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Case-control study on infant mortality in Southern Brazil

Estudo de caso-controle sobre mortalidade infantil em Caxias do Sul

ABSTRACT

OBJECTIVE: To identify risk factors associated with infant mortality and, more specifically, with neonatal mortality.

METHODS: A case-control study was carried out in the municipality of Caxias do Sul, Southern Brazil. Characteristics of prenatal care and causes of mortality were assessed for all live births in the 2001-2002 period with a completed live-birth certificate and whose mothers lived in the municipality. Cases were defined as all deaths within the first year of life. As controls, there were selected the two children born immediately after each case in the same hospital, who were of the same sex, and did not die within their first year of life. Multivariate analysis was performed using conditional logistic regression.

RESULTS: There was a reduction in infant mortality, the greatest reduction was observed in the post-neonatal period. The variables gestational age (<36 weeks), birth weight (<2,500 g), and 5-minute Apgar (<6) remained in the final model of the multivariate analysis, after adjustment.

CONCLUSIONS: Perinatal conditions comprise almost the totality of neonatal deaths, and the majority of deaths occur at delivery. The challenge for reducing infant mortality rate in the city is to reduce the mortality by perinatal conditions in the neonatal period.

KEYWORDS: Infant mortality. Neonatal mortality (public health). Prenatal care. Risk factors. Parturition. Epidemiology, descriptive.
CONCLUSÕES: As condições perinatais representam quase a totalidade das mortes neonatais, e a maioria das mortes ocorre no momento do nascimento. O principal desafio para redução da mortalidade infantil nesta cidade é a redução na mortalidade pelas condições perinatais que ocorrem no período neonatal.

INTRODUCTION

The decline in infant mortality seen in many developing countries is also evident in Brazil. According to estimates based on official birth and infant mortality records, in the last decades, there has been a general trend of decreasing infant mortality, despite a period of stagnation between 1984 and 1985. However, rates have decreased non-homogeneously in the different Brazilian geographical regions. The greatest reductions have been seen in the South, Southeast, and Mid-West regions. In the Southern state of Rio Grande do Sul, the infant mortality rate fell from 62.8 to 15.0 deaths per 1,000 live births between 1970 and 2000.

The overall decrease in infant mortality rate is a consequence of the reduction of mortality in its two components, neonatal and post-neonatal mortality. Neonatal mortality (zero to 28 days after delivery), and even perinatal mortality (week 22 of pregnancy to 7th day after delivery) reflect mostly the healthcare provided to mother and child during pregnancy and at delivery. On the other hand, post-neonatal mortality is related mostly to socioeconomic conditions, and, more generally, to quality of life. In areas with low infant mortality, the neonatal component accounts for the greatest proportion of deaths. In the last decades, the reduction of mortality in Southern Brazil has been attributed to the latter.

Some studies have evidenced the importance of socioeconomic factors in determining infant mortality. Other studies address healthcare during gestation and delivery, however, low birth weight is the strongest determinant of infant mortality, and is frequently associated with both neonatal and post-neonatal components.

A large share of the studies of infant mortality are based on secondary data, especially those collected by the Sistema de Informação de Nascidos Vivos - SINASC* (Brazilian Ministry of Health’s Information System on Live Births) and the Sistema de Informações sobre Mortalidade - SIM** (Information System on Mortality). Studies also are based on data from the Instituto Brasileiro de Geografia e Estatística - IBGE22 (Brazilian Institute of Geography and Statistics). Most of these studies are restricted to a descriptive analysis of the data, although analytical studies have been carried out based on these databases. The easy access to these secondary data, along with the wide coverage and good quality of information, have allowed for the development of simple low-cost studies for investigating factors associated with infant mortality.

METHODS

A case-control study was conducted in the municipality of Caxias do Sul, state of Rio Grande do Sul, Southern Brazil. The city’s population was 360,419 inhabitants in the year 2000. The study population included all live births in the years 2001 and 2002 with a completed live birth certificate and whose mothers lived in the municipality.

