Extreme prematurity in a public reference unit: morbidity, viability and mortality

Prematuridade extrema em uma unidade pública de referência: morbidade, viabilidade e

mortalidade

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Abstract

Premature birth is a public health problem due to the high mortality rate associated and risk of severe disabilities throughout life. The objective was to evaluate the morbidity and mortality in a high-risk maternity hospital and knowing the threshold of viability. The sample was selected in four stages: identification, selection, stratification of preterm infants by gestational age and birth weight, and structured data collection. Neonates up to 31 weeks of gestational age who had a death outcome were evaluated from August 2015 to August 2020 through a retrospective survey based on the descriptive analysis of variables related to pregnancy, childbirth, and the newborn. Absolute and relative percentages were described for the categorical variables and calculated mean, median and standard deviation, minimum and maximum value for continuous quantitative variables. Most newborns had a small gestational age (56.3%), extremely low birth weight (39.8%), and presented with asphyxia (38.7%). The main morbidities were respiratory distress syndrome (100%) and sepsis (40.6%). The overall mortality rate was 55.9% from 26% at 31 weeks to 100% at 22 weeks; most deaths (56.3%) occurred between 22 and 27 weeks. Of the 266 deaths, 25 (9.3%) still occurred in the delivery room and 237 (89%) in the neonatal unit. The early mortality rate was 0.77 deaths per 1,000 live births, and the late mortality rate was 0.22 deaths per 1,000 live births. Viability's limit found was 28 weeks. Death, in addition to fetal characteristics, was influenced by a series of modifiable risk factors. **Keywords:** Premature; Morbidity; Mortality; Fetal viability.

Resumo

O nascimento prematuro é um problema de saúde pública, pela elevada mortalidade e pelo risco de deficiências graves ao longo da vida. O objetivo foi avaliar a morbidade e a mortalidade numa maternidade de alto risco e conhecer o limiar de viabilidade. A amostra foi selecionada em quatro estágios: identificação, seleção, estratificação dos prematuros por idade gestacional e peso de nascimento e preenchimento de formulário estruturado. Foram avaliados neonatos até 31 semanas que tiveram desfecho óbito, no período de agosto de 2015 a agosto de 2020, através de levantamento retrospectivo, baseado na análise descritiva de variáveis relacionadas à gestação, ao parto e

ao recém-nascido. Foram descritos percentuais absolutos e relativos para as variáveis categóricas e cálculo de média, mediana e desvio-padrão, valor mínimo e máximo para as quantitativas contínuas. A maioria dos neonatos tinha baixa idade gestacional (56,3%), extremo baixo peso (39,8%) e sofreu asfixia (38,7%). As principais morbidades foram a síndrome do desconforto respiratório (100%) e a sepse (40,6%). O óbito atingiu 55,9% dos prematuros extremos. A mortalidade variou de 26% com 31 semanas a 100% com 22 semanas, a maioria (56,3%) entre 22 e 27 semanas. Dos 266 óbitos, 25 (9,3%) ocorreram na sala de parto e 237 (89%), na unidade neonatal. O índice de mortalidade precoce foi de 0,77 óbitos por 1.000 nascidos-vivos e o tardio, de 0,22 óbitos por 1.000 nascidos-vivos. O limite de viabilidade encontrado foi de 28 semanas. O óbito, além das características fetais, sofreu a influência de uma série de fatores passíveis de intervenção.

Palavras-chave: Recém-nascido prematuro; Morbidade; Mortalidade; Viabilidade fetal.

Resumen

El nacimiento prematuro es un problema de salud pública, debido a la elevada mortalidad y al riesgo de discapacidades graves a lo largo de la vida. El objetivo fue evaluar la morbilidad y la mortalidad en una maternidad de alto riesgo y conocer el umbral de viabilidad. La muestra se seleccionó en cuatro etapas: identificación, selección, estratificación de los recién nacidos prematuros por edad gestacional y peso al nacer, y cumplimentación de un formulario estructurado. Se evaluaron los neonatos de hasta 31 semanas que tuvieron un resultado de muerte, en el período entre agosto de 2015 y agosto de 2020, mediante una encuesta retrospectiva, basada en el análisis descriptivo de las variables relacionadas con la gestación, el parto y el recién nacido. Se describieron los porcentajes absolutos y relativos para las variables categóricas y el cálculo de la media, la mediana y la desviación estándar, el valor mínimo y el máximo para las variables cuantitativas continuas. La mayoría de los recién nacidos tenían una edad gestacional baja (56,3%), un peso extremadamente bajo (39,8%) y sufrieron asfixia (38,7%). Las principales morbilidades fueron el síndrome de dificultad respiratoria (100%) y la sepsis (40,6%). El 55,9% de los prematuros extremos murieron. La mortalidad osciló entre el 26% a las 31 semanas y el 100% a las 22 semanas, con la mayoría (56,3%) entre las 22 y las 27 semanas. De las 266 muertes, 25 (9.3%) se produjeron en la sala de partos y 237 (89%) en la unidad neonatal. La tasa de mortalidad temprana fue de 0,77 muertes por cada 1.000 nacidos vivos y la tasa de mortalidad tardía fue de 0.22 muertes por cada 1.000 nacidos vivos. El límite de viabilidad fue de 28 semanas. Además de las características fetales, la muerte estuvo influida por una serie de factores susceptibles de intervención. Palabras clave: Recién nacido prematuro; Morbilidad; Mortalidad; Viabilidad fetal.

