Early and late neonatal mortality: preventable causes and trends in Brazilian regions

Mortalidade neonatal precoce e tardia: causas evitáveis e tendências nas regiões brasileiras

Mortalidad neonatal temprana y tardía: causas evitables y tendencias en las regiones brasileñas

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Abstract

Objective: To analyze the main causes and trends in preventable early and late neonatal mortality according to Brazilian regions.

Methods: This is an ecological time series study carried out with records of neonatal deaths from 2000 to 2018 through the Mortality Information System. To classify the avoidable causes, the Unified Health System List of Preventable Causes of Death by Interventions (*Lista de Causas de Mortes Evitáveis por Intervenções do Sistema Único de Saúde*) was used. From mortality rates of early and late neonatal components, joinpoint regressions of the main causes were performed using the Annual Percentage Change and Average Annual Percentage Change.

Results: The highest avoidable mortality rates were found in the early neonatal phase. The South had the lowest avoidable mortality rates. The main causes according to groups on the list were tetanus of newborns, respiratory distress syndrome, birth asphyxia, bacterial septicemia, pneumonia and sudden death syndrome. The reduction in early neonatal mortality was higher from 2000 to 2004 (4.19% per year, p<0.001) and lower between 2012 and 2018 (1.80% per year, p<0.001). Considering late neonatal mortality, there was an average annual reduction of 2.02% (p<0.001). The Northeast had more than one turning point in the trend of mortality due to respiratory distress and asphyxia at birth and stability due to septicemia. In the South, a downward trend was identified for all the preventable causes studied.

Conclusion: There was a lower reduction in early neonatal mortality and inequalities in the trend of preventable neonatal mortality according to causes and regions of residence.

Resumo

Objetivo: Analisar as principais causas e a tendência da mortalidade neonatal precoce e tardia evitável segundo as regiões brasileiras.

Métodos: Estudo de séries temporais do tipo ecológico realizado com registros dos óbitos neonatais no período de 2000 a 2018 por meio do Sistema de Informação sobre Mortalidade. Para classificação das causas evitáveis utilizou-se a *Lista de Causas de Mortes Evitáveis por Intervenções do Sistema Único de Sa*úde. A partir das taxas de mortalidade dos componentes neonatal precoce e tardio foram realizadas regressões por *joinpoint*s das principais causas com indicação da variação percentual anual e variação percentual anual média.

Resultados: As maiores taxas de mortalidade evitável foram encontradas na fase neonatal precoce. A região Sul apresentou as menores taxas de mortalidade evitável. As principais causas segundo grupos da lista foram tétano do recém-nascido, síndrome da angústia respiratória, asfixia ao nascer, septicemia bacteriana,

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Conflicts of interest: nothing to declare.

pneumonia e síndrome da morte súbita. A redução na mortalidade neonatal precoce foi maior de 2000 a 2004 (4,19% ao ano, *p*<0,001) e menor, entre os anos de 2012 e 2018 (1,80% ao ano, *p*<0,001). Considerando a mortalidade neonatal tardia houve redução anual média de 2,02% (*p*<0,001). A região Nordeste apresentou mais de um ponto de inflexão na tendência da mortalidade por desconforto respiratório e asfixia ao nascer e estabilidade por septicemia. Na região Sul foi identificado tendência de redução para todas as causas evitáveis estudadas.

Conclusão: Houve menor redução na mortalidade neonatal precoce e desigualdades na tendência da mortalidade neonatal evitável segundo causas e regiões de residência.

Resumen

Objetivo: Analizar las principales causas y la tendencia de la mortalidad neonatal temprana y tardía evitable según las regiones brasileñas.

Métodos: Estudio de series temporales del tipo ecológico, realizado con registros de las defunciones neonatales en el período de 2000 a 2018, por medio del Sistema de Información sobre Mortalidad. Para la clasificación de las causas evitables, se utilizó la *Lista de causas de muertes evitables por intervenciones del Sistema Único de Salud*. A partir de las tasas de mortalidad de los componentes neonatal temprano y tardío, se realizaron regresiones joinpoints de las principales causas con indicación de la variación porcentual anual y variación porcentual anual promedio.