Three sources of information were used, according to each of the objectives specified in the study. In order to characterize prenatal and delivery care, the SINASC database was used; for profiling infant mortality in 2001 and 2002, the SIM database was used; and for investigating risk factors associated to...
Infant mortality, the expanded SINASC database and death certificates were used, both data obtained directly from the municipality’s epidemiological surveillance office.

Information on prenatal and delivery care and cause of death were descriptively evaluated, comparing the years 2001 and 2002. Cases were defined as all deaths of children living in the municipality which occurred during the first year of life, within the study period. In order to select cases, all of children’s death certificates were assessed. Through the mother’s full name in the death certificate, it was identified in the SINASC database babies born alive and who died within their first year of life. In the analysis of neonatal mortality, cases were restricted to deaths which occurred up to 28 days following delivery.

Controls were selected based on the identification of cases in the SINASC database. There were selected the two children born immediately after the case in the same hospital and who were of the same sex (paring criteria) and did not died within their first year of life. Twins were excluded from both cases and controls.

The sample included 118 cases and 236 controls.

The choice of risk factors was restricted to the variables recorded in the SINASC, namely mother’s schooling, marital status, mother’s age, deceased children, skin color, duration of pregnancy (weeks), prenatal care visits, route of delivery, 5-min Apgar, and birth weight.

Data were analyzed using Stata statistical package. The analysis was divided into two stages: (a) a descriptive analysis of the characteristics of prenatal and delivery care of all children born in 2001 and 2002; and (b) bivariate and multivariate analyses for identifying risk factors associated to infant and neonatal mortality, using conditional logistic regression.

The multivariate analysis was carried out according to the hierarchical model presented in the Figure. In this model, the distal determinants of infant mortality – socioeconomic and demographic variables – are placed in the highest level. The second level includes intermediate determinants such as reproductive history and care during pregnancy. Finally, the third level includes proximal determinants such as the characteristics of newborn and delivery. The same hierarchical model was tested in the study of neonatal mortality. The use of a hierarchical model allowed for controlling potential confounders. A variable was treated as a confounder when it was significantly associated (p≤0.10) with both the outcome and variables within its own level or in higher levels.

Studies using widely available secondary databases do not require approval by an ethics committee. In any case, all possible care was taken with respect to the anonymity and confidentiality of information in all stages of the study.

RESULTS

The data showed a predominance of neonatal over post-neonatal deaths although there was a greater reduction in the post-neonatal rate (13%) than in the neonatal rate (6%).

In Caxias do Sul, in 2001 and 2002, there were 155 deaths among infant children, 81 post-neonatal and 74 neonatal deaths, all included in the descriptive analysis. Twenty-three deaths were excluded from the study, six whose mothers did not live in the municipality (incorrectly registered), two of children living in Caxias do Sul but born in other cities, and 15 of twins (exclusion criterion). Of the 132 deaths eligible for the study, 14 (10%) were considered as losses due to incomplete newborn information.

Based on data obtained from SINASC, a number of indicators related to prenatal care and delivery were described. About 80% of pregnant mothers in both years were aged 20-39 years (Table 1). A comparison of the two years showed an increase in the percentage...
of women attending seven or more prenatal care visits, from 70.2% in 2001 to 79.7% in 2002. About 8% of pregnancies lasted up to 36 weeks and roughly half of the deliveries were by C-section.

In 2001, the three major causes of death (ICD-10) were the following: certain conditions originating in the perinatal period (58%); congenital malformations (14%); and diseases of the respiratory system (10%). In 2002, the three major causes were: certain conditions originating in the perinatal period (62%); congenital malformations (20.3%); and external causes of morbidity and mortality (5.4). In 2002 there was a reduction in the percentage of deaths due to diseases of the respiratory system (2.7%).

Table 2 presents the results of the paired bivariate analysis of infant mortality according to socioeconomic, demographic, reproductive, and care-related variables. There were no statistically significant differences in infant mortality in terms of mother’s schooling, mother’s age, number of living children, and number of deceased children. On the other hand, all variables related to delivery care showed significant differences with respect to infant mortality. Among controls, 93% were born after more than 37 weeks of pregnancy, whereas this proportion was 40% among cases. Cases had a threefold risk of having had less than seven prenatal care visits when compared to controls. Cases had a greater proportion of C-sections (58%) than controls (46%). Children delivered by C-section had an 80% greater chance of dying than those delivered vaginally, although the lower limit of the confidence interval for this ratio was very close to the unit.

