Research Square

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Influence of social, demographic, and clinical factors in live births with spinal dysraphism in Brazil: an ecological study of 21 years

Raissa Tereza Casseb Oliveira
Federal University of Pará (UFPA)

Diego Bessa Dantas
Federal University of Pará (UFPA)

Edila Monteiro de Andrade
Federal University of Pará (UFPA)

Márcio Vinicius de Gouveia Affonso
Federal University of Pará (UFPA)

Ana Beatriz Rocha de Marin
Federal University of Pará (UFPA)

Fabiana de Campos Gomes
São José do Rio Preto Medical School (FAMERP)

Nelson Veiga Gonçalves
State University of Pará (UEPA)

João Simão de Melo-Neto (jsmeloneto@ufpa.br)
Federal University of Pará (UFPA)

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Abstract

Objectives: This study aimed to verify possible associations between sociodemographic and clinical factors in live births with spinal dysraphism .

Methods: An analytical (descriptive and inferential), ecological study was carried out based on secondary data of 11,308 live births with spinal dysraphism registered in the Live Birth Information System (SINASC) in Brazil from 1999 to 2019. Demographic factors analyzed were age, education, mothers' marital status and geographic region. The clinical factors analyzed were duration, gestation period, birthweight and number of prenatal visits performed by women who underwent medical follow-up.

Results: There was an increase in the number of cases of spinal dysraphism in recent years in Brazil with an annual percentage variation of 3.52%. However, the period from 2005 to 2009 showed a reduction in live births with spinal dysraphism . The regions with the highest incidence were the South and Southeast. The risk increased in mothers born after 1980, older than 30 years and with a high level of education. The risk was increased in live births of whites and blacks, born from double pregnancy and with body weight less than 3,000 g. The absence of prenatal care was associated with a higher incidence.

Conclusion: Sociodemographic and clinical factors have specific characteristics that can predict spinal dysraphism in newborns in Brazil.

Synopsis

Study Question.

What sociodemographic and clinical characteristics are associated with spinal dysraphism in live births in Brazil?

What is already known.

The prevalence of spinal dysraphism varies between Asian and European countries and in different regions of the United States according to time period, race, ethnicity, age and sex. In Brazil, there are no studies on the prevalence of spinal dysraphism by number of inhabitants according to demographic variables. Also, there is lack of studies that address the risk factors related to this disease.

What this study adds.

The study highlights the association between clinical and sociodemographic factors and spinal dysraphism in live births in Brazil. In addition, the study identifies the risk factors for this disease in the country and collaborates with the prevention and formulation of public policies aimed at managing and reducing this disease in Brazil.

1. Background

Spinal dysraphism is a congenital malformation in which the spinal column is split (bifid) as a result of failed closure of the embryonic neural tube during the fourth week post-fertilization [1]. The prevalence of spinal dysraphism varies across Asian and European countries (per 1000 inhabitants) [2] and in different regions of the United States [3] according to time period, race, ethnicity, age, and sex [2, 3]. In Brazil, there are no studies on the prevalence of spinal dysraphism by the number of inhabitants according to demographic variables. According to an investigation by the Latin American Collaborative Study of Congenital Malformations (ECLAMC), Brazil has the highest prevalence of neural tube defects: (3.13) (1999), (3.32) (2000), and (3.36) (2001) per thousand live births, and an average of 0.81/thousand live births in the 2005–2007 period [4].

Children with spinal dysraphism carry complications that make it a serious public health problem, whose repercussions range from their families to the community with which they live. These complications include Arnold-Chiari malformation, neurogenic lower limb paralysis, neurogenic bladder, and bowel dysfunction, congenital clubfoot, hip dislocation, fractures, scoliosis, hydronephrosis, as well as vesicourethral reflux [5].

The defect can be covered by essentially normal skin(spinal dysraphism occulta), or be associated with a cystic protrusion, which may contain abnormal meninges, cerebrospinal fluid-meningocele, elements of the spinal cord and/or nerves, and myelomeningocele. Another clinical form is encephalocele, in which the brain and meninges herniate through a skull cap defect. [6].

Although neural tube closure defects have a heterogeneous etiology and several mechanisms have been described for their genesis, most cases are attributed to the interaction between various genes and environmental factors, which is called multifactorial inheritance [7, 8]. Several consistent factors have already been identified as risk factors for spinal dysraphism, including female sex, [9, 10] inadequate maternal folic acid intake, [11] family history of neural tube defect-affected pregnancies [2].

An extensive number of potential risk factors for the onset of spinal dysraphism has been studied, although there is insufficient evidence to confirm this association. Although there are well-defined risk factors for spinal dysraphism, there are no studies on the risk factors that are the focus of this study, which is of great importance in defining the most appropriate strategy for reducing its incidence. However, in Brazil, there are no comprehensive studies describing the association of demographic, social, and clinical characteristics in relation to spinal dysraphism .

The purpose of this study was to verify possible associations of sociodemographic and clinical characteristics in patients with spinal dysraphism, thereby providing a basis for policymakers to identify appropriate risk management measures to reduce the disease in Brazil.