Resultados: Las mayores tasas de mortalidad evitable se encontraron en la fase neonatal temprana. La región Sur presentó las menores tasas de mortalidad evitable. Las principales causas, según los grupos de la lista, fueron: tétanos neonatal, síndrome de dificultad respiratoria, asfixia al nacer, septicemia bacteriana, neumonía y síndrome de la muerte súbita. La reducción de la mortalidad neonatal temprana fue mayor del año 2000 al 2004 (4,19 % al año, *p*<0,001) y menor entre los años 2012 y 2018 (1,80 % al año, *p*<0,001). Considerando la mortalidad neonatal tardía, hubo una reducción anual promedio del 2,02 % (*p*<0,001). La región Nordeste presentó más de un punto de inflexión en la tendencia de la mortalidad por malestar respiratorio y asfixia al nacer y estabilidad por septicemia. En la región Sur se identificó una tendencia de reducción de todas las causas evitables estudiadas.

Conclusión: Hubo menor reducción de la mortalidad neonatal temprana y desigualdades en la tendencia de la mortalidad neonatal evitable según las causas y la región de residencia.

Introduction

Progress in the access and quality of health services as well as in the population's education and income conditions has contributed to reducing infant mortality in Brazil and in the world.[1,2] However, neonatal mortality remains at high rates, especially in its early phase, which is between birth and the sixth day of life.[3]

To combat this problem, international and national programs were implemented with the aim of organizing and qualifying care services during pregnancy and childbirth with an emphasis on risk situations.[4] Although they started decades ago, they still have weaknesses in terms of reducing neonatal mortality.[4-6] In this regard, the United Nations (UN) Sustainable Development Goals (SDGs) recommend actions to reduce child mortality, in particular to eradicate neonatal mortality from preventable causes by 2030.[7]

Deaths from preventable causes are those that can be reduced by actions available in the health system and reflect on the situation of access and quality of health services available to society, indicated in the Unified Health System List of Preventable Causes of Death by Interventions (*Lista de Causas de Mortes Evitáveis por Intervenções do Sistema Único de Saúde*).[8-10] Most preventable neonatal mortality is a consequence of the lack of adequate attention during prenatal care, childbirth and newborn care,[11] with differences in relation to the regions of residence.[12]

Even with evidence that there was a reduction in neonatal mortality in Brazilian cities and states,[13,14] studies that analyze the causes of death in the early and late neonatal periods separately were not identified in indexed databases. Identifying the main preventable causes in each neonatal phase can contribute to creating protocols and lines of care aimed at combating and assertively managing these causes, impacting their reduction, as suggested by the UN.

Given the priority of combating the causes of preventable deaths in the neonatal period, this study was proposed. Thus, the objective was to analyze the trend of early and late neonatal avoidable mortality and the main causes according to Brazilian regions.

Methods

This is an ecological-type annual time series study on neonatal mortality in the regions of Brazil according to the neonatal phase and preventable causes from 2000 to 2018. The country covers 5,570 municipalities in 27 federative units, 26 states and the Federal District, grouped into five regions:

North, Northeast, South, Southeast and Midwest (IBGE, 2019a). In Brazil, the Unified Health System (SUS - *Sistema Único de Saúde*) is organized to meet the population's health needs at all levels of care, based on the principles of comprehensiveness, equity and universality. Prenatal and postpartum consultations, home visits and monitoring of child growth and development are Primary Health Care (PHC) actions available to the maternal and child population.

From 2000 to 2018, there were 591,097 neonatal deaths in Brazil, with the study population consisting of infants (0-27 days) distributed according to the neonatal phase in which the deaths occurred, early (0-6 days) or late (7-27 days).

Data were extracted from the Mortality Information System (SIM - *Sistema de Informação sobre Mortalidade*) and the Live Births Information System (SINASC - *Sistema de Informação sobre Nascidos Vivos*), using the SUS Department of Informatics' official tabulator, TABWIN. The worksheets are available according to the year of death and birth. Data from 2000 to 2018 from all Brazilian states and the Federal District were selected. To identify the preventable conditions, the Unified Health System List of Preventable Causes of Death by Interventions for children under five years of age was used.[10] After coding the causes of death, deaths from preventable causes were selected.