In Table 2, it can be noted that 99% of controls had 5-min Apgar scores above 7, whereas this proportion was lower among controls (68%). The odds ratios for 5-min Apgar, as well as for gestational age and birth weight, were high and showed wide confidence intervals due to the sample size and mostly to the small number of exposed controls.

It was performed a paired bivariate analysis specific for neonatal mortality, i.e., considering only the 81 deaths occurring between 0 and 28 days after delivery. This analysis did not show statistically significant differences in terms of mother’s schooling, mother’s age, and number of deceased children between cases and controls (Table 3). However, there were statistically significant differences regarding number of prenatal care visits, gestational age, route of delivery, and birth weight. With the exception of 5-min Apgar, the factors associated with neonatal mortality were the same as those associated with infant mortality as a whole.

Children born after less than 37 weeks of pregnancy showed an almost 50-fold risk of neonatal death (Table 3). Cases of neonatal mortality were five times more likely to have had less than seven prenatal care visits than controls. As to mode of delivery, cases showed a greater proportion of delivery by C-section.
(65%) than controls (48%). Also in Table 4, 78% of cases were born weighing less than 2,500 g. Among controls, this proportion was only 8%. As to 5-min Apgar, 100% of controls scored more than six, making it not possible to calculate a measure of effect.

Multivariate analysis was performed using two independent models (Table 4), the first one with infant mortality (within first year of life) and the second one with neonatal mortality (until day 28 of life) as the outcome. In both models, it was not included the distal determinants (Figure 1), since these were not significantly associated (p ≤ 0.10) with each other or with any of the two outcomes in the bivariate analysis.

For infant mortality, the final model contemplated two levels. Level I considered the variables gestational age and number of prenatal care visits, but the latter lost its significance after adjustment. Level II (proximal) considered the variables route of delivery, birth weight, and 5-min Apgar. Route of delivery lost its statistical significance after adjustment. The adjusted odds obtained in the multivariate model were: gestational age (OR=36.61), birth weight (OR=23.64) and 5-min Apgar (OR=13.50).

For neonatal mortality, multivariate analysis showed a similar result as that obtained for infant mortality. The only difference in the model was 5-min Apgar, which was not included due to no exposed controls – 100% of controls scored above 6. Gestational age and birth weight in multivariate analysis were more strongly associated with neonatal mortality than with infant mortality.

**DISCUSSION**

The information and easy access to the databases available in Brazil have yielded a large body of descriptive studies of infant mortality.\(^6\),\(^15\),\(^18\),\(^22\) The analytical methodology usually applied in epidemiological studies to evaluate these databases, such as a case-control design, allowed for the simultaneous investigation of several risk factors for infant mortality in a relatively short time period and at low cost.

The disadvantage of using secondary databases is the lack of quality control and standardization in the procedures used for collecting this information. Compared to other parts of Brazil, or even to other regions within the state of Rio Grande do Sul, the coverage and quality of SINASC data are very good in the study municipality. According to a study\(^7\) conducted by the Brazilian Ministry of Health, the state of Rio Grande do Sul has 100% SINASC coverage. The use of this secondary database has the disadvantage of

