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EPIDEMIOLOGICAL OVERVIEW OF DEATHS FROM BACTERIAL SEPTICEMIA IN NEWBORNS AND THEIR RISK FACTORS IN THE NORTHERN REGION

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ABSTRACT

Bacterial neonatal sepsis is an important cause of preventable and neglected death in Brazil, especially in the North Region. The study aims to describe the number of deaths from bacterial septicemia in newborns in the North Region, relating them to birth weight, gestational age and type of delivery. It is an ecological, quantitative, and descriptive study, which used data from DATASUS in the North Region from 2013 to 2022, in the age groups 0-6 days and 7-27 days and the number of deaths from bacterial neonatal sepsis. A total of 3549 deaths of neonates due to bacterial septicemia were identified in the North Region, most of them in the state of Pará. There were 2077 deaths in the age group from 0 to 6 days and 1472 deaths from 7 to 27 days; 923 deaths were among neonates with a body mass of 500-999g; 810 in those born from 28 to 31 weeks of gestational age; and 1874 deaths in those born vaginally. Therefore, the reduction in the number of cases of death from bacterial neonatal sepsis is evident, however, they are more prevalent in the North in those born weighing 500 to 999g, vaginal delivery and premature infants.

Keywords: Septicemia, Bacterial. Preterm newborn. Normal delivery. Low Birth Weight Newborn.

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INTRODUCTION

Sepsis is an organ dysfunction generated by an exacerbated response of the individual to bacterial, viral, or fungal infection, with high mortality rates. In newborns, up to 28 days of life, it is a severe syndrome associated with meningitis, pneumonia, pyelonephritis, or gastroenteritis and develops early, in the first 48 to 72 hours of life, or late, after this period (Santos, Oliveira, and Sales, 2020).

In this sense, early neonatal sepsis is due to pathogens, most of which are bacterial in nature, acquired in the prenatal, antepartum or intrapartum period through hematogenous and transplacental dissemination of a maternal infection, including *Escherichia coli* in premature infants and *group B Streptococcus* in full-term newborns. These risk factors include: premature rupture of membranes for more than 18 hours prior to birth, maternal urinary tract infection, intrapartum fever, maternal chorioamnionitis, group B streptococcal colonization, and preterm delivery (Stoll *et al.*, 2020; Conceição *et al.*, 2024)

On the other hand, late-onset sepsis is due to postnatal factors, mainly from multiple care procedures, such as catheters, endotracheal tubes, venipunctures, and transmission through contact with the care team. Hospital microorganisms are the main agents, such as coagulase-negative *Staphylococcus aureus* and *Staphylococcus*, which form biofilms that are difficult to treat, hence the importance of early diagnosis. (Vilaça *et al.*, 2023; Niyoyita *et al.*, 2024; Kadan *et al.*, 2024).

The clinical picture is generally nonspecific and easily confused with conditions typical of the newborn's adaptation to the environment. Thus, the diagnosis is suspected when there is the involvement of three different systems associated with a maternal risk factor. These manifestations include respiratory disorders, thermal instability (hypo- or hyperthermia), and cardiovascular changes such as bradycardia or tachycardia, poor peripheral perfusion, and shock; endocrine such as hypo- or hyperglycemia; gastrointestinal disorders such as food intolerance, bloating, vomiting, and hepatomegaly; cutaneous diseases such as jaundice with no apparent cause, pallor, cyanosis or petechiae; and neurological with lethargy, irritability, and/or seizures (Procianoy and Silveira, 2019; Ayres, 2021; Conceição *et al.*, 2024).

A study carried out at Santa Casa de Misericórdia in Belém do Pará found a large number of neonatal infections in 2021, with a death frequency of 18.8% of newborns and a case fatality rate of 19.95 per 100 affected by neonatal sepsis. In these patients, the microbiological profile was evaluated, which resulted in the presence of bacteria in 91.16% of the cases, the most prevalent being Gram-negative *Klebsiella pneumoniae* and Gram-positive *Staphylococcus epidermidis*. Thus, the study of this pathology at the regional level

is important to reduce mortality in the North of the country (Santos, Sena, and Saraty, 2024).

In 2022, a total of 2,146 deaths from bacterial neonatal septicemia were verified in Brazil. This finding highlights the relevance of the theme at the national and regional levels, since it is an important cause of preventable, but neglected, death in Brazil and, especially, in the North Region. This reflects not only the quality of public policies for neonatal care, but also the quality of public policies for neonatal care. , 2024).