The analysis was performed based on the absolute and relative frequencies of the variables. Then, mortality rates per 1,000 live births (LB) were calculated according to early (0-6 days) and late (7-27 days) neonatal phase; region of maternal residence: North, Northeast, Southeast, South, Midwest; and group of causes reducible by: immunoprevention actions, care for women during pregnancy, childbirth, fetuses and newborns, diagnosis and treatment, and adequate health promotion actions, linked to health care actions.

For the main cause of the three most frequent groups, segmented regression models were built using the Joinpoint Regression Analysis program. The program performs segmented linear analysis, through value logarithmic transformation, verifying that a line with multiple segments is significantly better than a straight line or one with fewer segments. [15]

Each joinpoint means an turning point on the line, where zero joinpoint represents a linear line, one joinpoint represents two line segments, and two joinpoints represent three line segments.[15] The software calculated Average Annual Percentage Change (APPC) considering the entire period, and the Annual Percentage Change (APC), in the case of lines with one or more turning points. For cases with a straight line (no segments), AAPC is equal to APC. The trend was considered increasing for positive AAPC and APC, and decreasing for negative values. For both the AAPC and APC analysis, a statistical significance level of less than 0.05 was considered.

The year of occurrence was defined as an independent variable and the number of deaths according to cause of death and neonatal period as independent variables. LB were indicated as population and the rate per thousand inhabitants was considered. The study considered Resolution 510 of 2016 of the Brazilian National Health Council (CNS). Because it is the analysis of secondary data, from public consultation, without information that identifies the participants, it was exempted from analysis by the Research Ethics Committee, under Opinion 4,132,446 and CAAE (*Certificado de Apresentação para Apreciação Ética* - Certificate of Presentation for Ethical Consideration) 34084620.7.0000.0106.

Results

In Brazil, from 2000 to 2018, 453,411 infants from zero to six days old (76.71%) and 137,686 infants from seven to 27 days old (23.29%) died, considering all causes. Most deaths in the early neonatal and late neonatal phases occurred due to preventable causes, with respective proportions of 76.85% and 73.18% and a rate of 6.17 and 1.79 per thousand LB. The South had the lowest avoidable early neonatal mortality rates among the regions (4.84 per thousand LB) and late neonatal mortality (1.56 per thousand LB). On the other hand, the Northeast had the highest preventable early neonatal mortality

rate (7.58 per thousand LB), and the North had the highest rate in the late neonatal phase (1.91 per thousand LB). The predominant causes of preventable deaths in the early neonatal phase were from the groups reducible by actions during pregnancy, delivery and care of newborns. The groups of causes reducible by immunoprevention actions, adequate treatment and health promotion actions were more frequent in the late neonatal phase (Table 1).

Table 1. Distribution of early and late neonatal deaths according to the group of preventable causes through SUS interventions

Group of preventable causes	Early n(%)	Late n(%)
Immunoprevention actions	74(0.02)	162(0.16)
Care for women during pregnancy	166269(47.71)	31505(31.26)
Care during childbirth	73684(21.14)	10098(10.02)
Care for the fetus and newborn	104515(29.99)	52539(52.14)
Diagnosis and treatment actions	1275(0.37)	3261(3.24)
Health promotion actions	2657(0.76)	3205(3.18)

The main causes of preventable deaths, according to each group, were neonatal tetanus, respiratory distress syndrome, birth asphyxia, bacterial septicemia, pneumonia and sudden death syndrome. The five main causes of the groups were responsible for 57.44% to 91.15% of the total of each group (Table 2).