2. Methods

2.1. Type of study

An analytical (descriptive and inferential), ecological study was carried out based on secondary data on live births with spinal dysraphism registered in the Live Birth Information System (SINASC) of the Ministry of Health, Brazil.

2.2. Outcomes

Classification of the sociodemographic factors are as follows: geographic regions (North, Northeast, Midwest, South, and Southeast); age (≤ 19, 20 to 29, 30 to 39, 40 to 49, 50 to 59, 60 to 69, 70 to 79, ≥ 80 years); sex (Male and Female); and mother's educational level (no schooling to 12 or more years of education).

Duration of pregnancy (less than 22 weeks, 22 to 25 weeks, 28 to 31 weeks, 32 to 36 weeks, 37 to 41 weeks, and 42 weeks or more), type of pregnancy (single, double, triple or more), Birthweight (Less than 500 g; 500 to 999 g; 1000 to 1499 g; 1500 to 2499 g; 2500 to 2999 g; 3000 to 3999 g; 4000 g and more), and number of prenatal care (absent prenatal care; 1 to 3; 4 to 6; more than 7 prenatal care) were the clinical factors analyzed.

2.3. Data source and statistical analysis

SINASC is a secondary database available from the Ministry of Health's Database [12].Data on live births recorded from 1999 to 2019 in Brazil in the health information system were collected. A total of 11,308 newborns with spinal dysraphism and a corresponding number of mothers were studied.

The data were subjected to descriptive and inferential analyses. Relative and absolute frequencies were used to describe the data. The data were subjected to the Shapiro-Wilk test to verify the distribution of the normality of the data. The Pearson r correlation test (parametric) was used to verify the level of correlation between the rate of live births and spinal dysraphism per year.

The Spearman r correlation test (non-parametric) was used to verify the level of correlation between the rate of live births and the number of prenatal care. The R-squared (r^2) test was used to determine the coefficient of determination. In addition, linear regression was applied for data analysis. The chi-square test was used to examine associations between categorical variables. Odds ratios (ORs) with 95% confidence intervals (95% CI) were used to quantify the degree of association for the occurrence of spinal dysraphism in live births in Brazil.

An age-period cohort (APC) analysis using a suitable model for the identification problem due to independent effects of age groups, calendar time periods of birth of newborns with spinal dysraphism, and maternal birth cohorts was performed. For all analyzed variables in this study, the following functions were estimated: net drift, local drifts, all age, period, or cohort deviations, and all period or cohort rate ratios (RR).

The Wald test was used to verify the differences. These parameters were estimated using the APC Web Tool (Biostatistics Branch, National Cancer Institute, Bethesda, MD, USA) [13]. Results were considered significant at $p < 0.05$. QGIS software (version 2.6.1, Open Source Geospatial Foundation, Arizona) was used to depict the spatial distribution of the spinal dysraphism cases and prenatal care on an open Brazil map.

2.4. Ethics approval

This study analyzed secondary data available in the Department of Informatics of the National Health System (DATASUS) [12]. The data are publicized with unrestricted use and access. Ethical assessment of the research ethics committee is not required according to the terms of the National Health Council Resolution n. 510, April 7, 2016.

3. Results

The fee distribution of live births with spinal dysraphism (n = 11,308) per 100,000 inhabitants is shown in Fig. 1. It was observed that there was a positive correlation with an increase in the number of children with spinal dysraphism in recent years in Brazil ($p < 0.0001$; Pearson $r = 0.8022$; $r^2 = 0.6435$) and in the North ($p < 0.0001$; Pearson $r = 0.8646$; $r^2 = 0.7476$), Northeast ($p < 0.0001$; Pearson $r = 0.9419$; $r^2 = 0.8872$), South ($p = 0.0002$; Pearson $r = 0.7319$; $r^2 = 0.5357$), and Midwest ($p < 0.0001$; Pearson $r = 0.7747$; $r^2 = 0.6002$), except in the Southeast region ($p = 0.1305$; Pearson $r = 0.3498$; $r^2 = 0.1224$).

The distribution of live birth rates per 100,000 inhabitants by race and region is shown in Fig. 2. The incidence rate was higher in white and black newborns (Fig. 2A). Regarding children born with anomalies in the regions, it was possible to verify that the South and Southeast regions had the highest incidence rates (Fig. 2B).

Figure 3 shows the results obtained from the APC analysis. From 1999 to 2019, the net drift, which represented the annual percentage change in the expected age-adjusted rates, was 3.52% (95% CI: 2.43 to 4.62) per year. Regarding Cohort RR, it was observed that women who were born before 1980 had a low risk (1955: RR = 0.089, 95% CI = 0.01 to 0.66; 1960: RR = 0.441, 95% CI = 0.32 to 0.59; 1965: RR = 0.701, 95% CI = 0.61 to 0.80; 1970: RR = 0.795, 95% CI = 0.72 to 0.87; 1975: RR = 0.899, 95% CI = 0.83 to 0.96) and those who were born after 1980 had increased risk (1985: RR = 1.137, 95% CI = 1.07 to 1.20; 1990: RR = 1.267, 95% CI = 1.18 to 1.35; 1995: RR = 1.413, 95% CI = 1.30 to 1.52; 2000: RR = 1.495, 95% CI = 1.32 to 1.68; 2005: RR = 1.891, 95% CI = 1.17 to 3.05) (Fig. 3B).