Thus, the objective of the present study is to describe the number of deaths due to bacterial septicemia of newborns in the Northern Region, relating them to birth weight, gestational age, and type of delivery.

METHODOLOGY

The present study is an ecological, descriptive, observational and quantitative study that used data available in the Department of Informatics of the Unified Health System (DATASUS), contained in the TABNET platform. The epidemiological information referred to the number of infant deaths due to bacterial septicemia of the newborn, according to the numbering P36 classified by the 10th edition of the International Classification of Diseases (ICD-10).

The number of deaths from bacterial septicemia of newborns in the seven states of the North Region was collected, during the period from 2013 to 2022, and in the age groups of 0 to 6 days (early neonatal period) and 7 to 27 days (late neonatal period), which together correspond to the neonatal period in general. In addition, the number of deaths was collected according to the birth weight of the newborn, the type of delivery performed and the child's gestational age.

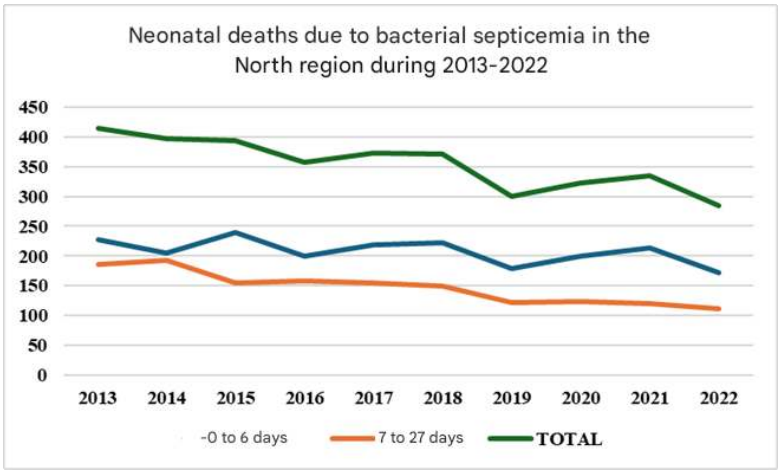
Subsequently, the data were recorded and organized in the Microsoft Excel platform, by calculating the percentage value according to the year, state, age group, birth weight, gestational age, and type of delivery. After that, the values found were transformed into graphs and tables for better elucidation of the study.

RESULTS

During the period from 2013 to 2022, 3,549 deaths of neonates due to bacterial septicemia of the newborn were identified in the North Region. The highest number of records occurred in 2013, with 414 deaths (11.66%), while the year with the fewest deaths was in 2022, registering 284 (8.00%). In addition, mortality in children in the age group of 0

to 6 days was higher in this decade, with 2,077 cases (58.52%), compared to those in 7 to 27 days, which had 1,472 deaths (41.47%).

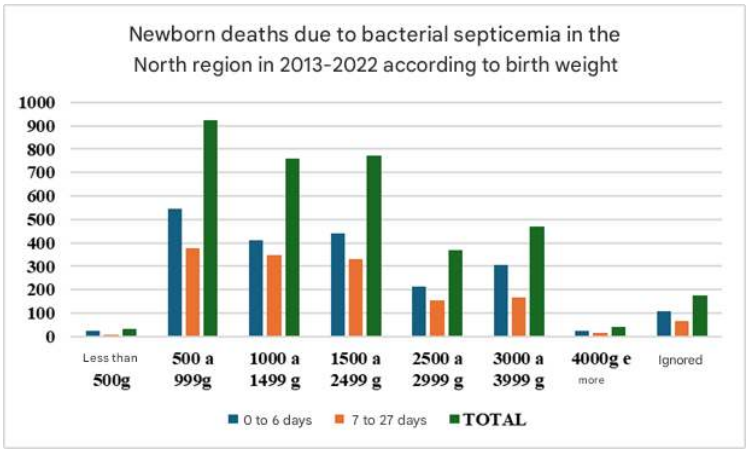
Figure 1. Graph of deaths from bacterial septicemia of newborns in the North Region from 2013 to 2022 (total and by age group).



Source: Authors, 2024.

Regarding weight at birth, it was found that most of the neonates who died from the disease, a total of 923 (26.00%), had a body mass between 500g and 999g. The minority consisted of less than 500g, with 35 deaths (0.98%) and over 4000g, with 42 (1.18%).

