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Original Article

Prevalence of fetal and neonatal mortality due to congenital anomalies in the state of Maranhão, Brazil, from 2001–2016

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Abstract

Introduction: The infant mortality rate (IMR) is an important health indicator directly associated with living conditions, prenatal care coverage, social development conditions, and parental education, among others. Worldwide, the infant mortality rate was 29/1000 live births in 2017. Therefore, this study aimed to evaluate the fetal and infant mortality rates due to congenital anomalies (CA) in Maranhão from 2001 to 2016.

Methods: Data were obtained from the SINASC, and SIM databases. We used simple linear regression, Poisson distribution, and ANOVA (Bonferroni's post hoc test). We analyzed the public data (2001–2016) of 1934858 births and determined the fetal, neonatal, perinatal, and post-neonatal mortality rates associated with CA by mesoregions.

Results: The IMR in Maranhão was 17.01/1000 live births (95%CI, 13.30-20.72) and CA was the cause of death in 13.3% of these deaths. Mortality due to CA (per 1000 live births) was 0.76 (95%CI, 0.74–0.85) for fetal mortality rate and 2.27 (95%CI, 1.45-3.10) for infant mortality rate. Geographic and temporal variations were observed with a slight increase in recent years for deaths attributable to CA, and in the northern part of Maranhão.

Conclusions: Mortality rates due to CA in Maranhão increased over the period 2001–2016 possibly as a result of improved maternal-infant health conditions eliminating other causes of death. Therefore, efforts to improve early diagnosis and better treatment of congenital anomalies should be considered to reduce its impact on child mortality.

Keywords: *Congenital abnormalities; Infant mortality; Live birth; Perinatal mortality*

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INTRODUCTION

The occurrence and severity of congenital anomalies (CAs) are determined by numerous genetic and environmental factors, often leading to serious disabilities or even death[1]. The worldwide infant mortality rate (IMR), or the number of deaths of children under 1 year of age, is an important health indicator directly associated with living conditions, prenatal care coverage, social development conditions, parental education, among others, as well as an indicator of the quality of public health[2-4]. Globally, the IMR decreased from 65 deaths per 1000 live births in 1990 to 29 deaths per 1000 live births in 2018[3]. A study by Victora et al.[4] showed that, in Brazil, infant mortality decreased from 47 deaths per 1000 live births in 1990 to 27/1000 live births in 2000, and 19/1000 live births in 2007. Ten years later, in 2017, this rate was 12/1000 live births[5]. Comparatively, in the European Region, IMR was only 9/1000 live births[6]. While this decline in Brazil in recent decades is reassuring, there are many regional differences. In 1990 the IMR in the Northeast region of Brazil was 2.6/1000 live births times higher than that in the South, and in 2007 it remained 2.2/1000 live births times higher[4].

The proportion of CAs associated with infant mortality is also an important health and social indicator[4,7]. In high-income countries, CAs are now the

leading cause of infant mortality. In most Latin American countries as well as in Brazil, CAs are already the second cause of infant mortality due to improved maternal and child care[7-9]. In a study with data from the European Surveillance of Congenital Anomalies (EUROCAT), for the period 2005–2009, the IMR due to CA was 1.1/1000 live births in 11 European countries[10]. In Brazil, deaths due to CAs were 2.48/1000 live births in 1996 and 2.74/1000 live births in 2008, and the proportion of IMR due to CA was 9.94% in 1996 and 18.22% in 2008[11].

Maranhão is one of the poorest states in Brazil with a Human Development Index (HDI) of 0.687 in 2017[12], and there is a shortage of studies on the impact of CA in IMRs in the Northeast region of the country[13,14]. Therefore, this study aimed to evaluate fetal and infant mortality rates due to CA in Maranhão from 2001 to 2016.

METHODS

This is a population-based ecological time-series analysis of fetal and infant deaths associated to congenital anomalies in the state of Maranhão from 2001 to 2016. Maranhão is located in the Northeast region of Brazil and has a geographical area of 329642170 km^2 and a population of 7075181 inhabitants[15]. The HDI was 0.639 in 2010 and 0.687 in 2017, and the monthly per capita household income in 2018 was US$ 144 dollars[12]. It has 217 municipalities in 5 geographic regions (Center, East, North, West, and South).