In relation to the period, it was possible to identify an increase in incidence in 1999 to 2004 (RR = 1.083, 95% CI = 1.00 to 1.16), 2010 to 2014 (RR = 1.380, 95% CI = 1.27 to 1.48), and 2015 to 2019 (RR = 1.732, 95% CI = 1.54 to 1.94) (Fig. 3C). However, when fitted temporal trends for period rate ratios were analyzed through the analysis of Period Deviations, we observed that the 1999 to 2004 (deviation: 0.102, 95% CI = 0.07 to 0.12) and 2015:2019 (deviation: 0.052, 95% CI = 0.03 to 0.07) an increase in spinal dysraphism incidence, while 2005 to 2009 (deviation: -0.151, 95% CI = -0.15 to -0.11) showed a reduction (Fig. 3D).

3.1. Demographic variables

3.1.1. Region

The association tests showed that children born in the north, northeast, and midwest regions of Brazil presented a lower association of developing spinal dysraphism, while children born in the Southeast region presented a high risk of spinal dysraphism (Table 1). Regarding the federation units, only Rondônia in the North region presented results considered to be a risk factor for spinal dysraphism. In the northeast, the states of Rio Grande do Norte, Pernambuco, and Sergipe were considered to be associated with spinal dysraphism. In the Southeast region, only the state of São Paulo showed a high association with spinal dysraphism. In the southern region, Rio Grande do Sul showed a high association for anomalies (Table 1). In the Midwest region, the state of Mato Grosso demonstrated a high risk of spinal dysraphism .

Table 1
Geographic regions of the mothers of live births with spinal dysraphism .

	spinal dysraphism Absent (n = 77,052,926)	spinal dysraphism Present (n = 11,308)	OR	95% CI
North	7,719,197	816	0.69	(0.65, 0.75)
Rondônia	729,971	110	1.49	(1.22, 1.82)
Acre	412,679	24	0.53	(0.35, 0.80)
Amazonas	1,822,478	217	1.16	(0.99, 1.35)
Roraima	256,268	12	0.43	(0.24, 0.76)
Pará	3,468,911	375	1.04	(0.90, 1.19)
Amapá	378,766	23	0.56	(0.37, 0.85)
Tocantins	650,124	55	0.78	(0.59, 1.03)
Northeast	22,124,293	2,739	0.79	(0.76, 0.82)
Maranhão	2,806,233	206	0.55	(0.48, 0.64)
Piauí	1,274,746	81	0.49	(0.39, 0.62)
Ceará	3,413,685	435	1.03	(0.93, 1.14)
Rio Grande do Norte	1,304,280	202	1.27	(1.10, 1.46)
Paraíba	1,145,641	191	1.06	(0.91, 1.23)
Pernambuco	3,839,064	792	1.93	(1.78, 2.10)
Alagoas	1,509,439	177	0.94	(0.81, 1.09)
Sergipe	956,030	185	1.60	(1.38, 1.86)
Bahia	5,564,175	470	0.61	(0.55, 0.68)
Southeast	30,540,009	5,468	1.42	(1.37, 1.42)
Minas Gerais	6,522,977	1,006	0.83	(0.77, 0.88)
Espírito Santo	1,430,575	150	0.57	(0.48, 0.67)
Rio de Janeiro	6,108,559	971	0.86	(0.80, 0.92)
São Paulo	16,477,898	3,341	1.34	(1.26, 1.41)
South	10,660,246	1,667	1.07	(1.02, 1.13)
Paraná	4,306,512	661	0.96	(0.87, 1.06)
Santa Catarina	2,366,154	318	0.82	(0.73, 0.93)

[a]. Chi-square test with Yates correction. OR: Odds ratio; 95% CI: confidence interval.

	spinal dysraphism Absent (n = 77,052,926)	spinal dysraphism Present (n = 11,308)	OR	95% CI
Rio Grande do Sul	3,987,580	688	1.17	(1.06, 1.29)
Midwest	6,609,181	618	0.62	(0.57, 0.67)
Mato Grosso do Sul	1,093,754	116	1.03	(0.84, 1.27)
Mato Grosso	1,320,366	176	1.41	(1.18, 1.68)
Goiás	2,416,425	243	0.96	(0.81, 1.13)
Distrito Federal	1,178,636	83	0.63	(0.50, 0.80)

[a]. Chi-square test with Yates correction. OR: Odds ratio; 95% CI: confidence interval.