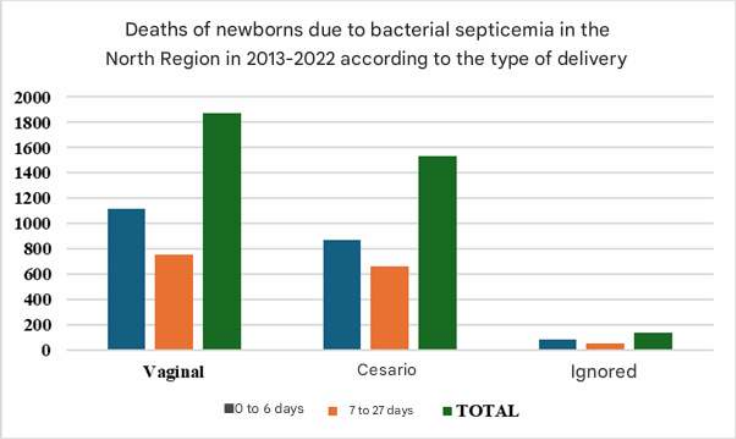
Figure 2. Graph of deaths from bacterial septicemia of newborns in the North Region according to birth weight.



Source: Authors, 2024.

Regarding the mode of birth, those performed vaginally had higher mortality from neonatal sepsis than those performed by cesarean section, accounting for 1,874 (52.80%) and 1,533 (43.19%), respectively. It is worth noting that most deaths from vaginal delivery occurred in newborns aged 0 to 6 days, with 1,119 cases (31.53% of the total cases).

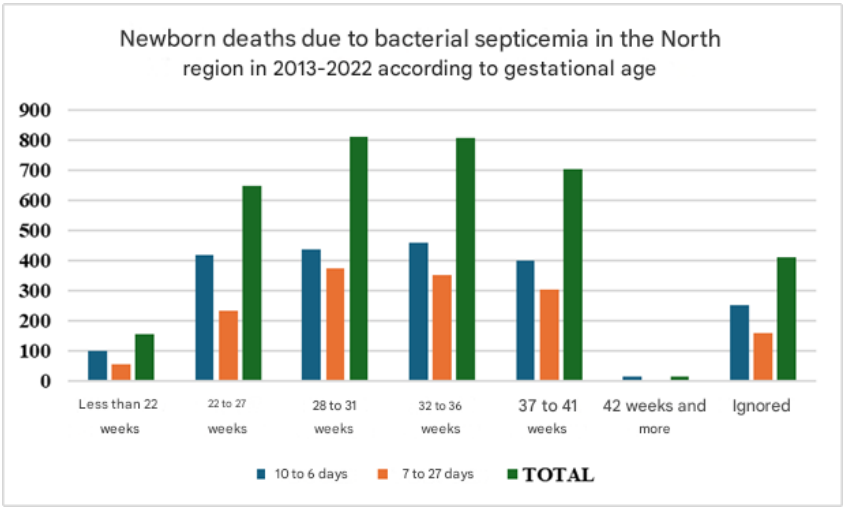
Figure 3. Graph of deaths from bacterial septicemia of newborns in the North Region according to type of delivery.



Source: Authors, 2024.

In addition, the analysis of the gestational age of deceased neonates showed a higher number of records in the range of those born at 28 to 31 weeks, with 810 deaths (22.82%), and lower rates in children from 42 weeks, with 16 cases (0.45%).

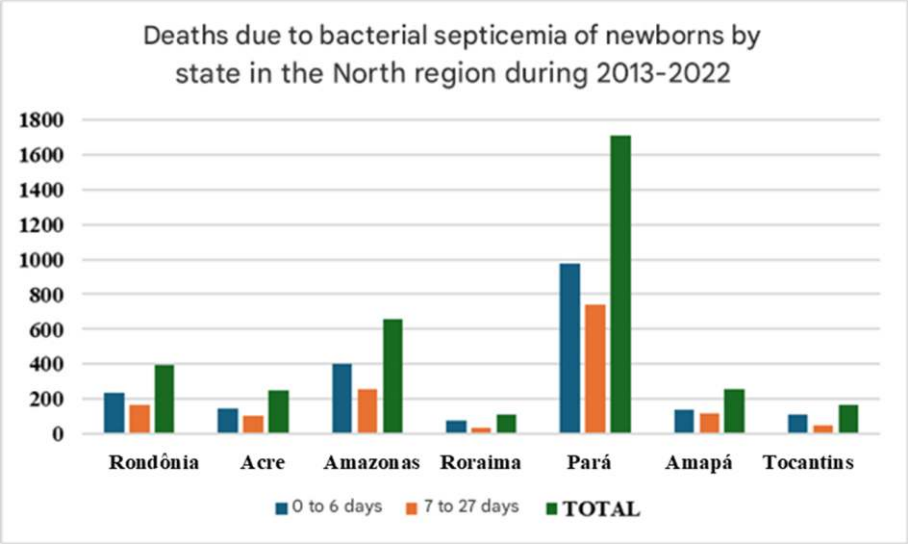
Figure 4. Graph of deaths from bacterial septicemia of newborns in the North Region according to gestational age.



