Spatial and temporal analysis of infant mortality from congenital malformations in Brazil (1996–2010)

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Introduction

While there are a number of studies on infant mortality in general and its risk factors, the contribution of congenital malformations and the mortality rates of children due to them has been less explored. Although individually rare, congenital malformations taken together have contributed significantly to infant mortality in populations where infectious diseases have been controlled and nutritional deficiencies have been corrected (Jenkins 1977).

Over the last decades, in countries at different stages of development, there has been a trend of decrease in total infant mortality accompanied by a reduction in the rate of infant mortality from congenital malformations (IMR-CM), that is, the number of deaths from malformations per 1,000 births. The proportion of congenital malformation deaths (CMD%) has also been increasing, that is, the number of deaths from malformations per 100 deaths, for children less than 1 year of age (Rosano et al. 2000; Copeland and Russell 2006). The previously described trend of deaths in children under 1 year of age was confirmed in Chile in the period from 1985 to 2001 (Szot 2004) and in Argentina in the period from 2002 to 2006 (Bronberg et al. 2009). According to Rosano et al. (2000), the

IMR-CM tends to be higher in the poorest countries, while the CMD% is higher in richer ones.

In most Latin American countries, congenital malformations as the cause of death for children less than 1 year of age has tended to increase, and it has occupied between second and fifth places as the cause of death, contributing between 2 % and 27 % to total infant mortality. According to Victora et al. (2011), in Brazil over the last three decades, there has been a persistent and substantial decrease in infant mortality—it decreased 5.5 % a year between 1980 and 1990, and it has decreased 4.4 % a year since 2000, attaining a rate of 20 deaths per 1,000 live births in 2008. According to these same authors, in the period between 1990 and 2007, there was no significant change in the IMR-CM throughout Brazil. Similar findings were reported by Victora and Celso (2001) when analyzing the behavior of infant mortality due to congenital malformations in Brazil between 1985 and 1987 and 1995 and 1997, thus demonstrating that, while the IMR-CM remained stable in both periods, the CMD% increased from 7.1 % for 1985–1987 to 11.5 % for 1995–1997. The same trend occurred at the regional level but with disparities between regions, particularly for the CMD%. However, Siedersberger Neto et al. (2012) found an increase in both the IMR-CM and the CMD% throughout Brazil in the period between 1996 and 2008.

This paper intends to broaden the analysis of the IMR-CM and CMD% trends in Brazil for 1996–2010 as well as their spatial variation at different levels of political-administrative structures (regions, Federative Units/States, and municipalities).

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Materials and methods

This is an ecological and populational study in which information was obtained from the DATASUS database of births and infant deaths occurring in Brazil).

DATASUS is responsible for the computerization of Brazil's Unified Health System (SUS, <http://www2.datasus.gov.br/DATASUS/index.php?area=01>), and it provides information that can be used to assist with objective analysis of the health situation, decision-making based on evidence, and the preparation of health programs. In this work, we used the data for Live Births and Infant Deaths (less than 1 year of age) collected through the SINASC (Information System for Live births) and the SIM (Mortality Information System), respectively.

The following variables for the place of births and deaths were used: (a) absolute number of deaths of children less than 1 year of age; (b) absolute number of live births; (c) number of congenital malformation deaths of children less than 1 year of age, identified by the International Classification of Disease (tenth Revision). Based on these data, regardless of gender, the IMR-CM (number of deaths from malformation for every 1,000 live births) and the CMD% (number of deaths from malformations for every 100 deaths of children less than 1 year of age) were calculated for the whole country, five geographical regions (North, Northeast, Southeast, South, and Center-West), 27 Federative Units/States (Rorônia, Acre, Amazonas, Roraima, Pará, Amapá, Tocantins, Maranhão, Piauí, Ceará, Rio Grande do Norte, Paraíba, Pernambuco, Alagoas, Sergipe, Bahia, Minas Gerais, Espírito Santo, Rio de Janeiro, São Paulo, Paraná, Santa Catarina, Rio Grande do Sul, Mato Grosso do Sul, Mato Grosso, Goiás, and the Distrito

Federal), and 5,600 municipalities in Brazil (Fig. 1) (IBGE 2002).

The trend for the entire period and for the variation of risk between the regions and Federative Units/States, for the periods 1996–2000, 2001–2005, and 2006–2010, was calculated using a Poisson regression model. In this model, deaths due to congenital malformation were the dependent variable, and the time (year of the study) was the independent variable, while live births and total deaths were the exposure variables. The trend was obtained from the coefficient of the independent variable (year of the study). A positive coefficient for “time” suggests an upward trend in the IMR-CM and CMD%, while a negative coefficient for “time” suggests a downward trend in the IMR-CM and CMD%.

In the same way, the relative risk related to the IMR-CM and CMD% is calculated between the subperiods 2001–2005 and 2006–2010, in relation to the subperiod 1996–2000, with a Poisson regression model, using deaths by congenital malformations as the dependent variable, the subperiods as independent variables, and the total births and deaths as the exposition variable, transforming the calculated coefficients into relative risks.