Table 2. Sex, race, age, and education level of the mothers of live births with spinal dysraphism .

	spinal dysraphism Absent (n =77,052,926)	spinal dysraphism Present (n = 11,308)	OR	95% CI
Sex				
Male	39,428,840	5,694	0.98	(0.95, 1.02)
Female	37,520,511	5,493	1.01	(0.97, 1.05)
Race				
White	27,520,990	5,381	1.22	(1.18, 1.27)
Black	2,190,132	428	1.11	(1.01, 1.22)
Yellow	344,933	35	0.57	(0.41, 0.80)
Brown	29,818,366	4,712	0.81	(0.78, 0.84)
Indigenous	413,349	43	0.59	(0.43, 0.79)
Mother's Age				
14 years or any less (-)	675,081	85	0.85	(0.68, 1.05)
15 to 19 years	15,051,859	1,909	0.82	(0.78, 0.87)
20 to 24 years	22,000,044	2,920	0.86	(0.82, 0.89)
25 to 29 years	18,237,220	2,706	1.00	(0.96, 1.04)
30 to 34 years	12,589,946	2,136	1.18	(1.12, 1.23)
35 to 39 years	6,266,027	1,177	1.30	(1.22, 1.38)
40 to 44 years	1,584,883	354	1.52	(1.37, 1.69)
45 to 49 years	114,161	20	1.18	(0.76, 1.83)
Mother's Education Level				
None	2,121,169	114	0.28	(0.23, 0.34)

1 to 3 years	4,962,631	660	0.71	(0.65, 0.76)
4 to 7 years	16,358,777	2,793	0.91	(0.87, 0.95)
8 to 11 years	27,541,510	5,672	1.26	(1.21, 1.30)
12 years or more (+)	9,812,651	1,861	1.04	(0.99, 1.09)

[a]. Chi-square test with Yates correction. OR: Odds ratio; 95% CI: confidence interval.

3.2. Social variables

The social variables are listed in Table 2. Sex was not associated with the occurrence of spinal dysraphism. The results demonstrated an association between spinal dysraphism in white and black newborns. In relation to maternal age, the results showed that mothers who had delivered before the age of 24 years indicated a protective factor against spinal dysraphism. Mothers who had children after 30 years of age had a greater chance of birthing children with spinal dysraphism. The results demonstrated that mothers who had a high education level (i.e., eight or more years of schooling) were associated with a high chance of spinal dysraphism in their neonates.

3.3. Clinical variables

Clinical variables are presented in Tables 3 and 4. The results showed that double pregnancy was highly associated with the disease (Table 3). The results on the duration of pregnancy revealed that women who had a gestation of 22 to 41 weeks maintained the risk of birthing children with spinal dysraphism (Table 3). Live births under 3000 g also have a higher chance of having spinal dysraphism (Table 3). In addition, we observed that a lower number of women with absent prenatal care had a higher incidence (Table 4). The higher number of women receiving prenatal care (1–6 medical care) resulted in a lower incidence (Table 4). However, the high number of prenatal care (7 or more medical care) is related to a greater incidence of live births with spinal dysraphism (Table 4). The spatial distribution of spinal dysraphism cases and prenatal care from 1999 to 2019 in Brazil is presented in Fig. 4.

Table 3. Type of pregnancy, duration of pregnancy, and birthweight of live births

with spinal dysraphism .

	spinal dysraphism Absent (n=77,052,926)	spinal dysraphism Present (n =11,308)	OR	95% CI
Type of Pregnancy				
One	73,583,694	10,959	0.66	(0.59, 0.74)
Double	1,401,290	318	1.52	(1.36, 1.70)
Triple and more (+)	71,247	12	1.11	(0.63, 1.97)
Duration of Pregnancy				
Less than 22 weeks (-)	45,009	6	0.87	(0.39, 1.94)
From 22 to 27 weeks	335,451	160	3.15	(2.69, 3.68)
From 28 to 31 weeks	512,498	324	4.22	(3.78, 4.72)
From 32 to 36 weeks	4,422,128	2,137	3.50	(3.50, 3.84)
From 37 to 41 weeks	66,086,419	8,413	3.16	(3.03, 3.30)
42 weeks or more (+)	1,673,397	131	0.50	(0.42, 0.60)
Birthweight				
Less de 500g	59,238	20	2.28	(1.47, 3.54)
500 a 999g	324,504	181	3.81	(3.29, 4.41)
1000 a 1499 g	529,040	334	4.36	(3.91, 4.86)

1500 a 2499 g	5,364,132	2,085	2.99	(2.85, 3.14)
2500 a 2999 g	17,319,539	3,390	1.46	(1.40, 1.52)
3000 a 3999 g	48,533,731	4,889	0.43	(0.42, 0.45)
4000g and more	4,074,647	377	0.61	(0.55, 0.67)

[a]. Chi-square test with Yates correction. OR: Odds ratio; 95% CI: confidence interval.

Table 4
Correlations between the number of prenatal care with incidence of spinal dysraphism in live birth in Brazil.