Data were obtained using the electronic database of the Department of Informatics of the Brazilian public unified health system (DATASUS)[16]. Information on stillbirths and infant deaths were available in the Mortality Information System (SIM—*Sistema de Informação sobre Mortalidade*, in Portuguese) and data on live births were available in the Live Birth Information System (SINASC—*Sistema de Informação sobre Nascidos Vivos,* in Portuguese). All data are public and can be accessed on the DATASUS website[16]. We extracted the yearly absolute number of live births, stillbirths and infant deaths, as well as the number of deaths of children under 1 year old with CAs in the period 2001–2016.

CAs are classified according to the 10th revision of the International Classification of Diseases (ICD-10th), grouped into the following categories: Q00–Q01 Anencephaly and Encephalocele; Q02 Microcephaly; Q04–Q07 Other CA of the nervous system; Q10–Q18 CA of the eye, ear, face and neck; Q20–Q28 CA of the circulatory system; Q30–Q34 CA of the respiratory tract; Q35–Q37 Cleft lip and cleft palate; Q38–Q45 Other CA of the digestive tract CA; Q50–Q56 Congenital malformations of genital organs; Q60–Q64 Congenital urinary tract abnormalities; Q65–Q79 CA and congenital deformities of the musculoskeletal system; Q80–89 Other congenital anomalies; Q90–Down syndrome; Q91–Edwards syndrome and Patau syndrome; Q92–Q99 Chromosomal anomalies not elsewhere classified[16].

We calculated the following indicators: (1) infant mortality rate (IMR: number of deaths of children under 1 year of age/total live births); (2) CA mortality rate (number of deaths due to congenital anomalies/number of births); (3) proportion of infant deaths attributable to CA (congenital anomaly mortality rate/IMR); (4) fetal CA rate (number of fetal deaths by CA/total number of stillbirths); (5) early neonatal CA mortality rate (number of deaths by CA from zero to the 6th day of age/number of live births); (6) perinatal CA mortality rate (fetal + early neonatal deaths/total births); (7) late neonatal CA mortality rate (number of deaths due to CA from the 7th to the 27th day of age/number of live births); and (8) post-neonatal CA mortality rate (number of deaths by CA from the 28th to the 364th day of age/number of live births).

Simple linear regression was used to detect annual temporal trends of fetal and infant mortality rates. Rates were the dependent variables (Y) and years the independent variables (X). The centralized variable (X–2008/2009), corresponding to the second semester of 2008 and the first semester of 2009, was selected to avoid autocorrelation between the equation terms. The equation formula was $Y = \beta_0 + \beta_1$ (X-2008/2009), where Y = mortality rate, β_0 = average rate for the period; β_1 = annual average rate and X = year. The fit of the model was by the determination coefficient (R^2)—that measures the proportion of variation of the dependent variables[11]. The ANOVA test was used to compare infant mortality rate (IMR), fetal mortality rate (FMR) percentage and IMR by CA from 2001 to 2016. Bonferroni's post hoc test was applied to analyze specific pairs of samples for stochastic dominance.

The data were organized in Microsoft Excel® 2016 spreadsheets, and spatial and temporal statistical analyses were performed using R studio, version 3.6.0. The confidence intervals of mortality rates were calculated using the Poisson distribution[17], using Epi Info™, version 7.2.3[18], and significance was set at $p < 0.05$.

This investigation does not contain any human or animal studies. The data included here refer to human births identified in the DATASUS system. All human individuals had anonymous records on the website. The Brazilian legislation (Resolution 466/12 of the Brazilian National Health Council) does not require Research Ethics Committee approval for data obtained from freely accessible public databases, such as DATASUS.