The spatial scan statistic for the Poisson model (Kulldorff et al. 2009) was used to determine geographical areas with rates that had either low or high statistical significance in comparison with the mean values—data on the number of

Fig. 1 Regions (North, Northeast, Center-West, Southeast, and South) and States of Brazil

Fig. 2 Rate of infant mortality by congenital malformations (IMR-CM) secular trend in Regions and States between 1996 and 2010 (**a** North, **b** Northeast, **c** Southeast, **d** South, **e** Center-West)

deaths due to congenital malformation (case group), the number of births (population), and the geographical coordinates of the exact location of each municipality are linked together. This analysis tests a circular area centered on each geographic point at a specific time, representing one of all the 5,600 municipalities (observational centers). Starting from an initial radius of 0, it was progressively enlarged by scanning the covered area, including observational centers, thus detecting centers with rates that were significantly higher or lower than expected. This test uses the maximum likelihood ratio test statistic to determine those areas with the smallest probability for the unusual rates observed that resulted from random sampling variation. The *P* value was obtained through multiple simulations, using the Monte Carlo model with 999

replications (Silva et al. 2009). The critical significance value was set at $P < 0.05$. The only two restrictions introduced into our analysis were: the number of births captured in a given area could not exceed 10 % of the total available births in our sample, and the resulting areas could not overlap.

Results

a. IMR-CM

For all of Brazil and for the entire period analyzed (1996–2010), the IMR-CM presented a statistically significant positive temporal trend ($P < 0.01$); see Fig. 2. In the periods 1996–

Table 1 Rate of infant mortality by congenital malformations (IMR-CM) by sub-periods and secular trend (ST) (1996–2010)

Political organization level	IMR-CM			ST	95 % CI ^a	<i>p</i> value ^b	<i>R</i> ² ^c
	1996–2000	2001–2005	2006–2010				
Brazil	2.42	2.56	2.71	0.010	0.009, 0.012	0.000	0.47
North	1.95	2.23	2.59	0.028	0.024, 0.033	0.000	0.51
Rondônia	1.99	2.64	3.26	0.049	0.035, 0.063	0.000	0.32
Acre	2.11	2.54	2.74	0.024	0.005, 0.043	0.00	0.32
Amazonas	2.47	2.49	3.15	0.027	0.018, 0.036	0.000	0.22
Roraima	3.45	3.13	2.67	−0.027	−0.050, −0.005	0.016	0.06
Pará	1.56	1.91	2.22	0.034	0.026, 0.041	0.000	0.38
Amapá	1.86	2.46	2.20	0.010	−0.011, 0.030	0.369	0.01
Tocantins	2.01	2.19	2.47	0.027	0.011, 0.042	0.001	0.09
Northeast	1.65	2.11	2.69	0.046	0.044, 0.049	0.000	0.82
Maranhão	1.28	1.82	2.24	0.050	0.041, 0.059	0.000	0.44
Piauí	1.23	2.12	3.21	0.089	0.077, 0.101	0.000	0.65
Ceará	1.89	2.31	2.67	0.031	0.024, 0.037	0.000	0.33
RG do Norte	1.96	2.33	2.61	0.029	0.018, 0.039	0.000	0.19
Paraíba	1.10	1.96	2.74	0.084	0.072, 0.096	0.000	0.60
Penambuco	2.28	2.54	2.98	0.025	0.019, 0.031	0.000	0.32
Alagoas	0.91	1.94	2.49	0.092	0.080, 0.103	0.000	0.6
Sergipe	1.86	2.45	2.84	0.041	0.029, 0.054	0.000	0.26
Bahia	1.52	1.83	2.66	0.056	0.050, 0.061	0.000	0.68
Southeast	2.80	2.71	2.62	−0.007	−0.010, −0.005	0.000	0.16
Minas Gerais	2.91	2.32	2.55	−0.010	−0.015, −0.005	0.000	0.03
Espírito Santo	2.38	2.87	3.06	0.026	0.017, 0.036	0.000	0.18
Rio de Janeiro	2.77	2.88	2.75	−0.001	−0.006, 0.003	0.615	0.00
São Paulo	2.87	2.82	2.57	−0.011	−0.014, −0.008	0.000	0.27
South	2.91	3.05	2.89	−0.001	−0.004, 0.003	0.666	0.00
Paraná	3.06	3.11	3.06	0.001	−0.004, 0.006	0.791	0.00
Santa Catarina	2.94	2.67	2.59	−0.013	−0.021, −0.006	0.001	0.09
RG do Sul	2.75	3.21	2.88	0.005	−0.001, 0.010	0.096	0.01
Center-West	2.79	3.14	3.08	0.012	0.008, 0.017	0.000	0.15
MG do Sul	2.82	3.33	3.40	0.017	0.006, 0.027	0.001	0.08
Mato Grosso	2.55	3.10	3.00	0.021	0.011, 0.031	0.000	0.11
Goiás	2.56	2.98	2.88	0.014	0.006, 0.021	0.000	0.09
Distrito Federal	3.48	3.34	3.28	−0.002	−0.011, 0.008	0.000	0.00

^a 95 % Confidence interval

^b *p* value

^c Coefficient of determination

2000, 2001–2005, and 2006–2010, the IMR-CM for Brazil was 2.42, 2.56, and 2.71, respectively (Table 1). Table 2 shows how the magnitude of the IMR-CM risk changes in the periods 2001–2005 and 2006–2010, in relation to the initial 1996–2000 period, for all of Brazil, both by region and Federative Unit/State. Nationally, the risk increased from 5.7 % for 2001–2005 to 11.8 % in the 2006–2010 period.