		Brazil	North	Northeast	Southeast	South
Absent	r	-3.922	-8.857	-6.255	-1.585	-466
	CI 95%	-0.71 to 0.06	-0.95 to -0.72	-0.83 to -0.25	-0.56 to 0.30	-0.75 to -0.02
	p	787	< 0.0001	24	4.926	332
1 to 3	r	-5.247	-6.282	-6.625	143	-4.262
	CI 95%	-0.78 to -0.10	-0.83 to -0.25	-0.85 to -0.31	-0.43 to 0.45	-0.73 to 0.02
	p	146	23	11	9.509	54
4 to 6	r	-5.351	-5.028	-5.377	-1.442	-461
	CI 95%	-0.79 to -0.12	-0.77 to -0.07	-0.79 to -0.12	-0.55 to 0.31	-0.75 to -0.02
	p	124	202	119	533	354
7 or more	r	787	8.312	8.961	4.052	7.327
	CI 95%	0.52 to 0.91	0.61 to 0.93	0.75 to 0.95	-0.04 to 0.71	0.42 to 0.88
	p	< 0.0001	< 0.0001	< 0.0001	684	2

95% CI: confidence interval.

4. Comments

4.1 Principal findings

This study shows that sociodemographic and clinical factors have specific characteristics that predict spinal dysraphism in live births in Brazil.

4.2 Strengths of the study

This study offers, in an objective language, information about social, demographic and clinical factors that predict spinal dysraphism in a Brazilian context of 21 years. In addition, another strength of the study is that its statistical analyzes were made with data available to everyone from the database of the Brazilian Unified Health System (SUS). Thus, given the need to understand the predictors of the disease in Brazil and to support the planning of public policies, this study contributes to the scarce scientific literature on this disease in the Brazilian context.

4.3 Limitations of the data

Although there is a reduction in data underreporting in Brazil, as in other developing countries, it is possible to observe a large number of unknown or unreported items that do much harm to the reliability of the analysis. Another limitation is the change in deadlines and items in billing spreadsheets, reducing standardization in the collection, and late release of data on the platform [14].

4.4 Interpretation

There has been an increase in the number of cases of spinal dysraphism in recent years in Brazil, with an annual percentage change of 3.52%. In addition, during the period from 2005 to 2009, there was a reduction in the incidence of the disease. In 2005, the National Iron Supplementation Program (PNSF) was implemented, which consists of prophylactic iron and folic acid supplementation for pregnant women [15].

The fortification of foods with folic acid is an unquestionable intervention in primary prevention, with a positive impact on the prevention of neural tube defects already demonstrated in several countries [16]. Thus, we believe that after 2009, the strategy for implementing this health program may have been modified, which influenced the progressive increase in the number of cases.

The prevalence of spinal dysraphism remains high in federation units: Rondônia, Rio Grande do Norte, Pernambuco, Sergipe, Mato Grosso, São Paulo, and Rio Grande do Sul. However, the South (São Paulo) and Southeast (Rio Grande do Sul) regions had a higher incidence of cases. Despite policies promoting prenatal folic acid supplementation and fortification of the food supply, health promotion strategies that encourage women of reproductive age to take folic acid supplements have failed, considering that the proportion of women taking their supplements has decreased over the years in other countries, such as England [17].

In addition, the heritability (the genetic component of risk) was estimated to be 60–70% based on the relative proportions of individuals affected among siblings of index cases [18]. The genetic causes as part of the disease process should be considered, which may imply a higher frequency of spinal dysraphism in these regions.

This study shows that the risk was increased in mothers born after 1980, aged over 30 years, and with a high education level, showing the demographic change that the country has presented over the past few years, in which women increasingly assume the posture of having children later and actively participating in the labor

market. Another possible explanation for this correlation is that the increase in the level of education of mothers allows them to become pregnant later than usual; for this reason, they are more likely to have neonates with the disease in question, since there is a positive correlation between the age of the mother and the disease [19].

The increased risk of live births with spinal dysraphism belonging to the White and Black race can be explained by the difference in dietary habits and practices of supplement intake between racial groups [20]. In addition, the difference in the level of education [21] and later pregnancy in white individuals may contribute to explaining this relationship. In Brazil, the income distribution is lower for black individuals, [21] which may imply worse eating habits and greater difficulties in accessing health care, making it difficult to monitor during prenatal care.

Regarding clinical factors, the results showed that one pregnancy was a protective factor for the occurrence of spinal dysraphism, but a double pregnancy was highly associated with the disease, as well as the body weight under 3,000 g of the newborn. This relationship probably occurs due to the deficiency of folic acid offered to neonates, [22] since the nutritional need is doubled in twin pregnancies. The use of multivitamins and folate during double pregnancy after a recognized twin pregnancy has been observed [23]. However, inadequate prenatal care can lead to inadequate nutritional intake or supplementation.

Finding ways to prevent more cases of spinal dysraphism is a priority for future research and public health implementation, and this study shows that absent prenatal care resulted in a higher incidence of spinal dysraphism. Thus, it affirms the concept that without adequate prenatal care, pregnant women do not have, by extension, adequate prevention and care for diseases, including spinal dysraphism. In this sense, the absence of prenatal care makes it difficult to carry out PNSF, [14] which may result in an increase in cases.

