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# TIME TREND OF INFANT MORTALITY DUE TO CONGENITAL MALFORMATIONS IN RECIFE, PERNAMBUCO, BRAZIL

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**ABSTRACT**

**Objective**: to analyze the time trend of infant mortality due to congenital malformations of residents of Recife, PE, during the period from 2001 to 2016. **Methods**: it is an ecological time-series study whose data sources were the Information Systems about Mortality (SIM) and Live Births (Sinasc). The rates and proportion of mortality due to congenital malformations were analyzed on a monthly basis by the autoregressive model of moving averages with an ancillary variable (ARMAX). **Results**: Out of a total of 1,194 child deaths due to congenital malformation, 527 (44.18%) occurred during the early neonatal period, 588 (49.25%) were male, 571 (47.8%) weighed ≥2,500 grams. The rate of child mortality due to congenital malformation showed a constant average, with a fairly stable result. As for the proportion of deaths due to congenital malformation, a growing trend was observed during the period analyzed, with significant growth from 2015 to 2016. **Conclusion**: the time-series analysis enabled the knowledge of the behavior of child mortality due to congenital malformation. These results may support healthcare actions and actions for the development of preventive measures in order to reduce that mortality.



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# INTRODUCTION

Congenital malformations represent a serious public health problem around the world. The concept of congenital malformations is related to disorders that modify the structure and functioning of organs present in the embryonic period or throughout the development of the child, and they may be physical, mental, or combined. (World Health Organization, 2015). It is estimated that 8.7% of the deaths during the first weeks of life are due to congenital malformations (World Health Organization, 2015). In the Latin-American countries, such anatomic or functional disorders are placed second in the infant mortality ranking, accounting for 2% to 27% of the deaths of children younger than one year of age (Bronberg *et al*., 2014). In Brazil, in 2010, the mortality rate due to malformations was 16.2 for every 1,000 live births (MENDES, 2015; Bando *et al*., 2014). The Northeast region presented a rate of 3.06 for every 1,000 live births, ranking second for causes of death in children younger than one year of age (França *et al*., 2017).

In the State of Pernambuco, in 2015, the mortality rate due to congenital malformations was 2.96 for every 1,000 live births. (BRASIL, 2016). To make it easier to observe or monitor the variation of the infant mortality rate due to malformations, time-series studies can be used, as they are valuable tools in epidemiology (Antunes and Cardoso, 2015). That analysis enables monitoring and assessing how a certain event acts over time and in regular periods (Antunes and Cardoso, 2015). The intention is to get to know which factors may have acted with cause and effect relationships in the behavior of the event in the past and are able to continue to have impacts in the future (Martins-Melo *et al*., 2014). Time trend studies allow us to comprehend the actions of a series over years, which may occur increasingly, decreasingly, or stationarily. Additionally, they show the velocity of such changes, identifying how their measures harmonize with each other or are associated with information on a certain phenomenon (Antunes and Cardoso, 2015). They also promote knowledge production, enabling better visibility of the main categories of deaths, their causes, and the possible contributing factors (Silva *et al*., 2016; Antunes and Cardoso, 2015).

Time series have an important role in supporting the planning of health care policies and decision making, in addition to providing epidemiological evidence of the health care needs of a population (Areco *et al*., 2016). Considered as the second-ranked cause of infant mortality, congenital malformations have an impact on the health of a population. This study aimed at analyzing the time trend of infant mortality due to congenital malformations that occurred in residents of Recife, PE, during the period from 2001 to 2016.