The North, Northeast, and Center-West regions showed a statistically significant positive temporal trend for the IMR-CM; however, it was negative in the Southeast and null in the South region (Table 1). Comparing the 2006–2010 and 1996–2001 periods, the North, Northeast, and Center-West regions showed IMR-CM increases of 31.9 %, 62.4 %, and 10.4 %,

respectively (Table 2). The Southeast region showed a decrease of 6.1 %, and the South region showed no significant changes (Table 2). As shown in Fig. 2, the IMR-CM values of the Center-West, South, and Southeast regions were generally higher than the rate for the entire country while those for the North and Northeast regions were below the national rate and tended to increase in the period analyzed.

The states of Piauí (0.089), Paraíba (0.084), and Alagoas (0.092) stood out with the highest positive trend values, while São Paulo (−0.11) and Santa Catarina (−0.013)—see Table 1—showed negative trend values. Comparing the sub-periods of 2006–2010 and 1996–2001, there were increases in the IMR-CM for Piauí, Paraíba, and Alagoas, of 152 %,

Table 2 Rate of infant mortality by congenital malformations (IMR-CM) risk for 2001–2005 and 2006–2010 sub-periods compared with 1996–2000 sub-period

Political organization level	2001–2005			2006–2010		
	RR	95 % CI ^a	<i>p</i> value ^b	RR	95 % CI ^a	<i>p</i> value ^b
Brazil	1.06	1.04, 1.07	0.000	1.12	1.10, 1.13	0.000
North	1.14	1.08, 1.20	0.000	1.32	1.26, 1.39	0.000
Rondônia	1.34	1.15, 1.55	0.000	1.65	1.43, 1.92	0.000
Acre	1.19	0.97, 1.47	0.096	1.29	1.05, 1.58	0.015
Amazonas	1.00	0.91, 1.11	0.976	1.27	1.15, 1.39	0.000
Roraima	0.92	0.73, 1.15	0.467	0.78	0.62, 0.99	0.042
Pará	1.23	1.13, 1.33	0.000	1.42	1.31, 1.55	0.000
Amapá	1.32	1.06, 1.66	0.015	1.19	0.94, 1.50	0.143
Tocantins	1.08	0.91, 1.28	0.372	1.22	1.03, 1.44	0.019
Northeast	1.27	1.23, 1.31	0.000	1.62	1.58, 1.67	0.000
Maranhão	1.45	1.31, 1.61	0.000	1.77	1.60, 1.96	0.000
Piauí	1.66	1.44, 1.91	0.000	2.52	2.41, 2.89	0.000
Ceará	1.21	1.13, 1.30	0.000	1.41	1.31, 1.51	0.000
RG do Norte	1.19	1.06, 1.33	0.003	1.33	1.19, 1.49	0.000
Paraíba	1.78	1.55, 2.05	0.000	2.49	2.18, 2.86	0.000
Pernambuco	1.11	1.04, 1.19	0.001	1.31	1.23, 1.39	0.000
Alagoas	2.11	1.84, 2.42	0.000	2.73	2.38, 3.12	0.000
Sergipe	1.32	1.15, 1.51	0.000	1.54	1.35, 1.75	0.000
Bahia	1.21	1.13, 1.29	0.000	1.76	1.66, 1.87	0.000
Southeast	0.97	0.95, 0.99	0.011	0.94	0.92, 0.96	0.000
Minas Gerais	0.87	0.83, 0.91	0.000	0.95	0.91, 0.99	0.035
Espírito Santo	1.20	1.09, 1.33	0.000	1.29	1.16, 1.42	0.000
Rio de Janeiro	1.04	0.99, 1.09	0.108	0.99	0.94, 1.04	0.694
São Paulo	0.98	0.95, 1.01	0.207	0.89	0.87, 0.92	0.000
South	1.05	1.01, 1.09	0.007	0.99	0.96, 1.03	0.691
Paraná	1.02	0.97, 1.07	0.509	1.00	0.95, 1.06	0.944
Santa Catarina	0.91	0.84, 0.98	0.015	0.88	0.82, 0.95	0.002
RG do Sul	1.17	1.11, 1.24	0.000	1.05	0.99, 1.12	0.103
Center-West	1.13	1.08, 1.18	0.000	1.10	1.05, 1.16	0.000
MG do Sul	1.18	1.06, 1.319	0.003	1.21	1.08, 1.35	0.001
Mato Grosso	1.22	1.10, 1.36	0.000	1.18	1.06, 1.31	0.003
Goiás	1.17	1.08, 1.26	0.000	1.13	1.04, 1.12	0.003
Distrito Federal	0.96	0.87, 1.06	0.382	0.94	0.85, 1.04	0.237

RR relative risk

^a 95 % Confidence interval

^b *p* value

149 %, and 172 %, respectively while São Paulo and Santa Catarina had a decrease of 10.6 % and 11.8 %, respectively (Table 2). In the North and Northeast regions, all states, except for Roraima, presented IMR-CM values that were generally lower than the national rate (Fig. 2) whereas in the South, Southeast, and Center-West regions, all the states, except for Minas Gerais, presented IMR-CM values that were generally higher than the national rate (Fig. 2).