1. Introduction

Premature birth occurring before 37 weeks, represents a serious public health problem as a result of its high worldwide prevalence – about 30 million preterm births per year – being responsible for approximately one million child deaths. In Brazil, about 323,000 infants are born preterm annually, representing 11.5% of all births and 54% of the 35,839 infant deaths recorded (Ambrósio et al., 2016; Al-Mouqdad et al., 2018; Aynalem et al., 2021).

Advances in neonatology and improvements in perinatal care have allowed the survival of newborns (NB) with increasingly lower gestational age (GA) and birth weight's (BW) thresholds, beside the emergence of new challenges such as the decision to start resuscitation in the delivery room, due to morbidities and medium and long-term outcomes. Prematurity consequences are more frequent at gestational ages below 32 weeks and become critical below 28 weeks (Apgar, 2015; Areia et al., 2018).

When considering low GA and BW, when newborns are too immature to survive, the provision of intensive care is unreasonable for those < 23 weeks and < 500 g. For newborns older than 25 weeks GA and with a BW > 500 g (grams), intensive care's measures initiation is considered justifiable, as most of these patients survive and at least 50% do so without major disability. For those born between 23 and 24 weeks of gestation with BW < 500 g, survival and morbidity are extremely uncertain; these infants lie in the so-called 'gray zone' of viability or periviability, in which post-delivery care involves extremely complex and multidisciplinary decision-making (Aziz et al., 2020; Bouzada et al., 2018; Brasil, 2014, 2020).

The different outcomes of prognosis and survival will depend on the structure, technology, organization, care practices and viability's threshold of each service. The most common complications include respiratory distress syndrome (RDS), periventricular/intraventricular hemorrhage (PVH/IVH), sepsis, necrotizing enterocolitis (NEC), bronchopulmonary

dysplasia (BPD), retinopathy of prematurity (ROP), and neonatal death (Alleman et al., 2013; Aziz et al., 2020; Barfield, 2018; Barros et al., 2018; Bartman et al., 2015; Bittar, 2018).

Mortality outcomes among extremely preterm infants are related to several variables. In Brazil, death within the first six days of birth is closely related to perinatal events, socioeconomic and care factors, which are considered preventable by health service actions (Apgar, 2015; Areia et al., 2018).

Given the complexity of the factors involved in conditions of extreme prematurity, this research aimed to evaluate morbidity and mortality in a public reference high-risk maternity, in order to know the viability's limits.

2. Methodology

This is a retrospective and observational study of data from a public referral maternity hospital which provides medium- and high-complexity obstetric and neonatal care. Ethical approval was obtained (opinion number 4393441). The population consisted of all preterm infants with GA until 31 weeks, admitted to the institution between August 2015 and August 2020, who had a lethal outcome. Newborns with severe malformations (cardiac, pulmonary, cerebral, gastrointestinal), sufficient to cause greater morbidity, were excluded (Carvalho et al., 2019; Castro et al., 2016).

Sample selection was a four-stage process. The first stage consisted of a survey of all births and deaths that occurred before the 28th day of life during analysis' period. The second stage consisted of data collection from all corresponding Infant Death Investigation Forms. In the third stage, infants < 32 weeks GA were selected and classified as very preterm (\geq 28 to < 32 weeks) or extremely preterm (\geq 22 to < 28 weeks) (Castro et al., 2016; Chawanpaiboon et al., 2019). Infants were further stratified on the basis of weight/gestational age ratio as appropriate for gestational age (AGA), small for gestational age (SGA), or large for gestational age (LGA) (Chun et al., 2017).