| Variable                      | Cases (%) | Controls (%) | OR     | 95% CI      | p-value |
|-------------------------------|-----------|--------------|--------|-------------|---------|
| Mother's schooling (years)    |           |              |        |             |         |
| 12 or more                    | 10.3      | 8.9          | 1.0    |             | 0.52    |
| 4-11                          | 83.8      | 87.7         | 0.85   | 0.40-1.81   |         |
| 0-3                           | 6.0       | 3.4          | 1.57   | 0.41-5.96   |         |
| Marital status                |           |              |        |             |         |
| Married, with partner         | 49.2      | 56.4         | 1.0    |             | 0.40    |
| Single                        | 48.3      | 41.9         | 1.33   | 0.85-2.10   |         |
| Separated, widowed            | 2.5       | 1.7          | 1.74   | 0.38-7.97   |         |
| Mother's age (years)          |           |              |        |             |         |
| 10-19                         | 25.4      | 22.9         | 1.0    |             | 0.44    |
| 20-35                         | 64.4      | 70.3         | 0.84   | 0.49-1.43   |         |
| 36 or older                   | 10.2      | 6.8          | 1.36   | 0.54-3.42   |         |
| Skin color                    |           |              |        |             |         |
| White                         | 89.0      | 92.8         | 1.0    |             | 0.22    |
| Nonwhite                      | 11.0      | 7.2          | 1.64   | 0.75-3.62   |         |
| Deceased children             |           |              |        |             | <0.01   |
| No                            | 94.1      | 95.3         | 1.0    |             |         |
| Yes                           | 5.9       | 4.7          | 1.29   | 0.49-3.44   |         |
| Prenatal care visits          |           |              |        |             | 0.02    |
| 7 or more                     | 47.8      | 67.9         | 1.0    |             |         |
| Up to 6                       | 52.2      | 32.1         | 3.37   | 1.84-6.06   |         |
| Duration of pregnancy         |           |              |        |             | <0.01   |
| ≥37 weeks                     | 40.2      | 93.2         | 1.0    |             |         |
| <36 weeks                     | 59.8      | 6.8          | 40.57  | 12.7-129.17 |         |
| Route of delivery             |           |              |        |             | <0.01   |
| Vaginal                       | 42.4      | 54.2         | 1.0    |             |         |
| C-section                     | 57.6      | 45.8         | 1.81   | 1.10-2.99   |         |
| 5-min Apgar                   |           |              |        |             | 0.61    |
| ≥7                            | 67.8      | 99.2         | 1.0    |             |         |
| ≤6                            | 32.2      | 0.8          | 74.51  | 10.23-542.74|         |
| Birth weight                  |           |              |        |             | <0.01   |
| ≥2,500 g                      | 28.8      | 92.4         | 1.0    |             |         |
| <2,500 g                      | 71.2      | 7.6          | 73.06  | 17.95-297.4 |         |

Source: SINASC
limiting the investigation to the risk factors and categories available in the database. Concerning deaths, the state has the lowest percentage of infant deaths attributed to ill-defined causes countrywide, and the percentage of underreporting is also low. The Human Development Index (HDI) for Caxias do Sul is 0.857, which ranks the municipality in 6th and 16th in the state and in the country, respectively.

The 10% loss observed among cases is at the limit of the values obtained in most epidemiological studies. The ratio of two controls for each case ensured an adequate statistical power without compromising efficiency. The sample size allowed, with 80% power and 95% confidence level, to detect statistically significant differences between odds ratios of 2.5 and above. Moreover, selecting three controls per case would increase the time period between the birth of the case and the third control. The use of gender-paired con-

Table 3 - Neonatal mortality according to socioeconomic, demographic, reproductive, and care-related characteristics, using conditional logistic regression. Southern Brazil, 2001-2002.