Six IMR-CM high-risk clusters and eight IMR-CM low-risk clusters that were significantly different from the rest of the country were detected (Table 3). Among the high-risk clusters, number 2, which is comprised of 1,050 municipalities located in the south of the country, stood out. Conversely, low-risk clusters tended to be located in the north of the country, especially clusters 1 and 8, which include the largest number of municipalities (Fig. 3).

b. CMD%

Over the entire period, CMD% in Brazil showed a statistically significant positive temporal trend (0.050)—see Table 3 and Fig. 2. In the 1996–2000, 2001–2005, and 2006–2010 periods, the CMD% in Brazil was 10.6 %, 13.8 %, and 17.9 %, respectively—see Table 4. Comparing the 2006–2010 subperiod with the initial 1996–2001 subperiod, we can see that the CMD% for Brazil rose by 71.3 %.

At the regional level, all regions showed a statistically significant positive temporal trend (Table 4). In terms of the

2006–2010 subperiod, in relation to the initial 1996–2001 subperiod, the regions with the highest increases were the North (84.6 %) and Northeast (158.6 %), while the Southeast, Center-West, and South regions exhibited comparatively lower increases of 54.3 %, 44.4 %, and 44.6 %, respectively. The South, Center-West, and Southeast regions presented CMD% above the national average, while it was below the national average in the North and Northeast regions (Fig. 4).

All states, except Roraima, experienced a statistically significant positive temporal trend (Table 4). Comparing the 2006–2010 subperiod with the 1996–2001 subperiod, the increase was highest in Paraíba (411 %) and lowest in the Distrito Federal (23.3 %)—see Table 5. Except partially for Roraima, all Federative Units/States of the North and Northeast regions generally showed CMD% values below the national percentage. However, for all states of the South, Southeast, Center-West regions (except the state of Minas Gerais), CMD% values were above the national percentage (Fig. 4).

Six clusters with high CMD% risk and six with low CMD% risk, which were significantly different from the rest of the country, were detected (Table 6). High-risk clusters tended to be located in the south of the country—cluster 2 comprising 1,154 municipalities stood out. Conversely, the low-risk municipalities were found in the north of the country—cluster 3 with 677 municipalities and cluster 1 with 367 municipalities (see Table 6 and Fig. 5).

Table 3 Characteristics of rate of infant mortality by congenital malformations (IMR-CM) clusters (2006–2010)

Risk classification	Cluster	CM ^a death	Birth	Risk ^b	95 % CI ^c	Nr. municipalities (states)	Regions	IMR-CM	95 % CI ^c
High	1	757	19,095	1.44	1.33, 1.55	2 (1)	North	3.71	1.48, 5.93
	2	4,085	1,337,379	1.14	1.10, 1.17	1,050 (5)	Southeast, South, Center-West	3.12	2.91, 3.31
	3	540	143,725	1.39	1.28, 1.52	51 (3)	Northeast	3.47	2.81, 4.14
	4	948	283,470	1.24	1.16, 1.32	8 (2)	Center-West	3.63	2.99, 4.27
	5	376	98,143	1.42	1.28, 1.57	3 (1)	Northeast	3.15	0.34, 5.93
	6	1,717	544,963	1.17	1.11, 1.23	130 (2)	Northeast	3.19	2.91, 3.46
Low	7	3,109	1,450,372	0.78	0.76, 0.82	581 (9)	North, Northeast, Center-West	2.06	1.91, 2.20
	8	1,851	785,449	0.87	0.83, 0.91	374 (2)	Southeast	2.28	2.06, 2.49
	9	49	38,877	0.47	0.35, 0.62	23 (1)	Northeast	1.18	0.63, 1.72
	10	434	211,029	0.76	0.69, 0.84	120 (2)	Northeast	1.93	1.67, 2.18
	11	2,795	1,139,960	0.91	0.87, 0.94	19 (1)	Southeast	2.29	2.09, 2.49
	12	148	82,442	0.66	0.57, 0.78	35 (2)	Northeast	1.99	1.48, 2.51
	13	684	306,026	0.83	0.77, 0.89	234 (4)	Northeast	2.12	1.88, 2.37
	14	35	26,995	0.48	0.34, 0.67	33 (2)	Northeast, Southeast	1.23	0.68, 1.83

^a Congenital malformation

^b Relative risk

^c 95 % Confidence interval

Fig. 3 Low and high risk of rate of infant mortality by congenital malformations (IMR-CM). Clusters (2006–2010) represented in a scatter plot of coordinates

Discussion

In order to analyze the behavior of infant mortality due to congenital malformations, this paper reviewed information from population databases containing birth certificates and infant deaths occurring for Brazil for the 1996–2010 period. While questioning the validity of these sources, due to the underreporting of congenital malformations (Rosano et al. 2000; Copeland and Russell 2006; Northam and Knapp 2006; Bronberg et al. 2009) caused by deficiencies in the capacity and quality of diagnosis (description, classification, and coding), this is the only population-level information collected in multiple countries which is used by World Health Organization (WHO) for comparative purposes. Indeed, WHO has regularly updated infant mortality tables of its Member States since 1990, and it provides estimates of total deaths by age, sex, and cause of death (WHO, Global Health Observatory Data Repository).