Source: Authors, 2024.

Regarding the study by federative unit in the North Region over 10 years, the most affected state was Pará, with 1,713 deaths (48.26%), followed by Amazonas, with 650 (18.56%). On the other hand, Roraima had fewer cases, registering 111 (3.12%). In Pará, the highest number of deaths was in the range of 0 to 6 days, with 974 cases (27.44% of the total cases in the North in both ages).

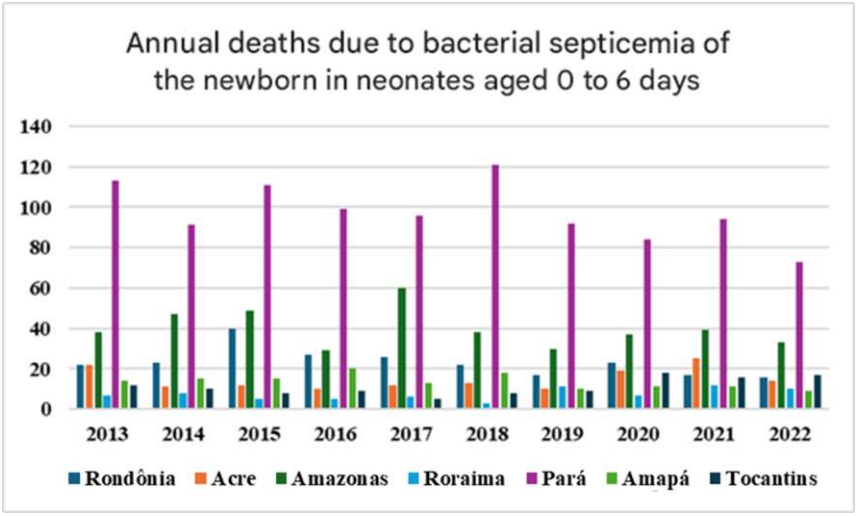
Figure 5. Graph of deaths from bacterial septicemia of the newborn in each state of the North Region.



Source: Authors, 2024.

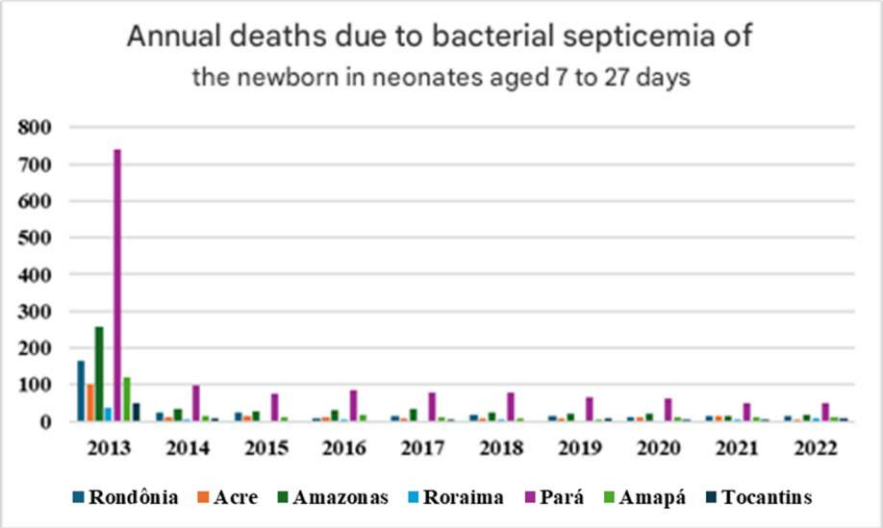
Finally, when analyzing the behavior of deaths in each state and in all years of the decade studied, it is noticed that the records in children aged 0 to 6 days showed similar behavior in all years, with Pará having a significant prevalence in these cases, followed by Amazonas. In relation to infants aged 7 to 27 days, the year 2013 presented a higher number of cases in most states, mainly in Pará and Amazonas, and there was a drastic decrease in 2014, which was constant in later years.