RESULTS

From 2001 to 2016, there were 1934858 live births in Maranhão and 25640 stillbirths, and the mean IMR was 2.23/1000 live births. Mortality rates due to CA (per 1000 live births) were: fetal mortality rate of 0.76 (95% confidence interval [CI], 0.74–0.85), early neonatal mortality rate of 1.06 (95%CI, 1.03–1.20), perinatal mortality rate of 1.82 (95%CI, 1.22–1.84), late neonatal mortality rate of 0.33 (95%CI, 0.29–0.73), and post-neonatal mortality rate of 0.87 (95%CI, 0.86-10.2) (Table 1).

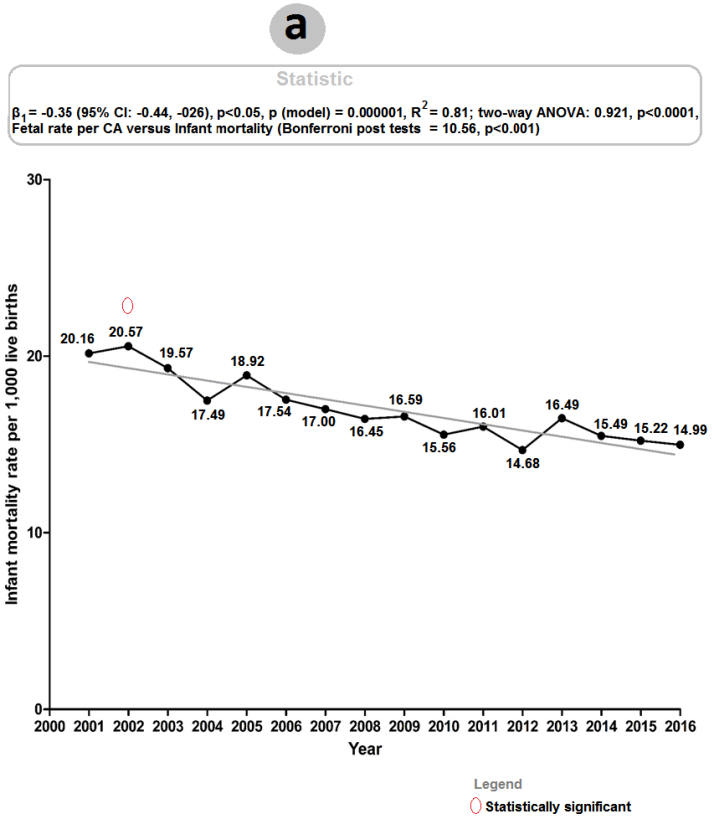
Table 1: Fetal, early neonatal, perinatal, late neonatal and post-neonatal mortality rates due to congenital anomalies, in the period 2001–2016 in the state of Maranhão, Brazil (Livebirths = 1934858; Stillbirths = 25640).

Mortality	Total deaths (N)	CA deaths (N %)	IMR-CA	(95%CI)
Fetal	25640	1462 (5.7%)	0.76	(0.74–0.85)
Early neonatal (0 to 6 days)	17251	2057 (11.9%)	1.06	(1.03–1.20)
Perinatal (fetal + early neonatal)	**27391**	**3519**	**1.82**	**(1.22–1.84)**
Late neonatal (7 to 27 days)	4126	642 (15.5%)	0.33	(0.29–0.73)
Post-neonatal (28 to 364 days)	11535	1684 (14.6%)	0.87	(0.86–1.02)
Infant (0 to 364 days)	**32912**	**4383 (13.3%)**	**2.27**	**(1.45–3.10)**
Infant Mortality Rate	**17.01 (95%CI, 13.30–20.72)**			

Note: CA deaths = Number of deaths with congenital anomalies and % of deaths due to CA;

IMR-CA = Infant Mortality Rate by Congenital Anomalies (per 1000 live births); CI = Confidence Interval.

The overall IMR in Maranhão decreased from 20.16/1000 live births in 2001 to 14.99/1000 live births in 2016, with a mean annual reduction of 0.35 (95% CI, -0.44–-0.26, p < 0.000001). In contrast, there was an increase in the FMR due to CA in the state during the same period, with a mean annual increase of 0.01 (95% CI, 0.002–0.017, p < 0.00933), as shown in Figure 1a and b. When comparing the FMR due to CA and the general IMR, (ANOVA = 0.921, Bonferroni = 10.66, p < 0.0001), there are higher rates in 2002 (general IMR) and 2015 (fetal mortality by CA) (Figure 1a).