According to Mathers et al. (2005), the quality of information on infant mortality and its causes in Brazil is only average, with a completeness (proportion of all deaths that are registered in the population covered by the vital registration system for a country) of 84 % and coverage (calculated by dividing the total number of reported deaths from the country's vital registration system for a year by the overall number of deaths for the national population estimated by WHO for that year) of 79 %. The Health Ministry's Mortality Information System (SIM), which supplies the data used in this work, was created in 1976 from the implementation of the standardized death certificate to substitute civil registry deficiencies (Landmann Szwarcwald 2002). These actions were reinforced by Ordinance No. 20 of Brazil's Health Ministry, dated October 3, 2003, which established data collection, data flow, and frequency of the information submitted to the central administrative level (Prado de Mello et al. 2007). According to Prado de Mello et al. (2007), the

Table 4 Proportion of congenital malformations deaths (CMD%) by sub-periods and temporal trend (ST) (1996–2010)

Political organization level	CMD%			ST	95 % CI ^a	<i>p</i> value ^b	<i>R</i> ² ^c
	1996–2000	2001–2005	2006–2010				
Brazil	10.6	13.8	17.9	0.050	0.049, 0.052	0.000	0.96
North	7.9	10.5	14.3	0.059	0.054, 0.063	0.000	0.83
Rondônia	8.3	12.7	18.0	0.078	0.065, 0.090	0.000	0.58
Acre	7.4	11.8	14.1	0.057	0.065, 0.090	0.000	0.58
Amazonas	8.4	12.1	18.6	0.076	0.069, 0.084	0.000	0.72
Roraima	16.2	19.1	15.7	0.005	−0.015, 0.026	0.595	0.00
Pará	6.8	8.6	11.9	0.057	0.050, 0.064	0.000	0.64
Amapá	7.5	11.2	10.3	0.027	0.009, 0.046	0.004	0.07
Tocantins	9.3	11.4	14.9	0.055	0.041, 0.069	0.000	0.33
Northeast	6.1	9.4	15.4	0.089	0.087, 0.092	0.000	0.95
Maranhão	7.3	9.5	13.5	0.069	0.061, 0.078	0.000	0.63
Piauí	7.4	10.1	17.4	0.089	0.077, 0.100	0.000	0.67
Ceará	6.3	10.5	17.0	0.091	0.085, 0.097	0.000	0.82
RG do Norte	8.9	12.6	18.2	0.067	0.058, 0.077	0.000	0.60
Paraíba	3.3	9.3	16.8	0.140	0.129, 0.150	0.000	0.83
Penambuco	6.7	10.4	17.3	0.092	0.087, 0.09	0.000	0.88
Alagoas	2.8	7.2	12.8	0.142	0.131, 0.153	0.000	0.82
Sergipe	6.4	9.4	16.1	0.089	0.078, 0.101	0.000	0.62
Bahia	6.5	8.1	13.9	0.076	0.071, 0.081	0.000	0.75
Southeast	12.8	16.9	19.4	0.040	0.039, 0.043	0.000	0.88
Minas Gerais	9.8	13.3	17.6	0.056	0.052, 0.061	0.000	0.81
Espírito Santo	12.2	17.9	22.9	0.064	0.055, 0.072	0.000	0.60
Rio de Janeiro	12.3	16.5	18.9	0.041	0.037, 0.045	0.000	0.70
São Paulo	14.6	18.8	20.2	0.032	0.030, 0.035	0.000	0.73
South	16.3	19.9	23.2	0.034	0.031, 0.037	0.000	0.76
Paraná	15.3	19.3	23.6	0.042	0.037, 0.046	0.000	0.69
Santa Catarina	17.4	18.9	22.1	0.026	0.019, 0.033	0.000	0.30
RG do Sul	16.9	21.1	23.4	0.030	0.025, 0.035	0.000	0.45
Center-West	14.6	18.4	21.1	0.036	0.032, 0.040	0.000	0.64
MG do Sul	11.1	15.9	19.2	0.051	0.042, 0.061	0.000	0.50
Mato Grosso	12.3	15.9	18.6	0.043	0.034, 0.052	0.000	0.40
Goiás	15.0	18.9	21.0	0.032	0.026, 0.039	0.000	0.39
Distrito Federal	21.4	24.0	27.2	0.024	0.016, 0.033	0.000	0.19

^a 95 % Confidence interval^b *p* value^c Coefficient of determination

SIM showed increased improvement, both qualitatively and quantitatively, with regional variations—in 1997, the coverage ranged from 56.2 % in the Northeast to 95.5 % in the Southeast while, in 2002, it exceeded 83 % for all of Brazil. According to Landmann Szwarcwald (2002), for 12 % of cases in 2001, there was inadequate information on the population for all of Brazil—in the North, this percentage was 35 %, followed by the Center-West with 29 %, while in the South there was information deficiency on infant mortality for only 1 % of the population.