# MATERIALS AND METHODS

The study area was Recife, the capital city of Pernambuco, located in the Northeast region of Brazil, with a land area of 218.5 km². The population of the study were all infant deaths whose underlying cause of death referred to congenital malformations, deformities, and chromosomal abnormalities, Chapter XVII (Q00-Q99) of the International Classification of Diseases and Related Health Problems, 10th revision (ICD-10). The deaths of residents of Recife that occurred during the period from 2001 to 2016 and were recorded in the Mortality Information System (SIM) were included. It is an ecological time-series study that allows assessing the evolution of the event of congenital malformations over time. The data were obtained from the SIM and from the Information System on Live Births (Sinasc), on the website of the Computing Department of the Unified Health System (DATASUS). The SIM was used to verify the number of deaths, and the Sinasc was used to calculate the mortality rates. In order to obtain projections for the epidemiological indicators infant mortality rate due to congenital malformations for every 1,000 live births and proportion of deaths due to congenital malformations, a dataset with the computed amounts of each indicator was provided.
This set has monthly data about the indicators for the city of Recife, PE, in the time interval of 2001 to 2016, amounting to 192 observations. To identify the models, time-series analysis was used, based on the statistical model; then it was possible to make assumptions about the behavior of the malformations for the next 24 months. A time series (Ts) is a set of data laid out in time. Its analysis consists of developing a statistical model to explain the behavior of the event over time; a time-series analysis begins with the observation of its chart.

A trend reveals the long-term performance of the series, that is, its average trajectory, considering a long period of time. In a time series, the main piece of data used in the modeling is the amount of the variable in past periods. Seasonality is the variation arising from specific moments. A random error implies that there is always a variation that occurs casually, and it cannot be anticipated. In this study for the analysis of the rate, the Box-Jenkins method was used, according to which the identification is made based on sample autocorrelation (ACF) and partial autocorrelation functions (PACF). This method must be applied to stationary series, i.e., series whose averages and variance do not depend on the time (constant). For a good adjustment to the data regarding the proportion, it was necessary to apply a more sophisticated model: the autoregressive model of moving averages with an ancillary variable (ARMAX). The ARMAX model is quite similar to the ARMA model, an autoregressive model of moving averages formed by the parameters autoregressive (AR) and moving average (MA). The value of the AR specifies the delay considered in the generation of the model. (Li, *et al*., 2014) The ARMAX is different than the others, because it takes into account not only the indicator of interest over time, but also other variables, as a regression (Li *et al*., 2014).

Because the model adopted for the estimate was the ARMAX, a regressing variable is necessary for the estimates to be made. The chosen variable is the number of deaths due to malformation, which had a higher correlation with the proportion indicator. The model was also applied for a forecast of the proportion of the mortality due to malformation for the period from January 2017 to December 2018.
A log transformation was also applied for the number of deaths. The following model was used to represent the proportion indicator:

$$\hat{Y}_t' = 0.1123Y_{t-1}' - 0.0499Y_{t-2}' - 0.0187Y_{t-3}' + 0.0387Y_{t-4}' + 0.0614Y_{t-5}' - 3.2179 + 0.0042T + 0.9139X_t$$

where, and and Y = Proportion and X = Number of deaths. The R Project for Statistical Computing version 3.501 was used. The study used secondary data in the public domain, available at www.datasus.gov.br, with no personal identification, which waived the need for submission to the ethics committee for researches involving human beings.

# RESULTS

During the study period, out of the 1,194 infant deaths with congenital malformation as a basic cause, 527 (44.14%) occurred during the early neonatal period, 588 (49.2%) were male, 734 (61.5%) were *Pardos*, 571 (47.8%) weighed ≤2.500 grams, and the place with the most frequent occurrence of the hospital, with 1.172 (98.16%). Regarding the characteristics of the mother, 739 (61.9%) mothers were of age 20 to 34, 716 (60%) mothers studied more than 8 years, 1,132 (94.8%) mothers had a single pregnancy, and there were 681 (57%) cesarean deliveries. (Table 1). In the distribution of the main causes of infant death due to congenital malformation, 244 (20.44%) deaths occurred due to other congenital malformations of the heart and 101 (8.46%) due to other musculoskeletal congenital malformations not elsewhere classified (Table 2).

