.80; p 0.001).

Table 4 – Poisson Regression Analysis to assess factors independently associated with congenital anomaly.

Variables	Prevalence Ratio (OR)	95% CI	p
Dead children	1,94	1,07 - 3,53	0,029
Prematurity (<37 weeks)	2,79	1,53 - 5,10	0,001
Apgar 5th minute	0,72	0,64 - 0,80	0,001

Discussão

The incidence of CA in the state of RS was 0.8%, close to the figure found in a previous study,[17] of 0.9%. According to official data, the incidence of CA in Brazil is 0.8%,[3] which is lower than the worldwide figure of 5%.[17] This may be evidence of the underreporting of cases in Brazil, which makes data analysis difficult, as well as demonstrating the difficulty in detecting certain anomalies that are not visible at birth.

There was a prevalence of musculoskeletal malformations in 32.3% of the sample, mainly polydactyly. The prevalence of this type of CA corroborates the findings in the literature[18] and may be related to the ease of diagnosis, since they are visible during the physical examination of the newborn.[4]

The study also showed that 61.2% of those born with CA were male, the same result found in previous evaluations.[10,19] In addition, the second most prevalent type of congenital anomaly was related to the genitourinary system (14.5%), which can be explained by maternal exposure to endocrine disruptors, causing fluctuations in female and male hormones during pregnancy and hindering genitourinary differentiation, leading to CA.[20] Anomalies related to the circulatory system also showed a prevalence of 14.5%, similar to official data for RS, which show the state as having the second highest prevalence of this type of CA.[3]

There was a statistically significant association between previous stillbirths, based

on the variable that includes stillbirths and previous miscarriages, and the occurrence of CA. This association shows dysfunctions in the gestational process, which may be genetic, environmental, infectious and/or due to obstetric complications.[21] Corroborating the results found, a time-series study[19] also found an association between the number of stillbirths and CA, as did a survey carried out in India,[8] which found that mothers who have had previous abortions are four times more likely to have children with CA.

In addition, the chance of having CA was higher in premature infants (<37 weeks), which is described in the literature as an expected outcome related to CA.[22] With regard to the Apgar score, it was observed that the higher the score in the 5th minute, the lower the chance of CA occurring. Since most newborns with anomalies have complications, such as dystocia, respiratory problems or infections,[9] it is inferred that their Apgar scores are lower when compared to newborns without anomalies.

There is evidence in the literature linking maternal exposure to pesticides with the occurrence of CA,[13,20] which is a factor that should be taken into consideration during prenatal

consultations. However, this association was not found in this study, leading to the assumption that contact with pesticides occurs regardless of occupation, whether through contaminated water, food or household pesticides, making it difficult to establish this relationship.

It is believed that the individual characteristics present in the social determinants of health, represented by gender, age and genetic factors, should be taken into consideration when studying CA. In a study carried out in Rio Grande do Sul,[23] black skin color was associated with a 20% increase in the chance of CA when compared to white skin color, which demonstrates the need to tackle structural racism, including in the health system. In addition, worse access to health, socioeconomic, housing and employment conditions show the vulnerability to which women are exposed and which can interfere with unfavorable outcomes for their offspring, such as infant mortality.[24] Among these outcomes, CA was strongly associated with infant mortality in the capital cities of Brazil.

Although the study did not include data on the use of folic acid during pregnancy,

it is known that its supplementation prevents the occurrence of CA, mainly related to neural tube defects.[9] Therefore, prenatal care should take this factor into account and ensure adequate supplementation according to the available scientific evidence.

Newborn screening through heart, eye, hearing and blood tests is essential for identifying diseases in newborns, including CA, especially those that are asymptomatic and not visible at birth. In addition, the tests play a fundamental role in the early diagnosis of comorbidities and the reduction of associated sequelae. However, despite the establishment of the National Newborn Screening Program in 2001, the prevalence of testing is unequal in Brazil, and is significantly higher among children whose guardians have a higher household income.[25]

Preparation for prenatal care must comply with established care protocols, but must also take into account the social dynamics and health-disease determinants in each territory. The role of nursing professionals in Brazil's Primary Health Care policy and their relevance in prenatal consultations is highlighted. In this way, thinking about prenatal care policy also means reflecting on the strengthening of nursing work in this scenario.[26]

Prenatal care in various contexts is linked to better birth outcomes. Above all, it is a complex and important health action. Considering the Brazilian context, we need to think about improving not only prenatal care policies,[27] but also reproductive planning.[28]

However, it is suggested that longitudinal studies be carried out to investigate risk factors for CA, in order to take into account other variables related to the issue. As this analysis uses secondary data, there are limitations in filling in and interpreting the data in relation to maternal characteristics and the diagnosis of CA, which in many cases can occur late.

Finally, the importance of the study in guiding prenatal consultations is highlighted, in order to ensure the development of pregnancy by identifying and advising on risk factors for developing CA.[14] In addition, health professionals, especially nurses, who are largely responsible for coordinating care, can be able to provide adequate and welcoming guidance to families who have had a child diagnosed with CA. It is essential to establish bonds and provide guidance on the available health network in order to help care for the newborn. The characterization of this outcome is also important for the development of new programs and protocols to assist families in this situation.

Conclusion

This study sought to analyze maternal and neonatal factors related to the occurrence of CA, finding an association with a maternal history of previous stillbirths, prematurity and a lower Apgar score at the 5th minute. This highlights the need to consider the specific characteristics of each woman and her living and working conditions during prenatal care. In addition, it is essential that the diagnosis of CA is made during the fetal period or at birth, with a view to communicating the prognosis to the family and referring them to specialized health facilities. It is also important that health professionals are made aware of the importance of identifying CA for the country's public health, in order to increase early diagnosis and proper registration.

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