As expected when using the same source for the whole of Brazil, the IMR-CM and CMD% behavior were similar to that reported by Siedersberger Neto et al. (2012) for the 1996–2008 period. These results indicate that, for the whole of

Brazil, the pattern observed in the 1996–2010 period was not characterized by an IMR-CM decrease and CMD% increase, as observed in Chile (Szot 2004) and Argentina (Bronberg et al. 2009). Particularly in Argentina, on a national level like in Brazil, IMR-CM had a positive trend that became negative after 1990 (Bronberg et al. 2009). Although there was probably no single cause for these differences, they could be explained by the trend, magnitude, and variations of total infant mortality. In Chile and Argentina, the infant mortality rate in 1990 was 16 per 1,000 and 24 per 1,000, respectively; and 8 per 1,000 and 13 per 1,000 in 2011. In Brazil, it went from 49 per 1,000 in 1990 to 14 per 1,000 in 2011 (WHO 2012a). This means that, compared with Chile and Argentina, in Brazil, the infant mortality rate remained high for most of

Fig. 4 Proportion of congenital malformations deaths (CMD%). Secular trend in Regions and States between 1996 and 2010 (**a** North, **b** Northeast, **c** Southeast, **d** South, **e** Center-West)

Table 5 Proportion of congenital malformations deaths (CMD%) risk for 2001–2005 and 2006–2010 sub-periods compared with 1996–2000 sub-period

Political organization level	2001–2005			2006–2010		
	Risk	95 % CI ^a	<i>p</i> value ^b	Risk	95% CI ^a	<i>p</i> value ^b
Brazil	1.30	1.28, 1.32	0.000	1.71	1.69, 1.74	0.000
North	1.33	1.26, 1.39	0.000	1.85	1.76, 1.94	0.000
Rondônia	1.52	1.31, 1.76	0.000	2.28	1.97, 2.62	0.000
Acre	1.62	1.32, 2.00	0.000	1.92	1.57, 2.37	0.015
Amazonas	1.40	1.27, 1.55	0.000	2.22	2.03, 2.43	0.000
Roraima	1.22	0.98, 1.54	0.081	1.05	0.84, 1.32	0.658
Pará	1.28	1.17, 1.39	0.000	1.81	1.68, 1.96	0.000
Amapá	1.49	1.19, 1.86	0.001	1.43	1.15, 1.78	0.001
Tocantins	1.21	1.02, 1.43	0.028	1.65	1.41, 1.93	0.000
Northeast	1.53	1.48, 1.57	0.000	2.59	2.51, 2.66	0.000
Maranhão	1.32	1.19, 1.46	0.000	2.00	1.81, 2.20	0.000
Piauí	1.34	1.17, 1.55	0.000	2.37	2.08, 2.70	0.000
Ceará	1.67	1.55, 1.79	0.000	2.74	2.26, 2.94	0.000
RG do Norte	1.42	1.26, 1.59	0.000	2.07	1.86, 2.30	0.000
Paraíba	2.76	2.40, 3.18	0.000	5.11	4.48, 5.84	0.000
Penambuco	1.55	1.45, 1.65	0.000	2.69	2.23, 2.85	0.000
Alagoas	2.49	2.17, 2.86	0.000	4.77	4.19, 5.45	0.000
Sergipe	1.44	1.26, 1.65	0.000	2.54	2.24, 2.89	0.000
Bahia	1.24	1.17, 1.32	0.000	2.18	2.06, 2.31	0.000
Southeast	1.32	1.30, 1.35	0.000	1.54	1.51, 1.58	0.000
Minas Gerais	1.36	1.29, 1.42	0.000	1.83	1.74, 1.91	0.000
Espírito Santo	1.46	1.32, 1.62	0.000	1.92	1.74, 2.12	0.000
Rio de Janeiro	1.35	1.29, 1.42	0.000	1.57	1.50, 1.64	0.000
São Paulo	1.30	1.26, 1.34	0.207	1.41	1.37, 1.45	0.000
South	1.22	1.18, 1.26	0.000	1.44	1.40, 1.50	0.000
Paraná	1.26	1.19, 1.33	0.000	1.57	1.49, 1.65	0.000
Santa Catarina	1.07	0.99, 1.16	0.074	1.31	1.21, 1.41	0.000
RG do Sul	1.25	1.18, 1.32	0.000	1.39	1.31, 1.47	0.000
Center-West	1.26	1.21, 1.33	0.000	1.47	1.39, 1.52	0.000
MG do Sul	1.44	1.29, 1.60	0.000	1.76	1.59, 1.96	0.000
Mato Grosso	1.28	1.16, 1.43	0.000	1.53	1.38, 1.70	0.000
Goiás	1.27	1.18, 1.38	0.000	1.41	1.31, 1.52	0.000
Federal District	1.12	1.02, 1.24	0.019	1.26	1.15, 1.39	0.000

RR relative risk

^a 95 % Confidence interval^b *p* value

the period analyzed, since deaths per 1,000 live births were 27 in 2000, 22 in 2005, and 19 in 2007 (Victora et al. 2011; WHO 2012b). Variations in the general infant mortality rate, at least in Latin American countries, are strongly related to infant mortality resulting from congenital malformations, given that these malformations have started to significantly contribute to infant mortality in societies that have completed the transition from the pattern of infant deaths through the control of preventable causes (infectious, perinatal, or nutritional), via economic development and the reduction of poverty and marginalization (Bronberg et al. 2012). It is therefore expected that the relationship between the two indicators used (IMR-CM and CMD%), as well as their temporal trend, will vary among

countries, based on the decrease in the infant mortality rate, the change in the trend of infant deaths due to causes, and the socioeconomical development attained.