**Table 1. Characteristics of infant deaths due to congenital malformation, Recife, PE, 2001 to 2016**

| Variables | No. | % | Variables | No. | % |
|---|---|---|---|---|---|
| **Age factor** | | | **Age of the mother** | | |
| Early neonatal | 527 | 44.1 | < 19 years old | 241 | 20.2 |
| Late neonatal | 183 | 15.3 | 20 to 34 years old | 739 | 61.9 |
| Post-neonatal | 484 | 40.5 | > 35 | 202 | 16.9 |
| **Sex** | | | Unknown | 12 | 1.0 |
| Male | 588 | 49.2 | **Education of the mother** | | |
| Female | 572 | 47.9 | None | 41 | 3.4 |
| Unknown | 34 | 2.8 | ≤ 8 years of study | 399 | 33.4 |
| **Race/color** | | | > 8 years of study | 716 | 60.0 |
| White | 353 | 29.6 | Unknown | 38 | 3.2 |
| Black | 21 | 1.8 | **Duration of the pregnancy** | | |
| *Pardo* (multiracial) | 734 | 61.5 | ≤ 36 weeks | 512 | 42.9 |
| Unknown | 86 | 7.2 | ≥ 37 weeks | 654 | 54.8 |
| **Weight at birth** | | | Unknown | 28 | 2.3 |
| ≤ 2,499 | 582 | 48.7 | **Types of pregnancy** | | |
| ≥ 2,500 | 594 | 49.7 | Single | 1132 | 94.8 |
| Unknown | 18 | 1.5 | Multiple | 46 | 3.9 |
| **Place of occurrence** | | | Unknown | 16 | 1.3 |
| Hospital | 1172 | 98.2 | **Type of delivery** | | |
| Another health facility | 3 | 0.3 | Vaginal | 494 | 41.4 |
| Domicile | 18 | 1.5 | Cesarean | 681 | 57.0 |
| Others | 1 | 0.1 | Unknown | 19 | 1.6 |

**Source**: Ministry of Health/Secretariat of Health Surveillance/General Coordination Office for Epidemiological Analyses and Information – MS/SVS/CGIAE – Mortality Information System (SIM)

**Table 2. Main causes of infant deaths due to malformation according to the ICD 10 classification. Recife, PE, 2001 to 2016**

| ICD-10 category | No. | % |
|---|---|---|
| Anencephaly and similar malformations (Q00) | 79 | 6.6 |
| Congenital hydrocephalus (Q03) | 41 | 3.4 |
| Other congenital malformations of brain (Q04) | 32 | 2.7 |
| Congenital malformations of cardiac chambers and connections (Q20) | 33 | 2.8 |
| Congenital malformations of cardiac septa (Q21) | 54 | 4.5 |
| Other congenital malformations of heart (Q24) | 244 | 20.4 |
| Congenital malformations of great arteries (Q25) | 33 | 2.8 |
| Congenital malformations of lung (Q33) | 52 | 4.4 |
| Congenital malformations of esophagus (Q39) | 30 | 2.5 |
| Renal agenesis and other reduction defects of kidney (Q60) | 20 | 1.7 |
| Congenital malformations of musculoskeletal system, not elsewhere classified (Q79) | 101 | 8.5 |
| Other congenital malformations, not elsewhere classified (Q89) | 137 | 11.5 |
| Down Syndrome (Q90) | 78 | 6.5 |
| Trisomy 18 and Trisomy 13 (Q91) | 38 | 3.2 |

**Source**: MS/SVS/CGIAE – Mortality Information System (SIM)
**Note**: malformations with records smaller than 20 were removed

To identify the models, the Box-Jenkins method was used, based on their sample autocorrelation (ACF) and partial autocorrelation functions (PACF). The analysis of the estimates for autocorrelation and partial autocorrelation calculated up to *lag* 50 shows them inside the significance range equal to zero (Figure 1). Thus, there is evidence that the model to be adopted for the rate can be $Y_t = y + Z_t$.