During the fourth stage, collected data was based on the following variables: a) maternal/gestational characteristics – age, marital status, housing conditions, education, occupation, addictions, and complications; b) birth characteristics – birth place, antenatal corticosteroids, delivery way, gestational age, birth weight; c) neonatal characteristics – surfactant, morbidity, death cause, death timing (early vs. late), and neonatal viability.

A descriptive analysis of all variables was carried out according to GA in weeks (from the 22 to 31). Categorical variables had absolute and relative frequencies described, and means, standard deviations, medians, and ranges (minimum-maximum) were described for continuous quantitative variables. Statistical analyses were carried out in SPSS Version 20.0 and Microsoft Excel 2016.

To analyze factors associated with the unfavorable outcome of preterm infants in this cohort, variables were evaluated according to the characteristics of each group and the chronology of related events, namely: maternal/gestational factors, childbirth-related factors, and neonatal factors.

3. Results

In analyzed period, 6961 newborns were admitted to the reference maternity hospital, of which, 634 (9.1%) were extremely preterm infants. There were 542 deaths, 303 (55.9%) in premature infants with GA until 31 weeks. Of these, 37 neonates were excluded due to the presence of severe malformations. Over the 5-year period of interest, the analyzed sample comprised 266 participants (Figure 1).

Figure 1. Flowchart of admissions of preterm infants up to 31 weeks of gestational age and deaths at the Maternidade Escola Santa Monica, from August 2015 to August 2020.





Figure 1 showed that the percentage of preterm infants up to 31 weeks corresponded to less than 10% of all births, representing more than 50% of neonatal deaths and significantly impacting institution's high neonatal mortality results.

The number of preterm births in the state from 2015 to 2020 was approximately 25,900, corresponding to a prematurity rate of approximately 10.7% (Cnattingius et al., 2020). There were 2,572 admissions of preterm infants at the maternity hospital, accounting for 37% of all live births (75.3% moderate and late preterm, 16.7% very preterm, and 7.8% extremely preterm).

3.1 Maternal/gestational factors

Regarding maternal characteristics, most of the mothers (66%) came from the state capital; 60.9% were between 20 and 34 years old; 54.1% were single; and 59.4% had less than 8 years of formal schooling. In 66.1% of records, there was no information regarding maternal addictions. Regarding marital status, 54.1% did not have a steady partner, most of them (76.7%) attended fewer than six antenatal visits, and 38% were diagnosed with antenatal infection. Among complications recorded during pregnancy, premature rupture of membranes (PROM) (35.6%), infections (27.8%), and hypertensive syndromes (26.8%) were the most prevalent, in decreasing order of frequency.

3.2 Childbirth-related factors

Vaginal deliveries accounted for 64.7% of all births, mainly at extremes of gestational age. Antenatal corticosteroids were used by only 32.7% of mothers, and there were no changes in this rate over the five-year study period. An overall lack of monitoring regarding the number of administered doses was observed, and there was no reference of this therapy in 24.4% of

medical records. Among neonates who were transferred from other facilities (10%), all had been delivered vaginally and none had received corticosteroids before birth.

Regarding perinatal asphyxia, an Apgar score < 7 in the 5th minute of life was observed in 38% of newborns (n=103). The need for neonatal resuscitation was stratified by gestational age. 37.5% of preterm infants were resuscitated at 22 weeks; 53.8% at 23 weeks; 95.7% at 24 weeks; 100% between 25 and 26 weeks; and ranging from 92.9% at 27 to 90.2% at 31 weeks GA (Graph 1).

Graph 1. Need for neonatal resuscitation in the delivery room, stratified by gestational age in weeks, of extremely premature infants at the Maternidade Escola Santa Monica, from August 2015 to August 2020.



Source: Research data (2020).

In graph 1, we can see that more than 50% of preterm infants up to 23 weeks and 90 to 100% of those born between 24 and 31 weeks were resuscitated, which represents the high need for help to start the cardiorespiratory transition among the preterms of the study, for adequate adaptation to extrauterine life.

3.3 Neonatal factors

Regarding neonatal characteristics, 84% (n=224) of included infants were born at the study hospital, and more than half (56%) were male. Birth's distribution by GA range increased from 8 (3%) at 22 weeks to 38 (14.2%) at 25 weeks, and subsequently ranged from 36 (13.5%) at 28 weeks to 25 (9.3%) at 31 weeks. BW ranged from 315 g at 22 weeks to 1730 g at 30 weeks. The mean BW at 28 weeks was 879 g.