5. Conclusions

In this study, we observed that sociodemographic and clinical factors present specific characteristics that predict spinal dysraphism in live births in Brazil. There has been an increase in the number of cases of spinal dysraphism in recent years in Brazil, with an annual percentage change of 3.52%. However, the period of 2005 to 2009 showed a reduction in live births with spinal dysraphism. The units of the federation with the highest incidence were Rondônia, Rio Grande do Norte, Pernambuco, Sergipe, São Paulo, Rio Grande do Sul, and Mato Grosso. However, the highest incidence was observed in the South (Rio Grande do Sul) and Southeast (São Paulo) regions. The risk was increased in mothers born after 1980, aged over 30 years, and with a high education level. The risk was increased in live births in white and black, double pregnancy, and body weight under 3,000 g. Absent prenatal care was also associated with higher incidence. These findings can be used to reformulate professional practices and improve guidelines for public health policies.

Declarations

The authors claim there is no conflict of interest

6.2 Ethics approval and consent to participate

Not applicable.

6.3 Consent for publication

The authors approve the manuscript for publication.

6.4 Availability of data and material

Not applicable.

6.5 Competing interests

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6.7 Authors' contributions

Conception and design of study: João Simão de Melo-Neto, Fabiana de Campos Gomes, Nelson Veiga Gonçalves.

Acquisition of data: Raissa Tereza Casseb Oliveira, Edila Monteiro de Andrade, Diego Bessa Dantas, Márcio Vinicius de Gouveia Affonso; Ana Beatriz Rocha de Marin.

Analysis and/or interpretation of data: João Simão de Melo-Neto, Raissa Tereza Casseb Oliveira Oliveira, Edila Monteiro de Andrade, Diego Bessa Dantas, , Márcio Vinicius de Gouveia Affonso; Ana Beatriz Rocha de Marin, , Fabiana de Campos Gomes, Nelson Veiga Gonçalves

Drafting the manuscript: João Simão de Melo-Neto, Raissa Tereza Casseb Oliveira Oliveira, Edila Monteiro de Andrade, Diego Bessa Dantas, , Márcio Vinicius de Gouveia Affonso; Ana Beatriz Rocha de Marin, , Fabiana de Campos Gomes, Nelson Veiga Gonçalves

Revising the manuscript critically for important intellectual content: João Simão de Melo-Neto, Fabiana de Campos Gomes, Nelson Veiga Gonçalves.

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References

1. Copp AJ, Adzick NS, Chitty LS, Fletcher JM, Holmbeck GN, Shaw GM. Spina bifida. Nature reviews. Disease primers 2015; 1: 15007. doi:10.1038/nrdp.2015.7

2. Mitchell LE, Adzick NS, Melchionne J, Pasquariello PS, Sutton LN, Whitehead AS. Spina bifida. The Lancet 2004; 364(9448): 1885–95. doi: 10.1016/S0140-6736(04)17445-X
3. Shin M, Besser LM, Siffel C, Kucik JE, Shaw GM, Lu C et al. Prevalence of spina bifida among children and adolescents in 10 regions in the United States. Pediatrics 2010; 126: 274–9. doi: 10.1542/peds.2009-2084
4. Honein MA, Paulozzi LJ, Mathews TJ, Erickson JD, Wong LY. Impact of folic acid fortification of the US food supply on the occurrence of neural tube defects. JAMA 2001; 285: 2981–6. doi: 10.1001/jama.285.23.2981
5. Gaiva MAM, Neves AQ, Siqueira FMG. The care of the child with spina bifida by the family at home. Escola Anna Nery Revista Enfermagem 2009; 13: 717–25. doi: 10.1590/S1414-81452009000400005
6. Hunter GW. Brain and Spinal Cord. In: Human malformations and related anomalies. Editors: Stevenson ER, Hall JG, Goodman RM. New York: Oxford University Press, 1993; pp. 109–31
7. Online Mendelian Inheritance in Man. *NEURAL TUBE DEFECTS, FOLATE-SENSITIVE; NTDFS* (2015) https://omim.org/entry/601634?search=601634&highlight=601634 [Accessed June 1, 2021]
8. Online Mendelian Inheritance in Man. *GRAINYHEAD-LIKE 3; GRHL3* (2018) https://www.omim.org/entry/608317 [Accessed June 1, 2021]
9. Shaw GM, Carmichael SL, Kaidarova Z, Harris JA. Differential risks to males and females for congenital malformations among 2.5 million California births, 1989–1997. Birth Defects Research Part A Clinical and Molecular Teratology 2003; 67: 953–8.
10. Rittler M, López-Camelo J, Castilla EE. Sex ratio and associated risk factors for 50 congenital anomaly types: clues for causal heterogeneity. Birth Defects Research Part A Clinical and Molecular Teratology 2004; 70: 13–9. doi: 10.1002/bdra.10131
11. Botto LD, Moore CA, Khoury MJ, Erickson JD. Neural-tube defects. The New England Journal of Medicine 1999; 341: 1509–19. doi: 10.1056/NEJM199911113412006
12. Ministry of Health. *DATASUS*. Health Information (2008). http://www2.datasus.gov.br/DATASUS/index.php?area=02 [Accessed June 1, 2021].
13. Rosenberg PS, Check DP, Anderson WF. A web tool for age-period-cohort analysis of cancer incidence and mortality rates. *Cancer epidemiology, biomarkers & prevention: a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology* 2014; 23(11):2296–2302. doi: 10.1158/1055-9965.EPI-14-0300
14. Bessa Dantas D, da Costa D, Andrade E, Bastos MDS, Gomes F, de Melo-Neto JS. Sociodemographic and clinical factors associated with cryptorchidism in live births in Brazil: A 20-year analysis. Journal of public health research 2021; 10(1):1850. doi: 10.4081/jphr.2021.1850
15. Ministry of Health. National Program for Iron Supplementation: manual of general conduct. Brasília: Editora MS, 2013; pp. 24.
16. National Health Surveillance Agency. RDC n. 269, of September 22, 2005, 2019; https://www.gov.br/agricultura/pt-br/assuntos/inspecao/produtos-vegetal/legislacao-1/biblioteca-de-normas-vinhos-e-bebidas/resolucao-rdc-no-269-de-22-de-setembro-de-2005.pdf/view
17. Bestwick JP, Huttly WJ, Morris JK, Wald NJ. Prevention of neural tube defects: a cross-sectional study of the uptake of folic acid supplementation in nearly half a million women. PLoS One 2014; 9(2):e89354. doi:

10.1371/journal.pone.0089354

18. Carter CO, Evans K. Spina bifida and anencephalus in greater London. Journal of medical genetics 1973; 10(3):209–34. doi: 10.1136/jmg.10.3.209
19. Biney AAE, Nyarko P. Is a woman's first pregnancy outcome related to her years of schooling? An assessment of women's adolescent pregnancy outcomes and subsequent educational attainment in Ghana. Reproductive health 2017; 14:123. doi: 10.1186/s12978-017-0378-2
20. Williams LJ, Rasmussen SA, Flores A, Kirby RS, Edmonds LD. Decline in the prevalence of spina bifida and anencephaly by race/ethnicity: 1995–2002. Pediatrics 2005; 116(3):580–6. doi: 10.1542/peds.2005-0592
21. Andrade CY, Dachs JNW. Acesso à educação por faixas etárias segundo renda e raça/cor. Cadernos de Pesquisa 2007; 37:399–422. doi: 10.1590/S0100-15742007000200009
22. Office for National Statistics (UK). Health Statistics Quarterly, No. 10, Summer 2001. Trends in neural tube defects. https://webarchive.nationalarchives.gov.uk/20160111211122/http://www.ons.gov.uk/ons/rel/hsq/health-statistics-quarterly/no–10–summer-2001/index.html [Accessed June 1, 2021].
23. Vollset SE, Gjessing HK, Tandberg A, Rønning T, Irgens LM, Baste V, Nilsen RM, Daltveit AK. Folate supplementation and twin pregnancies. Epidemiology (Cambridge, Mass.) 2005; 16(2):201–5. doi: 10.1097/01.ede.0000152914.84962.13

Figures

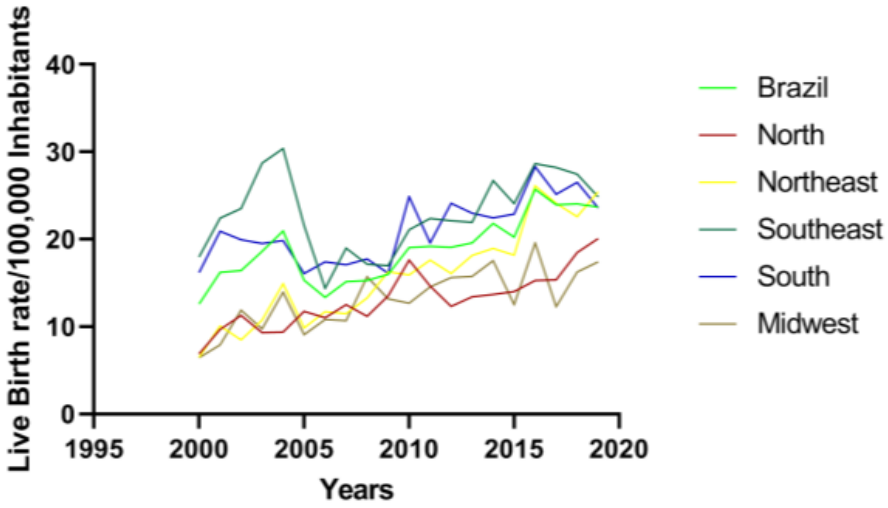

Figure 1

Distribution of the live birth rate / 100,000 inhabitants with spinal dysraphism per year.