In contrast, the pattern of decreased IMR-CM and increased CMD% appeared regionally in the Southeast region and partially in the South region and the states of Minas Gerais, Rio de Janeiro, São Paulo, Santa Catarina, and the Distrito Federal. These regions and states are characterized by a high Human Development Index (HDI) of over 0.800 (PNUD 2012) and the location of the most economically and demographically important urban centers in the country. Roraima is the only state of Brazil where the IMR-CM and CMD% have a negative trend, which sets a unique pattern that

Table 6 Characteristics of proportion of congenital malformations deaths (CMD%) clusters (2006–2010)

Risk classification	Cluster	CM ^a death	Total death	Risk ^b	95 % CI ^c	No. of municipalities (states)	Regions	CMD%	95 % CI ^c
High	1	5,108	21,760	1.41	1.37, 1.46	1,154 (5)	Southeast, South, Center-West	24.7	23.3, 26.1
	2	4,495	20,754	1.27	1.23, 1.32	667 (4)	Southeast, Center-West	19.4	17.8, 20.9
	3	4,565	21,833	1.22	1.18, 1.26	85 (1)	Southeast	21.3	19.6, 23.0
	4	487	1,837	1.49	1.38, 1.61	21 (1)	Southeast	30.9	25.4, 36.4
	5	1,541	7,336	1.18	1.13, 1.23	75 (5)	Southeast, Northeast	20.8	17.4, 24.3
	6	1,186	5,608	1.19	1.13, 1.25	1 (1)	Southeast	21.2	–
Low	7	2,529	21,925	0.60	0.58, 0.63	367 (6)	North, Northeast, Center-West	10.9	9.9, 11.8
	8	2,885	21,908	0.70	0.67, 0.73	677 (9)	North, Northeast	12.9	12.2, 13.7
	9	228	2,318	0.50	0.44, 0.58	39 (2)	North	9.3	7.7, 10.9
	10	898	6,656	0.72	0.67, 0.77	131 (3)	Northeast	13.1	11.9, 14.8
	11	944	6,730	0.78	0.74, 0.84	183 (3)	Northeast, Center-West	13.3	11.9, 14.8
	12	654	4,544	0.81	0.75, 0.87	226 (3)	Southeast	14.1	12.3, 16.0

^a Congenital malformation^b Relative risk^c 95% Confidence interval

has not been previously described for the behavior of infant mortality resulting from congenital malformations. Although Roraima is characterized by an HDI with a mean value >0.70 , it is located in the North region, which is one of the poorest regions of Brazil, and with poor quality of vital information (Landman Szwarcwald 2002). Interestingly, it is the state that has the largest indigenous population (11 %) as a percentage of its total population (IBGE 2012). It is likely that the pattern of infant mortality due to congenital malformation observed in this state resulted from the combination of these contributing elements.

Historically, Brazil has been characterized as a country with profound socioeconomic inequalities in terms of income distribution and economic activity throughout the country. This inequality is manifested by lower socioeconomic development and greater poverty in the North and Northeast regions of the country. If the recent economic growth, which placed Brazil among the four largest emerging economies in the world (with China, Russia, and India), has changed this situation globally, it has not had a substantial impact on regional economies. Indeed, the reduction of regional disparities is modest, because economic activity continues to be focused in the South and Southeast regions of the country (Crocco et al. 2013).

When analysis of the behavior of infant mortality due to congenital malformation was concentrated, Brazil presented a clear contrast between the north and south of the country, and also for the two indicators used. Indeed, the IMR-CM and CMD% values for the northern regions and northern Federative Units/States were generally lower than those for the south and for Brazil as a whole. Excluding these differences as a source of disparities between the north and south of the country in the coverage and quality of information of the previously

considered death certificates (Landman Szwarcwald, 2002), they can be explained by the great demographic and socioeconomic heterogeneity among Brazil's regions. When Azis dos Santos et al. (2006) analyzed the differences of subnational government spending per capita within Brazil, they observed that, despite presenting the highest levels of poverty, the Federative Units/States of the Northeast region had lower public spending for both social (education and health) and territorial (public infrastructure) assets, that is, for the same fiscal effort, the country's poorest and most needy communities in the northern regions spent less on social and regional public assets per capita. Regional differences were also evidenced by GDP per capita—the highest amount was observed in the Distrito Federal and the lowest amounts, with a ratio above 7, were in Maranhão and Piauí, which were the lowest in both the Northeast Region and for all of the Federative Units/States of Brazil (Guisan and Cardim Barta 2003). Also, for the last census in 2010, the North and Northeast regions of the country had the highest percentage of people with no formal education or incomplete primary education, as well as the lowest economically active population (IBGE 2010). While the North and Northeast regions showed a sharp decline in the rate of infant mortality between 2000 and 2010 (more than 45 %), they recorded the highest rates among the five regions—21.8 deaths per 1,000 births for the Northeast region and 20.1 deaths per 1,000 births for the North region (Health Ministry/Ministerio de Saúde 2011).