There was a downward trend in early and late neonatal mortality rates in Brazil. The early neonatal component showed a reduction of 4.19% (APC) per year from 2000 to 2004 ($p<0.001$), 3.13% (APC) per year from 2004 to 2012 ($p<0.001$) and 1.80% (APC) per year between 2012 and 2018 ($p<0.001$). Considering the period from 2000 to 2018, reduction was 2.93% (AAPC) per year ($p<0.001$). Late neonatal mortality showed a reduction of 2.02% (AAPC) per year ($p<0.001$), considering all years of the study. The reduction pattern in death rates due to respiratory distress syndrome was common in the South, Southeast, Midwest and North, as they showed a linear reduction. In Brazil, there was a reduction, but with 2 turning points, demonstrating different rates of decline during the study period. There was stability in deaths from neonatal asphyxia from 2000 to 2004 in the Northeast ($p=0.191$) and in Brazil ($p=0.252$). With the exception of

Table 2. Distribution of preventable neonatal deaths according to main causes preventable by SUS interventions

Group/ preventable causes of death	Early n(%)	Late n(%)	Total n(%)
Reduced by immunoprevention actions			
Neonatal tetanus	25(33.78)	72(44.44)	97(41.1)
Congenital viral diseases	35(47.3)	41(25.31)	76(32.2)
Whooping cough	0(0)	41(25.31)	41(17.37)
Diphtheria	9(12.16)	5(3.09)	14(5.93)
Bacterial meningitis	5(6.76)	1(0.62)	6(2.54)
Total group	74(100)	160(98.77)	234(99.15)
Reducible by adequate care during pregnancy			
Respiratory distress syndrome	58358(35.1)	8554(27.15)	66912(33.83)
Related to short gestation or low birth weight	45651(27.46)	1988(6.31)	47639(24.09)
Maternal conditions not mandatory for pregnancy	20703(12.45)	6111(19.4)	26814(13.56)
Maternal complications during pregnancy	19758(11.88)	3702(11.75)	23460(11.86)
Complications of the placenta, umbilical cord and membranes	7614(4.58)	1293(4.1)	8907(4.5)
Total group	152084(91.47)	21648(68.71)	173732(87.84)
Reducible by adequate care during childbirth			
Asphyxia at birth	24981(33.9)	3935(38.97)	28916(34.51)
Neonatal aspiration syndrome	15369(20.86)	2942(29.13)	18311(21.86)
Intrauterine hypoxia	13503(18.33)	936(9.27)	14439(17.23)
Complications of the placenta, umbilical cord and membranes	12624(17.13)	1328(13.15)	13952(16.65)
Complications of labor	5900(8.01)	739(7.32)	6639(7.92)
Total group	72377(98.23)	9880(97.84)	82257(98.17)
Reduced by adequate newborn care			
Bacterial septicemia of newborns	33392(31.95)	31136(59.26)	64528(41.09)
Respiratory conditions in the perinatal period	32464(31.06)	3505(6.67)	35969(22.9)
Specific infections of the perinatal period	7962(7.62)	3392(6.46)	11354(7.23)
Congenital pneumonia	5592(5.35)	3812(7.26)	9404(5.99)
Other conditions originating in the perinatal period	6463(6.18)	1075(2.05)	7538(4.8)
Total group	85873(82.16)	42920(81.7)	128793(82.01)
Reducible by proper diagnosis and treatment			
Unspecified pneumonia	275(21.57)	1816(55.69)	2091(46.1)
Down syndrome	585(45.88)	378(11.59)	963(21.23)
Bacterial meningitis	72(5.65)	247(7.57)	319(7.03)
Meningitis from other causes	58(4.55)	234(7.18)	292(6.44)
Other septicemias	113(8.86)	144(4.42)	257(5.67)
Total group	1103(86.51)	2819(86.45)	3922(86.46)
Reduced by health promotion actions			
Sudden childhood death syndrome	700(26.35)	436(13.6)	1136(19.38)
Diarrhea and gastroenteritis	184(6.93)	852(26.58)	1036(17.67)
Inhalation of gastric contents	125(4.7)	308(9.61)	433(7.39)
Assault by unspecified means	371(13.96)	15(0.56)	386(6.58)
Unspecified facts or events and undetermined intent	238(8.96)	138(4.31)	376(6.41)
Total	1618(60.9)	1749(54.66)	3367(57.43)

Table 3. Trend in preventable neonatal mortality rates according to main causes and regions of residence