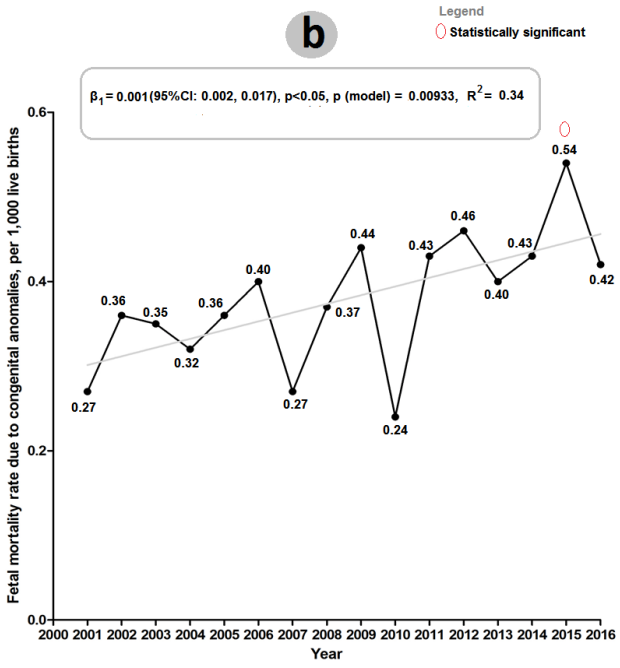
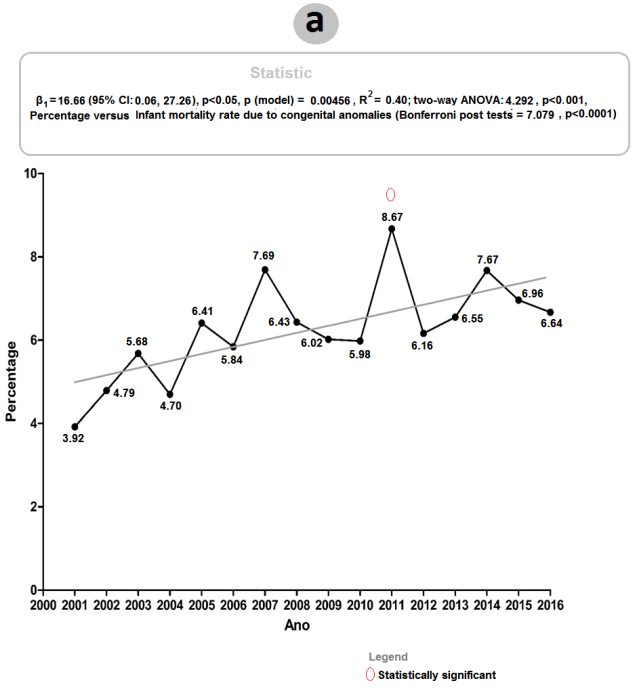


Figure 1: A: Time trend general infant mortality rate; B: Fetal mortality rate due to congenital anomalies, in the period 2001–2016, in the state of Maranhão, Brazil.

There was an increase in infant mortality due to CA from 1.58/1000 live births (2001) to 2.63/1000 live births (2016), with a mean annual increase of 0.07/1000 live births (95% CI, 0.04–0.10, p < 0.00025) (Figure 2a). The proportion of infant deaths due to CA increased from 3.92% in 2001 to 6.64% in 2016, with a mean annual increase of 19.66% (95%CI, 6.06%–27.26%, p < 0.00456), as shown in Figure 2b. When comparing the percentage of deaths due to CA and overall IMR by CA, it was found to be statistically significant (ANOVA = 4.292, Bonferroni = 0.079 with higher rates in 2011, p < 0.0001) (Figure 2a).