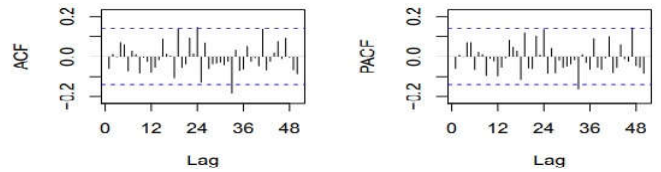


**Figure 1. Autocorrelation and partial autocorrelation charts for the rate variable**

Before making any estimates, a linear regression model was estimated to identify the seasonality. The model to be estimated is represented by $Y_t = M_i + s$, where $M_i$ represents the months. As no estimate showed significance, it is possible to conclude that the rate did not show seasonality in its months. To check whether the model was consistent, their residuals were analyzed. The residuals were analyzed through a histogram (Figure 2), and it was noted that there were good chances that the residuals were normal, as the histogram (Figure 2a) and the boxplot (Figure 2b) proved to be quite symmetrical and showed an average and median close to zero. To validate the normality of the residuals, the Shapiro-Wilk test was used, whose results were $W = 0.9887 \Rightarrow \hat{\alpha} = 0.1318$. As the descriptive level was not lower than the significance level, the null hypothesis for the normality of the residuals is not rejected.

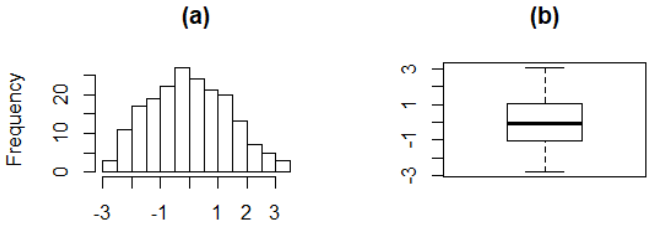


**Figure 2. (a) Histogram of the residuals; (b) Boxplot of the residuals**

By investigating the autocorrelations and partial autocorrelations, it was possible to note that most lags were in the significance range. (Figure 3) To confirm whether all ACFs were really statistically equal to zero, the Ljung-Box test was calculated for all lags. Figure 4 showed that the descriptive levels for all lags were higher than 0.1. However, this method must be applied to stationary series, i.e., series whose averages and variance do not depend on the time.

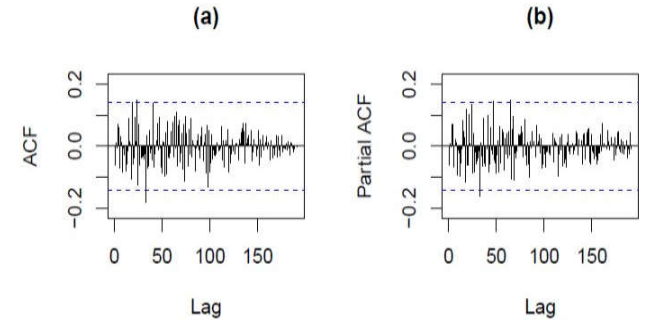


**Figure 3. (a) Autocorrelation of the residuals up to lag 191 (maximum lag); (b) Partial autocorrelation of the residuals up to lag 191 (maximum lag)**

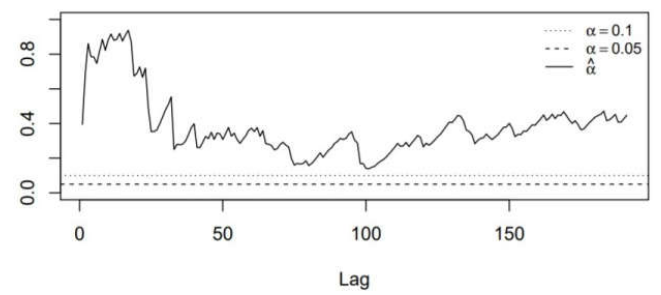


**Figure 4. Descriptive levels for the Ljung-Box tests in all lags**

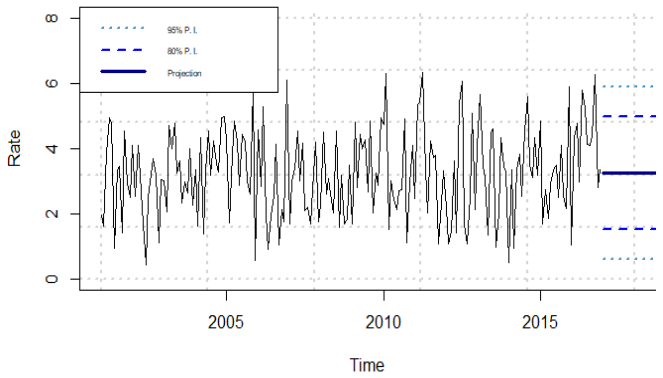


**Figure 5. Monthly mortality rate due to congenital malformation with adjustments Recife, PE, 2001 to 2006**

The infant mortality rate due to congenital malformations showed a stationary behavior. (Figure 5) For purposes of confirmation, the unit root test was used, resulting in $T = -2.15 < \tau_1 = -2.58$. The model adopted was a Gaussian white noise model, the model estimated for this indicator is only its own average over time, and $Y_t = 3.25$ (the average).