Cause/ region	♯APC1	p-value	TPY*	♯APC2	p-value	TPY*	♯APC3	p-value	◊AAPC	p-value
Respiratory distress syndrome										
South	-7.58	<0.001							-7.58	<0.001
Southeast	-6.46	<0.001							-6.46	<0.001
Midwest	-7.64	<0.001							-7.64	<0.001
Northeast	3.72	0.411	2002	-8.56	<0.001	2008	-5.82	<0.001	-5.74	<0.001
North	-4.02	<0.001							-4.02	<0.001
Brazil	-2.53	0.017	2003	-9.65	<0.001	2006	-5.89	<0.001	-5.98	<0.001
Asphyxia at birth										
South	-5.26	<0.001							-5.25	<0.001
Southeast	-5.47	<0.001							-5.47	<0.001
Midwest	-6.66	<0.001							-6.66	<0.001
Northeast	1.98	0.191	2004	-4.19	0.002	2010	-6.76	<0.001	-4.02	<0.001
North	-5.71	<0.001							-5.71	<0.001
Brazil	-1.35	0.252	2004	-5.83	<0.001				-4.85	<0.001
Septicemia										
South	-2.85	<0.001							-2.85	<0.001
Southeast	3.07	0.149	2004	-3.94	<0.001				-2.42	<0.001
Midwest	4.25	0.196	2004	-3.64	<0.001				-1.94	0.012
Northeast	2.25	0.235	2005	-2.03	<0.001				-0.86	0.146
North	-0.47	0.726	2006	-4.53	<0.001				-3.2	<0.001
Brazil	1.68	0.088	2005	-3.48	<0.001				-2.07	<0.001

♯APC - Annual Percentage Change; ♯APC1- First turning point; ♯APC2 - Second turning point; ♯APC3 - Third turning point; *TPY - Year of turning point; ◊AAPC - Average Annual Percentage Change

the South, deaths from septicemia remained stable in the regions from 2000 to 2004 and 2006. The Northeast showed points of oscillations in the reduction of mortality rates due to respiratory distress and asphyxia at birth, although the reduction is significant, and stability in deaths from septicemia (p=0.146) (Table 3).

Discussion

The main results lead to the conclusion that most neonatal deaths in Brazil occurred in the early neonatal phase and due to preventable causes through SUS interventions.

Although there was a reduction in early and late neonatal mortality in Brazil over the 19 years of study, there was a higher drop in early preventable neonatal mortality rates at the beginning of the period, with a subsequent deceleration in the following years. Differences were also found in neonatal mortality trends according to preventable causes.

Neonatal deaths continue to be a major public health challenge worldwide and are responsible for the majority of deaths that occur among children under five years of age.[2,16] In this context, the early neonatal phase is considered the most vulnerable and frequent[13,17] and has tended to increase in some countries.[18]

The South had the lowest avoidable mortality rates per thousand LB, both for the early and late phases. In the North, the highest avoidable late neonatal mortality rate was observed. The Northeast was the region with the highest rate of preventable early neonatal mortality. The Ministry of Health announced an increase in early and late neonatal mortality in several regions of Brazil, except the South, the only one that presented a decrease in both components.[5] Differences in relation to economic development, financial incentives, job offer, level of education and expansion of the health care network are aspects that influence these indicators.[8,9,19] A study carried out in Brazil identified that there was a reduction in neonatal mortality in all Brazilian regions, as well as in most states, except Amazonas, Roraima, Distrito Federal, Goiás, Sergipe and Maranhão, where there was stability in deaths.[20]

Regarding deaths, the groups of causes reducible by care during pregnancy, childbirth and care for newborns were prevalent both in the early and late phases. The literature indicates that these causes were prevalent in a state in midwestern Brazil.[17]

Even in places with other cultures, similar causes of neonatal deaths were identified, as in China, where the main causes were complications of premature birth (33.6%), congenital anomalies (21.3%), infections (12.6%) and asphyxia at birth (9.1%),[18] conditions that suit the groups on the Brazilian list and are close to the results found.

The higher the organization and quality of care since pregnancy, the better the neonatal outcomes found.[21] Prenatal care has wide coverage in Brazil;[22] however, the quality of this care needs to be analyzed.[11] Close fetal monitoring is essential to prevent fetal or newborn death, especially in high-risk pregnancies.[23] It was recently shown that only 13% of pregnant women received adequate care for the advanced level of prenatal care, which considers the number of consultations, initiation of prenatal care, procedures performed during prenatal care and laboratory tests.[24] Other findings indicate that adequate prenatal care prevailed among white women and that women residing in the North had the lowest frequencies of adequate prenatal care, while in the Southeast, the highest,[25] corroborating with regional inequalities observed in the present study.