Regarding neonatal care, surfactant replacement therapy was offered to 84.8% (n=226) of preterm infants, specifically 9% (n=24) of those < 24 weeks; 36% (n=96) of those at 25 to 27 weeks; and 39.8% (n=106) for those born > 28 weeks GA. The most common early complication was respiratory distress syndrome, which occurred in 100% of newborns and was strongly related on GA at birth and was associated with death in the first week of life, followed by sepsis, which accounted for 40.6% of late mortality.

Among 266 deaths analyzed, 25 (9.3%) occurred in the delivery room and 237 (89%) in the NICU. Birth weight < 1,000g observed until the 26th week of GA carried a high mortality rate (45.4%). Lethality was inversely proportional to GA, with death occurring in 55.9% of very preterm infants; mortality ranged from 26% at 31 weeks to 100% at 22 weeks GA (Graph 2).





Source: Research data (2020).

Graph 2 shows that the highest mortality occurred in the lowest gestational age range, with 100% of death between 22 and 24 weeks, and that there was a gradual decrease from 25 to 31 weeks.

Analysis of death timing showed a predominance in the period of 1 to 6 days of life, with an early neonatal mortality rate of 77.1%; Considering these deaths, 31.6% occurred in the first 24 hours, with a higher prevalence among those younger than 24 weeks GA. On the other hand, late mortality occurred in 22.8% of preterm infants from 27 weeks GA age onwards. The early neonatal mortality rate was 0.77 deaths per 1,000 live births, while late neonatal mortality rate was 0.22 deaths per 1,000 live births.

The survival rate increased progressively with each additional week of GA, increasing from 0% between 22 and 24 weeks to 72% at 31 weeks GA. However, mortality was lower at the 30th week compared to the 31st week of GA, probably due to the influence of accuracy in determining GA.

Most of the deaths were observed in those born between 22 and 24 weeks of gestation. Most deaths (56.3%) occurred in premature infants born between 22 and 27 weeks, and only those born after 28 weeks had a survival rate over 50%. Viability's limit or threshold in the studied population was 28 weeks of gestational age. Thus, based on our findings of mortality rates according to each gestational age range, study sample neonates's prognosis can be categorized into three groups – extremely high risk, high risk and moderate risk. Regarding fetal viability, they were classified as: unviable, possibly viable with a high chance of severe sequelae and viable (Table 1).

Gestational age	Mortality rate	Risk categorization	Viability
22ª	100%	Extreme high risk	
23ª	100%	More than 90% chance of dying or	Not viable
24ª	100%	surviving with severe disability	
25ª	84%	High risk	Dessible visble, but with high shapees
26ª	74%	50 to 90% chance of dying or surviving	of sorious socuels
27ª	51%	with severe disability	of serious sequers
28ª	38%	Modonoto viele	
29ª	29%	Less than 50% chance of dying or surviving with severe disability	Viable
30 ^a	28%		
31ª	26%		

Table 1. Description of mortality rates by gestational age, risk categories and viability of extreme preterm infants at the

 Maternidade Escola Santa Monica, from August 2015 to August 2020.

Table 1 shows that until 24th week of gestational age, newborns are at extreme high risk and do not survive hospital discharge, being considered unviable. Between 25 and 27 weeks, they still have significant mortality rates, being possibly viable, but at high risk of developing serious sequelae. Only at 28 weeks pregnancy, more than 50% manage to survive in hospital, with mortality moderate risk and less than 50% chance of serious sequelae, representing the found viability limit.

Despite the conditions associated with the high risk of morbidity and mortality in the analyzed sample, it's not possible to define individual prognosis of an extremely premature infant. In this way, the uncertainties must be shared with the parents for involvement with the team in the care of newborn's best interest. Thus, we can suggest graphic visual presentation of mortality and survival's information, to assist communication between health professionals and parents (Figure 2).

Figure 2. Infographic for parents on the mortality results among extreme premature infants at Maternidade Escola Santa Monica, from August 2015 to August 2020.



Survival

Source: survey data (2020). Adapted from Guillen (2019).

Figure 2 shows illustrative content on mortality results in each gestational age group, aiming to inform and guide parents in the processes that involve very immature newborns' care.

Source: Research data (2020). Adapted from Mactier et al. (2020).

4. Discussion

The extreme prematurity rate of 16.7% was high compared to the total rate of 13.6% found in Brazil in 2019 (Aynalem et al., 2021). However, still much higher than those found in Europe and the United States, with 11.3% and 1.6% very preterm and 4.1% and 0.67% extremely preterm infants, respectively (Ambrósio et al., 2016; Cristina et al., 2021). This is probably explained at least in part by the fact that the study hospital is a statewide referral center for high-risk pregnancies, as well as by possible interference with estimates of preterm birth rate arising from differences in GA assessment methods, definitions of prematurity, and the quality of vital statistics (Ambrósio et al., 2016; Bartman et al., 2015).