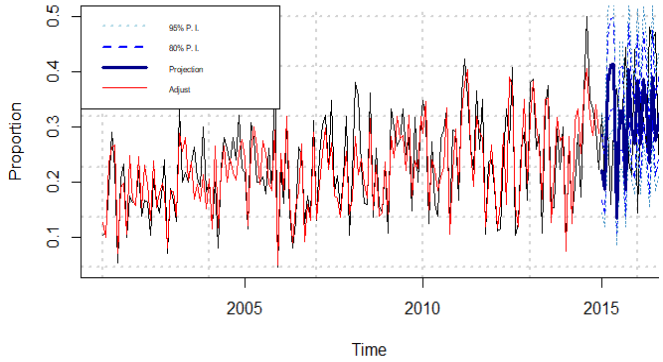


**Figure 6. Proportion with adjustments of infant mortality due to congenital malformation for every 1000 live births during the period from 2001 to 2016**

Regarding the proportion of deaths due to congenital malformation, no univariate model showed reasonable estimates, quite possibly due to the complexity of that indicator. The regressing variable informed a proportional growth for each month, i.e., if in a certain month there was a great number of deaths, then the proportion tends to be higher for the same month. It also showed a notable increasing trend. Therefore, a drift term was adopted to intercept that growth; the proportion showed slow growth, and it is possible to note a significant increase in the period from 2015 to 2016 (Figure 6).

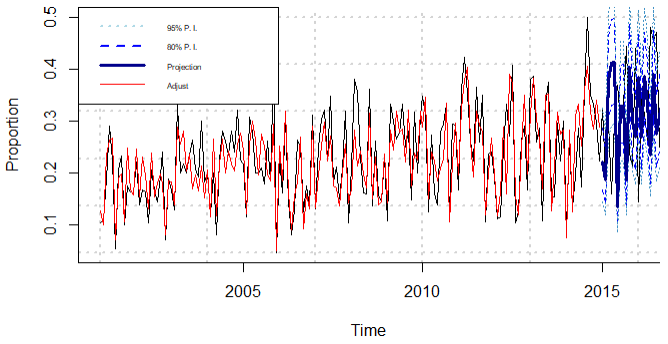


**Figure 6. Proportion with adjustments of infant mortality due to congenital malformation for every 1000live birthsduring the period from2001 to 2016**

The projections for the following 24 months expect a prediction interval, in which for 95% confidence, the average is between 0.6 and 5.9.

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| Down Syndrome (Q90) | 78 | 6.5 |
| Trisomy 18 and Trisomy 13 (Q91) | 38 | 3.2 |

Source: MS/SVS/CGIAE – Mortality Information System (SIM) Note: malformations with records smaller than 20 were removed

**Table 3. Forecast of the monthly mortality rates due to congenital malformation in Recife from January 2017 to December 2018**