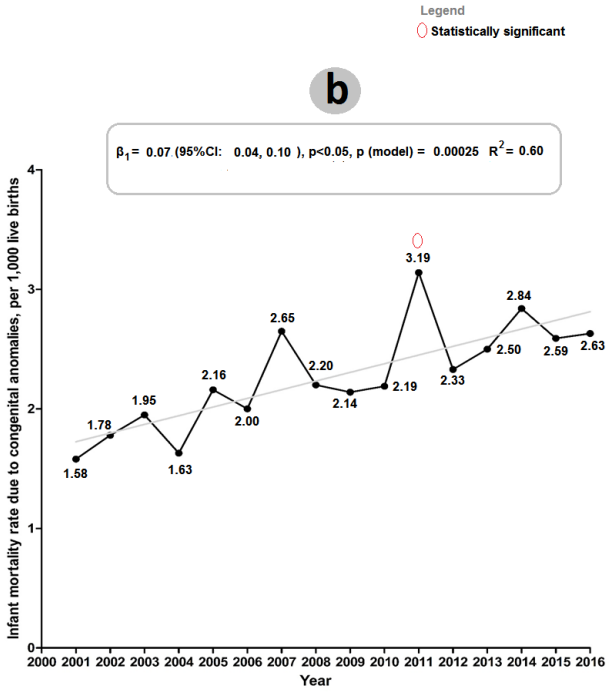


Figure 2: A: Time series of the percentage of deaths due to congenital anomalies; B: Infant mortality rate due to congenital anomalies, in the period 2001–2016, in the state of Maranhão, Brazil.

The spatial distribution of IMR due to CA showed differences across geographic regions: lower (0.88/1000 live births) in the West and higher (1.88/1000 live births) in the North (Figure 3).

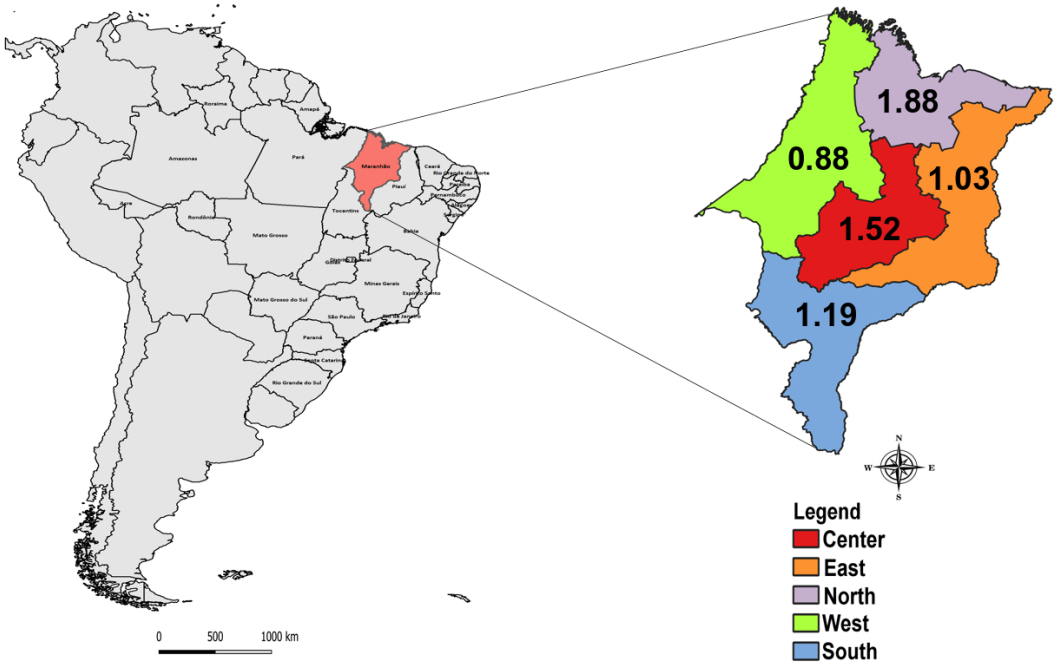


Figure 3: Distribution of infant mortality rates by congenital anomalies in the mesoregions of Maranhão, from 2001–2016.