| Variable                        | Cases (%) | Controls (%) | OR | 95% CI | p-value |
|--------------------------------|-----------|--------------|----|--------|---------|
| Mother’s schooling (years)      |           |              |    |        |         |
| 12 or more                      | 12.5      | 9.9          | 1.0| 0.73-1.19| 0.42    |
| 4-11                            | 80.0      | 86.3         | 0.75| 0.32-1.97|         |
| 0-3                             | 7.5       | 3.7          | 1.54| 0.36-6.68|         |
| Marital status                  |           |              |    |        |         |
| Married, with partner           | 51.9      | 58.6         | 1.0|         | 0.45    |
| Single                          | 44.4      | 39.2         | 0.72| 0.38-1.40|         |
| Separated, widowed              | 3.7       | 1.9          | 2.10| 0.45-11.83|         |
| Mother’s age (years)            |           |              |    |        |         |
| 10-19                           | 21.0      | 22.6         | 1.0|         | 0.79    |
| 20-35                           | 67.9      | 68.5         | 1.0| 0.87-1.27|         |
| 36 or older                     | 11.1      | 8.6          | 1.45| 0.49-4.28|         |
| Skin color                      |           |              |    |        |         |
| White                           | 88.9      | 92.6         | 1.0|         | 0.32    |
| Nonwhite                        | 11.1      | 7.4          | 1.61| 0.62-4.19|         |
| Deceased children               |           |              |    |        |         |
| No                              | 95.5      | 94.4         | 1.0|         | 0.82    |
| Yes                             | 4.5       | 5.6          | 0.88| 0.56-2.09|         |
| Prenatal care visits            |           |              |    |        | <0.00   |
| Up to 6                          | 49.4      | 73.9         | 1.0|         |         |
| Duration of pregnancy           |           |              |    |        | <0.00   |
| ≥37 weeks                       | 27.5      | 91.4         | 1.0|         |         |
| ≤36 weeks                       | 72.5      | 6.6          | 4.95| 2.22-11.03|         |
| Route of delivery               |           |              |    |        | <0.00   |
| Vaginal                         | 34.6      | 52.5         | 1.0|         |         |
| C-section                       | 56.4      | 47.5         | 0.77| 1.41-5.44|         |
| 5-min Apgar                     |           |              |    |        |         |
| ≥7                              | 61.7      | 102          | 1.0|         |         |
| ≤6                              | 38.3      | 0            | -  |         |         |
| Birth weight                    |           |              |    |        | <0.00   |
| ≥2,500 g                        | 22.2      | 92.0         | 1.0|         |         |
| <2,500 g                        | 77.8      | 8.0          | 1.0| 110.05-152.87|         |

Source: SINASC

Table 4 - Multivariate analysis for neonatal and infant mortality using conditional logistic regression. Southern Brazil, 2001-2002.

| Variable                        | Neonatal mortality | Infant mortality | p-value | p-value |
|--------------------------------|--------------------|------------------|---------|---------|
| Level I                         | ORadj 95% CI       | ORadj 95% CI     |         |         |
| Prenatal care visits*           | 0.533              | 0.582            |         |         |
| Gestational age*                |<0.00               |<0.00             |         |         |
| ≥37 weeks                       | 43.9               | 10.26-183.97     |         |         |
| ≤36 weeks                       | 36.1               | 11.25-119.17     |         |         |
| Level II                        | Route of delivery**| 0.16             | 0.62    |         |
| Vaginal                         | 2.36               | 0.70-7.61        |         |         |
| C-section                       |<0.00               |<0.00             |         |         |
| Birth weight**                  | 34.6               | 3.84-311.50      |         |         |
| ≥2,500 g                        | 23.6               | 5.14-108.66      |         |         |
| ≤6                              | 13.50              | 1.69-107.80      |         |         |

*Adjusted for the variables in the same level
**Adjusted for the variables in the same level and for those in Level I
Results in bold type correspond to the final model for each of the outcomes.
tors is due to the greater mortality observed among males during the first year of life. Twins were not included in the sample due to the high prevalence of low birth weight and preterm birth in this population. Twins are excluded from the majority of studies of risk factors for infant mortality for that reason.\(^{15}\)

The percentage of women who attended more than seven prenatal care visits (79%) and the percentage of children born with adequate weight (89%) and with 37 or more weeks of pregnancy (90%) were noteworthy. However, the study results indicate a high percentage of C-section deliveries (58%), which is higher than those found in most studies.\(^{4,16}\) That value was similar to that reported by Olinto et al. (2003) for a municipality in the metropolitan area of Porto Alegre, state of Rio Grande do Sul. All the values found in recent studies are above the 20% of deliveries by C-section recommended by the Brazilian Ministry of Health.

As to the causes of death among infants, it was observed a predominance of perinatal conditions and congenital malformations. The study results confirm the trend in developing countries of infant mortality lower than 10 per 1,000 live births, where the main cause of death among infants is congenital malformations.\(^{17}\)

According to the hierarchical model of this case-control study, the distal determinants (socioeconomic and demographic variables) showed no significant differences. In contrast, other studies have indicated an association between socioeconomic and demographic variables and infant mortality.\(^{8,13}\) The explanation for the study findings probably has to do with the low number of post-neonatal deaths, which are more directly related to socioeconomic characteristics or, more generally, to quality of life. The present study also shows that schooling did not discriminate between socioeconomic categories, given that 86% of the sample had between four and 11 years of schooling.