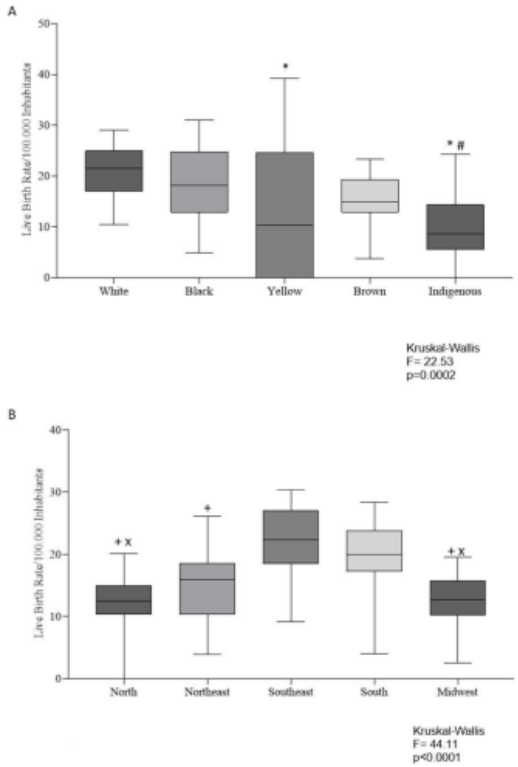

Figure 2

Distribution of the live birth rate/100,000 Inhabitants with spinal dysraphism per race/color (A) and region (B).

* $p < 0.05$, compared to white. # $p < 0.05$, compared to black. $^{+}$ $p < 0.05$. compared to the southeast. ^{X} $p < 0.05$. compared to the South.

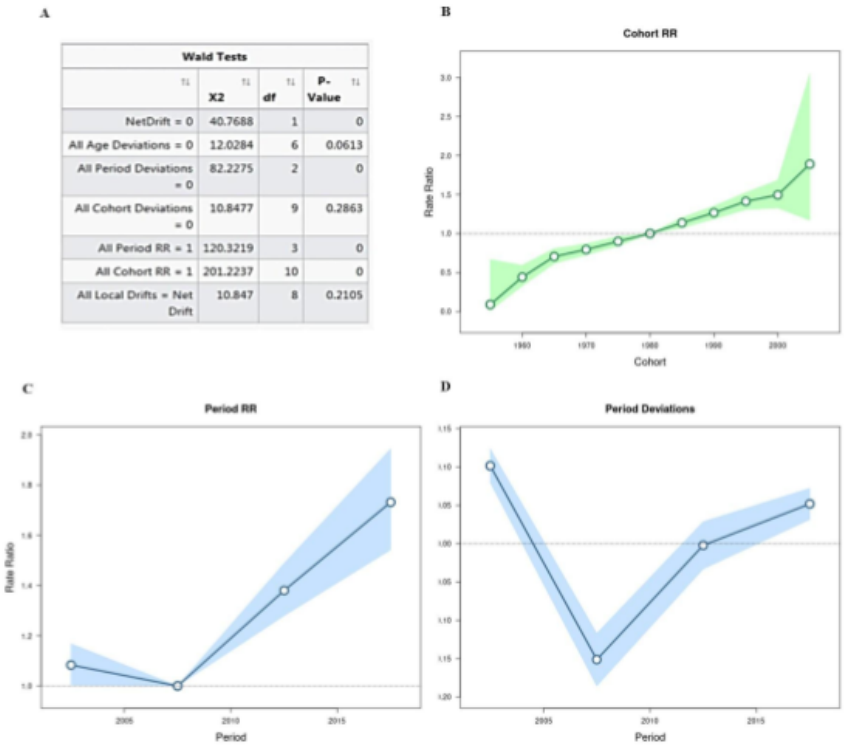

Figure 3

APC analysis with Wald test (A), Cohort RR (B), and Period (RR [C] and deviations [D]).

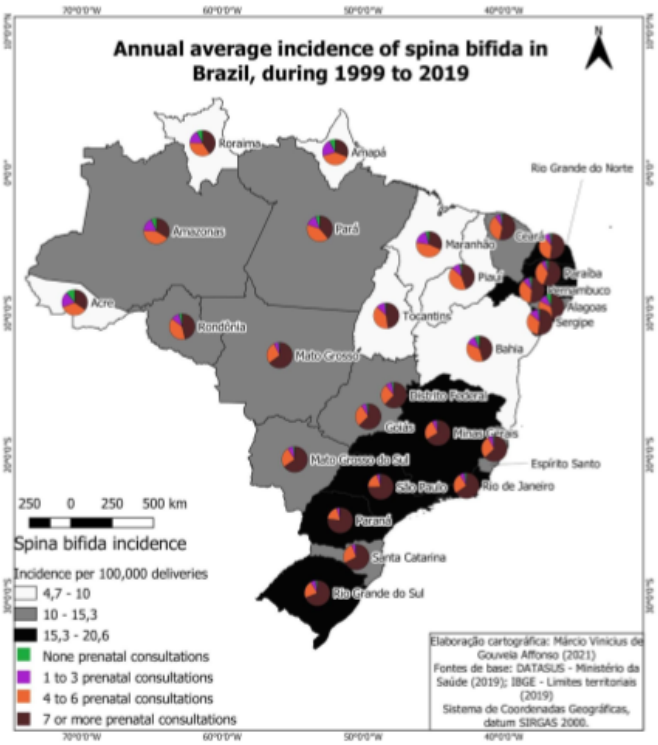

Figure 4

Spatial distribution of spinal dysraphism cases and prenatal care, 1999 to 2019, in Brazil.