IMRs by type of CA were analyzed (Table 2), and the highest IMRs were due to congenital heart defects (0.94/1000 live births; 95%CI, 0.48–0.95).

Table 2: Infant mortality rate associated to congenital anomalies in children under 1 year according ICD-10th categories, from 2001–2016, in the state of Maranhão, Brazil.

Congenital anomalies types (ICD-10th)	N	IMR-CA (95%CI)
Q00–Q01 Anencephaly and Encephalocele	328	0.17 (0.15–0.17)
Q02–Microcephaly	31	0.02 (0.00–0.03)
Q03–Congenital Hydrocephalus	184	0.10 (0.09–0.11)
Q04-Q07 Other nervous system CA	279	0.14 (0.12-0.15)
Q10–Q18 CA Eye, Ear, Face and Neck	01	0.00 (0.00–0.00)
Q20–Q28 Congenital circulatory system abnormalities	1827	0.94 (0.48–0.95)
Q30–Q34 Congenital respiratory tract abnormalities	181	0.09 (0.07–0.09)
Q35–Q37 Cleft lip and palate	22	0.01 (0.00–0.02)
Q38–Q45 Other congenital anomalies of digestive tract	321	0.17 (0.15–0.17)
Q50–Q56 Congenital anomalies of genital organs	03	0.00 (0.00–0.00)
Q60–Q64 Congenital urinary tract abnormalities	66	0,03 (0.02–0.04)
Q65–Q79 CA of the musculoskeletal system	350	0.18 (0.17–0.25)
Q80–Q89 Other congenital malformations	672	0.35 (0.26–0.47)
Q90–Down syndrome	74	0.04 (0.03–0.06)
Q91–Edwards syndrome and Patau syndrome	32	0.02 (0.00–0.03)
Q92–Q99 Chromosomal anomalies, not elsewhere classified	12	0.01 (0.00–0.02)

Note: ICD-10th = International Classification of Diseases; N = Number of deaths in children under 1 year; IMR-CA = Infant Mortality Rate by Congenital Anomalies (per 1000 live births).

DISCUSSION

This study described the spatial and temporal IMR due to CA in the state of Maranhão. Despite the steady decline in IMR in Brazil as a whole, there are different levels of decline in rates across the country and among the population groups within Brazilian states. A reduction from 24.47/1000 live births to 15.03/1000 live births in IMR was observed in an ecological study from 1996 to 2008 conducted in Brazil[11]. Comparatively, in our study in Maranhão, in 2001, overall IMR was 20.16/1000 live births, and in 2006, 14.99/1000 live births. Another study identified the largest declines in overall IMR in the Southeast and South regions of the country[4].

Mortality due to CA was already the first among the causes of death in almost all Brazilian states throughout the second decade of the 21st century[19]. In the present study, we observed that the IMR from CAs in the state of Maranhão increased in the period 2001–2016, which can be attributed to 3 situations: (1) improved infant mortality records; (2) national and local health policies aimed at reducing infant mortality[20]; and (3) the outbreak of Zika Virus associated congenital microcephaly, which occurred mainly in the Northeast of Brazil[21]. In addition to mortality related to brain damage secondary to prenatal Zika infection, the outbreak likely caused more reporting and surveillance in both births and the number of deaths from CA and others causes. Between 2000 and 2015, an annual average of 164 cases of microcephaly were registered[21], and 71% (n = 1142 cases) of live births were to mothers in the Northeast. The incidence of microcephaly in Maranhão was 8.23/10000 live births[21].

According to the United Nations Inter-agency Group for Child Mortality Estimation (UNIGME), infant mortality rates dropped from 46/1000 live births to 16/1000 live births between 1990 and 2015 in Latin America and the Caribbean, consequently the proportion of infant deaths secondary to CA is expected to have increased[22], as observed in our study. Like our results, Bronberg et al. observed an increase in the IMR due to CA in Maranhão, between the 2001–2005 and 2006–2010 periods[7].