The spatial distribution at the municipal level for the IMR-CM and CMD% indicators could also be explained by the socioeconomic conditions of the places where child deaths occur due to congenital malformations. From an international perspective, the most important antecedent for this issue is the work of Rosano et al. (2000), who used the IMR-CM and

Fig. 5 Low and high risk of proportion of congenital malformations deaths (CMD%). Clusters (2006–2010) represented in a scatter plot of coordinates

CMD% to analyze data on infant mortality due to congenital malformations from 36 countries in Europe, the Middle East, America, Asia, and the South Pacific and then related this to the GDP per capita. Rosano et al. (2000) found that the IMR-CM presented a strong negative correlation with GDP per capita, while the CMD% was positively correlated with this indicator of economic development. More recently, Bronberg et al. (2012) analyzed the IMR-CM and CMD% in relation to socioeconomic and demographic characteristics, which is summarized in a single indicator of development in Argentina, at regional and district levels. The IMR-CM did not significantly associate with the country's marked socioeconomic heterogeneity, but the highest CMD% values were observed in the more developed populations in the central and southern parts of the country. Because of this association between CMD% and the socioeconomic development of the population, Bronberg et al.

(2012) suggested using this indicator to represent the wellbeing and quality of life. The spatial distribution of the IMR-CM and CMD% in Brazil partially coincided with the findings of Rosano et al. (2000), since the clusters of high IMR-CM and CMD% tended to be distributed in the municipalities of the more developed South and Southeast regions and Federative Units/States of the country. These findings account for the importance of considering the IMR-CM and CMD% parameters as a simple and inexpensive statistical resource for obtaining information and monitoring the progress of various general and specific health policies and programs for congenital malformations.

Since the majority of congenital malformation deaths consist of major structural malformations, particularly defects in neural tube closure and cardiac malformations, interregional differences of IMR-CM and CMD% can also be interpreted in

terms of efforts to treat these diseases and reduce their prevalence. In 2004, the Brazilian Health Ministry established a national policy for highly complex cardiovascular care with a focus on cardiovascular surgery. According to a performance evaluation of this program done in 2008 using several indicators, there were clear inequalities between the north and south of the country (to the detriment of the north) in the distribution of cardiovascular surgery services, in relation to the size of the population, number of births, treatment capacity, and efficiency (Valdester Cavalcante 2010). In a cross-sectional study that examined the prevalence and spatial distribution of neural tube defects before and after folic acid fortification of wheat flour and maize in the state of São Paulo, a temporary reduction was confirmed in most of the state, except in some municipalities in the west (Fujimori et al. 2013).

There is specific policy in Brazil regarding supplementation, and the lower impact of folic acid fortification in Brazil, when compared with other Latin-American countries, could be due to differences in dietary habits, the concentration of folic acid in flour, as well as the characteristic composition of the ethnic population (Orioli et al. 2011).

The Millennium Development Goal 4 (UNDP 2010; WHO 2010) has proposed reducing infant mortality by two thirds for children under 5 years of age. The neonatal component (0–27 days) in Brazil represents 70 % of infant mortality (França et al. 2009). In 2010, 3.1 million children died worldwide in the neonatal period. Of these deaths, congenital malformation was the cause of death in 270,000 cases, with 6,255 of these deaths occurring in Brazil. In 2000, this number was 8,879 (Liu et al. 2012). While Brazil registered a negative trend for neonatal infant mortality and the number of children dying from congenital malformations in the neonatal period, the relative percentage of this cause of death in Brazil increased from 7.1 % for 1983–1985 to 14.4 % for 2003–2005, with large regional disparities—its increase was most significant in the country's southern regions (França et al. 2009). These facts, together with the results obtained in this work, reveal the importance of broadening the analysis and interpretation of spatial and temporal behavior of infant mortality from congenital malformations in Brazil, in order to contribute to the formulation of a specific national policy on birth defects (Horovitz et al. 2005, 2012).

The main limitations encountered in this epidemiological study did not arise from the two indicators for mortality from congenital malformations (IMR-CM and CMD%), or from the methodology used for its calculation, but rather from the quality of the data sources in relation to their previously analyzed coverage. Since the infant mortality rate is the preferred indicator of the risk of dying from any cause during the first year of life, then the IMR-CM would also be a valid indicator of congenital malformation deaths for children less than 1 year of age. There are other measures of infant mortality, such as infant deaths (deaths of persons aged 1 year or more),

but these data are not available for Brazil in DATASUS, and it is not universally used, thus making intra- and interpopulation comparisons difficult. While the Poisson distribution used in this paper provides a model for discretizing events that infrequently occur in time or space as congenital defects, perhaps in order to broaden this analysis for future works, analytical solutions could include stratified analysis, simulations, or Bayesian Models, etc.

In conclusion, we have shown that the pattern of infant mortality in Brazil, from 1996 to 2010, is characterized by an increase both of the rate of infant mortality from congenital malformations (IMR-CM) as well as of the rate of congenital malformation deaths (CMD%). However, it is noteworthy the deep regional disparities with states from the South presenting a pattern more similar to that observed in high-income countries with a decrease in IMR-CM and an increase in CMD%.

Ethical standards This study complies with the current laws of the country in which they were performed.

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