Figure 6. Graph of deaths from bacterial septicemia in neonates aged 0 to 6 days in each state of the Northern Region.



Source: Authors, 2024.

Figure 7. Graph of deaths from bacterial septicemia in neonates aged 7 to 27 days in each state of the Northern Region.



Source: Authors, 2024.

DISCUSSION

In Brazil, between 2011 and 2020, bacterial septicemia of the newborn was the second leading cause of early neonatal death and the leading cause of late neonatal death. When this information is subdivided to the Brazilian regions, the highest neonatal mortality rates are found in the North and Northeast regions due to the great social inequality in the country and the precariousness of the health system (Pasquini *et al.*, 2022).

In the period from 2000 to 2018, Brazil showed a significant reduction in neonatal mortality in all regions, however, the states of Amazonas and Roraima (both in the North Region) did not follow this statistic, keeping the number of deaths from neonatal septicemia still high, as the data collected by the survey corroborate, with Amazonas being one of the states with the highest incidence of deaths from the disease (Prezotto *et al.*, 2023).

In general, the highest number of deaths from bacterial neonatal sepsis in all states in the North Region occurred in 2013, with some stability during the decade, and the lowest number in 2022. This is due to an improvement in diagnostic techniques and therapeutic management during prenatal care, delivery rooms, and neonatal Intensive Care Units (ICUs). However, there are still challenges, especially for the care of newborns with risk factors, as mortality is still significant among this group (De Freitas *et al.*, 2024).

It is worth noting that the highest infant mortality rates are related to weight below 2500g and birth before 37 weeks of gestation, as well as in the present study, in which prematurity and low birth weight were the groups with the highest infant mortality rates. However, it is believed that 56% of these deaths are preventable through adequate care for pregnant women, that is, prenatal, childbirth and postpartum care are key factors for reducing infant mortality (Fernandes *et al.*, 2023).

On the other hand, a study carried out in Guanambi-BA analyzed 712 neonates, of which 410 were diagnosed with neonatal sepsis and, in relation to birth weight, the highest percentage of deaths was present in those weighing less than 1000g. As well as the study carried out in Londrina-PR, in which the highest number of deaths was in the population < 1000g (Costa and Borges, 2022; Oliveira and Sorte, 2022).

These findings are justified because, as in premature infants, low birth weight neonates have immunological dysfunction and absence of transplacental acquired maternal IgG antibodies, explaining low birth weight as one of the most important risk factors for infant mortality. This group is also more prone to hypothermia, hyaline membrane disease, greater water loss through the respiratory tract, and patent ductus arteriosus, which generate pathological weight loss and important hemodynamic repercussions. In addition, they have a skin and mucosal barrier that is ineffective to the invasion of microorganisms, their skin is thinner and susceptible to ruptures, and the need for continuous feeding to avoid hypoglycemia inhibits gastric acidity that protects against invasion (Oliveira and Sorte, 2022; Medeiros, 2022).

It is also worth noting that, in a study on the evaluation and impacts of neonatal sepsis, biochemical markers of worse prognosis for sepsis were identified in very low birth weight newborns. An increase in plasma levels of IL-1 and TNF-alpha was found in the cerebrospinal fluid of this population, concluding an association between the increase in these inflammatory markers and probable negative neonatal outcomes, such as increased death in this population or changes in neuroimaging in very low birth weight preterm infants (Santos *et al.*, 2020).

There are also cases of neonatal sepsis due to the need for invasive interventions such as parenteral nutrition, central venous catheter and mechanical ventilation. These cases present late and are related to sepsis caused by multidrug-resistant bacteria, such as *Staphylococcus aureus*. A study conducted at the State University of Campinas (UNICAMP) analyzed 99 very low birth weight neonates with late-onset sepsis, of whom 21 died as a result of sepsis, generating a mortality rate of 21.2% in this group (Lobo, 2023). In Brazil and worldwide, one of the greatest predictors of risk for deaths from neonatal sepsis is low-weight newborns undergoing such procedures (Medeiros *et al.*, 2022).

Regarding gestational age, in the North Region, a higher incidence of deaths due to neonatal sepsis was found in those who were very preterm infants, in line with the study carried out in Bahia with 1114 deaths due to neonatal sepsis, of which most were neonates between 22 and 31 weeks of gestational age (AGUIAR *et al.*, 2021). Internationally, studies conducted in Tanzania, the United States of America, China, and Ethiopia, have defined a

3.36 times greater chance of developing neonatal sepsis when compared to preterm and term neonates (Belachew and Tewabe, 2020).