In the city of Recife, in the northeastern state of Pernambuco, a study in 2004 and 2005 found that the perinatal mortality rate due to CA was 59.4/1000 live births with higher rates for perinatal and early neonatal mortality[23]. Arruda et al., also in Pernambuco, found higher mortality rates due to CAs in the perinatal and early neonatal periods from 1993 to 2003[20]. Another study conducted in Brazil in 2011–2012 observed the highest neonatal mortality rates from CAs in the South and Southeast of the country[24].

The different mortality rates for CAs in the spatial distribution of regions in Maranhão can be explained by the socioeconomic conditions. From a national perspective, Maranhão has one of the lowest HDIs in Brazil and ranks first in the lowest per capita household income in the Northeast Region[25]. Historically, Brazil presents significant socioeconomic inequalities in relation to income distribution. In this sense, the regions of Maranhão are not very different from the national reality. Accordingly, the lowest infant mortality rates due to CAs are evident in the west, east, and south (mainly) of Maranhão, probably because these areas concentrate more economic activities, mostly by migrants from the South and Southeast of Brazil[26].

In South America, a study of five Argentinian regions from 2002 to 2006 observed an association between mortality rates due to CAs and socioeconomic and demographic characteristics, which are factors that indicate a country's regional developmen[27].

In another study in Maranhão, Cacau et al. detected that 10.5% of the primary causes of mortality were due to CAs[14]. In addition, a further study observed that prematurity, regional inequalities, inadequate maternal care during pregnancy, infectious diseases (e.g., congenital syphilis, congenital rubella, and cytomegalovirus), labor complications, and alcohol use during pregnancy are factors that increase infant mortality rates[28-31]. In this perspective, high infant mortality rates reflect the poor health conditions of the population[28]. Mazzu-Nascimento et al. reported the following data in Brazil: fetal deaths (annual mean of 1530), infant hospitalizations (annual mean of 82452), deaths of hospitalized infants (annual mean of 2175), and the mean cost of hospitalizations by CAs (annual cost of $ 7758) between 2008 and 2014[31].

Recently, Reis et al. concluded that estimates of the incidence of infant mortality rate due to CAs and of rates of CA at birth using time and spatial series can help the specialized team to identify local causes, appropriate conditions for interventions, as well as the cost-benefits of the interventions[30]. In this sense, IMR due to CA and the rates for live births with CAs impact quality of life and increase the costs of specialized care for those affected and their families[31].

In another study in the Northeast, weaknesses were identified in the operation of the SIM—it signaled for possible changes in the work process at the local level (e.g. more partnerships with other sources of information)[32]. However, Figueiroa et al. already observed an increase in over 90% of the SIM coverage[32,33]. For this reason, the information in the studies by Figueroa et al.[32,33], partially explains the results observed in Figures 1 and 2 of this study.

In other Brazilian studies, malformations of the nervous system had the highest proportions in causes of general IMR[20,23]. A study in Colombia reported that circulatory system (cardiac) CAs had the highest proportions (32.0%) in infant deaths, followed by nervous system CAs (15.8%) and chromosomal abnormalities[34]. These differences might be explained by the fact that cardiac anomalies might be more variable reported due to difficulties in its diagnosis at birth.

Limitations of this study

The main limitation found in our retrospective study was that this research was based on public data from DATASUS, SINASC, and SIM databases. For this reason, the IMRs due to CA may be underestimated due to underreporting. Moreover, CAs were present only in groups at DATASUS, so it was not possible to study individualized ICD-10th codes. Outside the limitations, the research had some strengths, e.g., we obtained a significant number of cases, in addition to investigating mortality over a long series of time.

CONCLUSION

In conclusion, mortality rates due to CAs in Maranhão increased over the period 2001–2016 possibly as a result of improved maternal-infant health conditions eliminating other causes of death. Therefore, efforts to improve early diagnosis and better treatment of congenital anomalies should be considered to reduce its impact on child mortality.

Conflicts of Interest

The authors declare no conflicts of interests.

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