There was found a consistency between the study findings and those in the literature with respect to proximal determinants. Confounder control, carried out using multivariate analysis, reinforces the validity of the study findings.\(^3\) Proximal variables related to prenatal and delivery care showed statistically significant differences. After analysis, gestational age, birth weight, and 5-min Apgar were maintained in both infant mortality and neonatal mortality models. The 5-min Apgar was excluded from the multivariate model of neonatal mortality since 100% of controls scored above 6.

Low-birth weight and preterm birth are the risk factors described in the literature that show the strongest association with infant mortality.\(^{15}\) Preterm and low-birth weight children show a significantly higher risk of mortality than those born after week 37 and weighing 2,500 g or more.\(^{11}\) Birth weight reflects the quality of care provided to the mother, her nutritional status prior to and during pregnancy, and the effect of risk factors to which the mother is exposed. Thus allows for identifying risk areas and situations and for targeting specific health and nutrition programs and policies.\(^1\)

There is little information available on the evolution of birth weight in Brazil. There are no time series that allow going back in time in order to compare and understand the current figures.\(^{12}\) In Caxias do Sul, the prevalence of low-birth weight was 11.3%. In São Paulo, it was 8% in the same period. Comparisons among developed countries are easier due to the availability of this statistical datum. Studies from some of these countries report the following prevalences: Norway, Finland, and Spain 4%; Sweden, France, Italy, and Portugal 5%; Denmark, and Canada 6%, and United States 7%.\(^{14}\) Recent Brazilian studies on the distribution of birth weight conducted in the city of Pelotas, Southern Brazil, (all live births in 1993) and in Ribeirão Preto, Southeastern Brazil, (a probabilistic sample of live births in 1994) report prevalences of low-birth weight of 9.8% and 10.6%, respectively.\(^{10,20}\)

Low-birth weight is related mostly to biological and nutritional problems and to preterm birth, which, in turn, are associated with maternal events, either chronic or acute, during pregnancy.\(^6\) One of the potential causes for preterm delivery is the interruption of pregnancy before term, which may occur by medical actions, including C-section and induction of delivery, or due to maternal infections that trigger preterm labor.\(^3\) This is supported by the high percentage of C-sections in Caxias do Sul (58%).

Regarding 5-min Apgar, several studies indicate shortcomings in this indicator record. In a study by Costa et al\(^3\) (2002), 68.2% of records did not include this information, impairing the statistical data analysis. In the present study, there were no losses regarding this information. This indicator is directly related to the quality of care at delivery. Poor care during delivery, resulting in fetal distress, may lead to low Apgar scores, even if the baby is born at term and with adequate weight.\(^4\) The 5-min Apgar score was included given this is an indicator that informs on the newborn prognosis and showed significant association with infant mortality in the final model. Although this variable was not entered in the final logistic
model for neonatal mortality, its importance should be pointed out.

According to a study by D’Orsi & Carvalho (1998), at the individual level, low-birth weight is an adequate predictor of infant risk. For identifying regions or population groups, especially when the greatest differential is access to health care, though somewhat underrated, the Apgar score seems to be more useful, hence the importance of recording this indicator.

The greatest challenge for reducing the infant mortality rate is the reduction of the mortality by perinatal conditions in the neonatal period. Excluding congenital abnormalities, perinatal conditions comprise almost the totality of neonatal deaths, and the majority of deaths occur at delivery. Such a reduction is feasible by means of an adequate monitoring of women during the gestational period, whereby risk factors may be identified and minimized, and by the qualification of delivery care.

Therefore, improved prenatal care may promote immediate results in terms of a reduction in the prevalence of low-birth weight and/or preterm delivery, and qualified delivery care will allow for interventions by the health care team, thus reducing the high number of children that die due to perinatal conditions.

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