| 2017 | | | | 2018 | | |
|---|---|---|---|---|---|---|
| Month | Forecast | Lower Limit (L.I.) 95%** | Upper Limit (L.S.) 95%** | Forecast | Lower Limit (L.I.) 95%** | Upper Limit (L.S.) 95%** |
| January | 0.242 | | | 0.411 | 0.195 | 0.408 |
| February | 0.202 | 0.159 | 0.350 | 0.291 | 0.292 | 0.541 |
| March | 0.402 | 0.131 | 0.299 | 0.413 | 0.196 | 0.410 |
| April | 0.446 | 0.285 | 0.532 | 0.360 | 0.294 | 0.543 |
| May | 0.452 | 0.323 | 0.575 | 0.254 | 0.250 | 0.487 |
| June | 0.148 | 0.328 | 0.582 | 0.416 | 0.168 | 0.365 |
| July | 0.352 | 0.093 | 0.227 | 0.296 | 0.297 | 0.546 |
| August | 0.353 | 0.243 | 0.479 | 0.332 | 0.199 | 0.415 |
| September | 0.202 | 0.244 | 0.479 | 0.365 | 0.228 | 0.457 |
| October | 0.432 | 0.130 | 0.300 | 0.334 | 0.254 | 0.493 |
| November | 0.324 | 0.310 | 0.562 | 0.157 | 0.229 | 0.459 |
| December | 0.290 | 0.221 | 0.448 | 0.336 | 0.099 | 0.239 |

# DISCUSSION

This study evidenced that most deaths occurred during the early neonatal period, in males, predominantly of *Pardo* race/color, and weight equal to or heavier than 2,500 g. The predominance was of children whose mothers of reproductive age between 20 and 34 years of age, with more than 8 years of study, in most cases, with gestational age equal to or greater than 37 weeks, with a single pregnancy and cesarean delivery. According to other studies, males face a higher risk for certain more lethal congenital defects, which can be an inferred justification for the slightly greater number of deaths. In the literature, the *Pardo* race in a population with a lower socioeconomic status shows the highest infant mortality rate (Fontoura and Cardoso, 2014; Rodrigues, 2014; Pal *et al*., 2015). Similar data identified that almost all deaths have occurred in a hospital environment, most conditions may be related to insufficient high-complexity assistance in the country (Bando *et al*., 2014; Kassar *et al*., 2013; Rodrigues, 2014). The mothers with more than eight years of education did not show a lower risk of death as compared to those with less education found in other researches (Bando *et al*.,

2014; Kassar *et al*., 2013). Regarding the categories of the malformations, the greatest frequency occurs in the Q24 classification (other congenital malformations of heart), which shows an inaccuracy in the diagnosis. According to other national and international studies with similar results considering the main cause of death indicated in this study, we understand that the survival of children with cardiovascular abnormalities depends on high-complexity assistance and surgical services that can save the patients' lives. Among the other malformations mentioned, the emphasis on those that affect the musculoskeletal system can be explained by the fact that such abnormalities are easier to perceive during the prenatal period or at the physical examination at birth (Lima *et al*., 2018).

The behavioural malformation mortality rate observed in this study was stationary. In an international study, the mortality rates due to congenital anomalies also remained fairly stable, similarly to the result provided in this study (Roncancio *et al*., 2017). In another international study, the infant mortality rate due to congenital abnormalities decreased, and a decreasing trend was identified, differently than the results provided in this study. (Navaneelan *et al*., 2016) The result identifies the proportional increase that occurs gradually in the behavior of mortality due to congenital malformation. During the period from 2015 to 2016, a significant increase was verified in the trend. Time-series studies carried out in Brazil showed an increase in the proportion of infant mortality due to congenital malformations, deformities, and chromosomal abnormalities, similarly to the results of the study. (Raia *et al*., 2017; Siedersberger Neto *et al*., 2012).

The fact that the results of the deaths due to malformation show this behavior may be associated with the inaccuracy in the diagnosis of the pathology; the earlier the diagnosis and implementation of proper assistance measures, the better the prognosis of the newborn will be. In this regard, the diagnosis of the malformation should be made during the prenatal period, as it allows advance planning of the measures to be adopted by the medical team immediately after delivery, which would greatly increase the survival of the affected newborns. Additionally, most deaths may be related to insufficient high-complexity assistance (Lima *et al*., 2017; Roncancio *et al*., 2017; Welander*et al*., 2015). Based on past data, a continuous increase in congenital malformations can be observed in several regions around the world. Forecasts made by this model may contribute to the implementation of prevention and assistance measures aimed at a reduction in the occurrence of such malformations. From this perspective, the use of time series and statistical techniques such as the ARMAX is useful to support health care actions to combat this event and may contribute to new epidemiologic studies.

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