However, other authors found a different statistic evaluating 838 neonates with neonatal sepsis, in whom the mean gestational age was 36.91 weeks and of these, 76.47% were born at term, which is in line with the data collected, possibly due to the fact that they were cases of hospitalizations that did not evolve to death in all patients (Dortas *et al.*, 2019).

A possible perceived relationship between preterm neonates and neonatal sepsis is the presence of an immature and nonspecific immune system, with a vulnerable skin barrier, low neutrophil reserve, low IgG production with or without absence of IgA or IgM, early bone marrow depletion, and production of an inadequate immune response to prevent disease manifestation (Belachew and Tewabe, 2020; Guo *et al.*, 2023; Alejandra, 2023). In addition, premature and very low birth weight neonates have a reduced ability to pump and reserve breast milk, facilitating the occurrence of hypoglycemia, one of the main causes of mortality related to neonatal sepsis (Guo et al, 2023).

Another plausible explanation would be the relationship between mothers with premature rupture of the amniotic membrane and the incidence of neonatal sepsis in preterm infants. The study by Ocvivanti and Wahono carried out in this group of women noted 21 neonates with sepsis, of whom 20 had a preterm delivery and, of these, 13 had a gestational age between 28 and 34 incomplete weeks and 5 were less than 28 weeks (Ocviyanti and Wahono, 2018).

In addition, several factors were also related to the development of neonatal sepsis in preterm infants due to the characteristics of this group, such as: 5th minute ≤ 3 Apgar scores and the need for invasive therapies, such as mechanical ventilation, central venous catheter and surgical interventions to support the immaturity of these patients' body development (Dortas *et al.*, 2019).

Regarding the analysis of the type of delivery performed, a study carried out in Peru analyzed 480 patients, of whom 240 neonates had neonatal sepsis, and in this group, 79.2% were born by cesarean section. The relationship studied in this mode of delivery would be the absence of contact with the vaginal canal, which helps in the maturation of the immune system and in the function of the intestinal barrier against pathogens, which can increase the risk of neonatal sepsis (Alejandra, 2023). However, this differs from the data found in the study.

In this study, most cases of neonatal sepsis were present early in newborns born vaginally, as well as in the study carried out in the state of Bahia, in which most deaths from

neonatal sepsis were related to vaginal delivery (Aguiar *et al.*, 2021). It is believed that maternal infection by *Streptococcus* group B hemolytic beta can disseminate hematogenous and transplacental pathway or ascend from the vaginal canal to the amniotic fluid during labor or it can colonize the skin and mucous membranes of the neonate during its passage through the birth canal and is one of the factors most related to neonatal sepsis (Nunes, 2019; Vilaça *et al.*, 2023).

In addition, another maternal pathology associated with symptomatic neonatal sepsis is premature rupture of amniotic membranes for more than 18 hours with or without the presence of chorioamnionitis. Analyzing 36 symptomatic neonates, 53% of them were born vaginally, of which 50% of the mothers suffered from premature rupture of the amniotic membrane (Dortas *et al.*, 2019; Nunes, 2019).

Finally, it is worth noting that other maternal factors considered to be at risk for the occurrence of neonatal sepsis are: dystocic delivery, maternal genitourinary tract infection during pregnancy, presence of meconium amniotic fluid, less than 6 prenatal visits, need for corticosteroids for fetal lung maturation, and hospitalization before labor (Salinas, 2021; Rosa *et al.*, 2022; Alejandra, 2023).

CONCLUSION

Therefore, according to the information mentioned above, it was found that, despite the reduction in the number of cases of deaths from bacterial neonatal sepsis, they are still prevalent in the North Region, especially in those born weighing 500g to 999g, vaginal delivery and premature infants due to the low immunity of this group and the exposure to bacteria from the maternal genital tract and the hospital environment.

Such factors, especially low birth weight and prematurity, seem to be closely related, as well as maternal conditions during prenatal care and childbirth, and may assist in the implementation of government public policies aimed at reducing neonatal mortality. As an example of possible measures, more effective follow-up during prenatal care to detect possible risk factors for bacterial septicemia is essential for the population of these federative units.

Thus, analyzing this epidemiological profile in the North region is essential to know the reality and its regional particularities, contributing to possible questions about the high incidence and the reasons for such neglect of this population.

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