Regarding childbirth, an assessment of the birth process indicated the weakness of health systems in different Brazilian regions, especially in relation to the provision of early care for the poorest population.[26] In several studies, it was found that factors such as excessive interventions during childbirth, lack of a companion, commuting between maternity hospitals are some of the factors that can influence this cause.[3,4]

Respiratory distress syndrome, asphyxia and septicemia were the most frequent causes in the groups of causes reducible by adequate care during pregnancy, childbirth and newborn care. They deal with problems linked to prematurity with implications for longer hospital stays and rigorous treatments.[27] Specialized care is expected to prevent these conditions and is closely linked to neonatal survival [28-30] and should prioritize accessibility and quality of care for newborns.[16]

From 2000 to 2018, there was a reduction in neonatal deaths due to respiratory distress, neonatal asphyxia and septicemia in the regions of Brazil, except the Northeast, which showed stability in the analysis of deaths due to septicemia. In the Northeast, stability was also observed due to asphyxia from 2000 to 2004 and fluctuations in mortality rates due to respiratory distress and asphyxia at birth, contrary to the linear trend of reduction in other regions.

The causes reducible by immunoprevention and health promotion actions were more frequent in the late neonatal phase. The present study identified a significant number of deaths due to sudden death syndrome and neonatal tetanus, conditions mainly related to PHC's work through vaccination actions and postpartum guidance at home.

To meet neonatal health's needs, PHC and hospital services must include directive actions for the causes of preventable mortality. There is a need for intensive interpersonal interventions with counseling focused on the reality of each family and community where the family is inserted.[31,32] Knowledge about newborn care is critical to their safety, but it can be a challenge for healthcare systems around the world. It was found in a survey in Nepal that 48.7% of mothers did not have adequate knowledge about infant care, with the mother's age and education, number of prenatal consultations and proximity to the health unit factors that impacted on maternal knowledge.[16]

Pneumonia accounted for 46.10% of deaths in the group of causes reducible by proper diagnosis and treatment. Even though it is not frequent in neonatal mortality, it is one of the main causes of post-neonatal morbidity and mortality. Neonatal care services should consider its occurrence when risk factors are present, such as prematurity, hospitalization, low weight, family economic situation and access to health services.[33]

On the other hand, complications resulting from Down syndrome had a prevalence of 21.23% within their group. Complications resulting from the syndrome are well documented in the literature, such as persistent pulmonary hypertension in newborns, atrioventricular septal defect and pulmonary hypertension, with a prevalence of 55% in patients and a mortality rate of 23%.[34] When identifying the development of a fetus with the syndrome, the team must be prepared to act in the main complications, avoiding death after birth.

As limitations of this study, it is noteworthy that the study analyzes secondary data where the typing of deaths and births is performed in a decentralized way, with possible mistyping. However, the results of epidemiological studies that use SIM and SINASC portray the profile of mortality and birth in Brazil and the large number of records contribute to minimize their possible failures. In several locations, secondary data sources have been used to study preventable deaths.[9,11]

Conclusion

A trend towards a reduction in early and late neonatal avoidable mortality was identified. Common causes of preventable neonatal mortality were respiratory distress syndrome, birth asphyxia, and septicemia that showed a downward trend in the Brazilian regions, although some with periods of stability, with the exception of septicemia in the Northeast, which showed stability throughout the study period. Health teams must be qualified to assist infants in the main causes of death to promote their prevention. These are frequent causes and, regardless of the region of residence, infants need prenatal care, delivery care, postnatal care and resolving immunizations through solid policies and assistance from qualified professionals.

Collaborations

Prezotto KH, Bortolato-Major C, Moreira RC, Oliveira RR, Melo EC, Silva FRT, Abreu IS and Fernandes CAM declare that they contributed to the study design, data analysis and interpretation, article writing, relevant critical review of the intellectual content and approval of the final version to be published.

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