Most mothers of preterm infants had low economic status, little education, and limited antenatal care; consequently, they were at greater risk of perinatal complications, which is consistent with preterm birth high rates, PROM, and concomitant infection observed (Cupen et al., 2017; Ellsbury et al., 2016). In addition, there was a high prevalence of hypertensive disorders of pregnancy (HDP), which can lead to intrauterine growth restriction (IUGR) and worse outcomes (Fenton & Kim, 2013), as shown in previous studies carried out in Mexico (Fiorenzano et al., 2019), Trinidad and Tobago (Gagliardi & Bellù, 2017), the United States (Gibelli, 2019), and China (Guimarães, 2019). These conditions highlight the need of investment on health networks to care for women during pregnancy and municipal health services quality improvement (Guimarães et al., 2017).

In terms of care practices, there was no improvement in the rate of mothers receiving antenatal corticosteroid therapy during the course of the study. This stands in contrast to what was observed at RBPN-affiliated centers, where the rate of antenatal corticosteroid use increased from 70% in 2011 to 85% in 2018, and in the Vermont Oxford Network (VON), where it rose from 86% in 2009 to 92% in 2016 (Bartman et al., 2015; Guillén et al., 2019). A meta-analysis of 30 studies found that antenatal corticosteroid therapy resulted in reductions in RDS (44%), need for mechanical ventilation (32%), sepsis (4%), NEC (50%), and perinatal death (28%) (Guinsburg et al., 2016).

The low 5-minute Apgar scores and high mortality observed during the study period were consistent with those reported by Bartman et al. (2004 to 2010) (Guinsburg et al., 2016) and Myrhaug et al. (2000 to 2017) (Guinsburg et al., 2021) in the U.S. and by Cnattingius et al. (1992 to 2016) (Helenius et al., 2018) in Sweden, who observed a greater association between low 5-minute Apgar scores and neonatal mortality in preterm infants with a GA of 23 to 28 weeks. Birth attendants training in neonatal resuscitation should thus be a priority measure to reduce neonatal mortality.

Neonatal resuscitation procedures were required by 92.9% of newborns at 27 weeks and 90.2% at 31 weeks (**Graph 1**). Thus, given the high possibility of interventions necessary at birth and the greater risk of complications, additional resources need to be prepared to attend extreme preterm infant delivery, and it is essential to have adequate material and a team trained in resuscitation (Apgar, 2015).

At the same time, the beneficial impact of extremely preterm neonate resuscitation cannot be estimated in our sample, since 100% of infants with GA < 24 weeks died within the first 24 hours of extrauterine life. According to the neonatal viability guideline proposed by Seri et al., comfort measures should be offered to neonates under 23 weeks; resuscitation and initiation of ICU care are warranted for those over 25 weeks. For neonates in the "gray zone" (between 23 weeks and 24 weeks and 6 days), clinicians should consider the patient's condition at the time of delivery and involve the parents in decision-making, always with ongoing reassessment of the neonate's response to treatment (Hon et al., 2018).

This study population included preterm infants at the extreme threshold of viability, and more than half of all deaths (56.3%) occurred among those born at < 28 weeks GA (Graph 1). Preterm infants in this category have different degrees of development, which can directly influence their chances of survival and risk of complications (Jung et al., 2019). As expected, each additional week of pregnancy resulted in increased survival.

The extremely low birth weight of sample's neonates also had a major influence on mortality rate (45.4%), which was far higher than that reported in the Lansky et al. (2014) cohort (30% mortality). This highlights the importance of low BW as an isolated determinant of neonatal mortality in Brazil.

Neonates transferred from outside hospitals, despite limited information on delivery and transport conditions, showed similar morbidity and mortality from those born in the study hospital, probably due to the predominance of risk factors specific to the analyzed population.

Regarding morbidities, the high incidence of respiratory distress syndrome stood out among the causes of early mortality, and reflects the importance of greater use of antenatal corticosteroids, both to reduce disease's severity and to optimize the effect of surfactant therapy (Leal et al., 2016).

As for neonatal care, surfactant was commonly offered to all preterm infants, regardless of gestational age. In this sense, it is important to avoid invasive procedures and unnecessary treatments, and it is essential to adopt preventive measures such as the use of prenatal steroids and CPAP as ventilatory support, with subsequent surfactant indication, according to preterm infant's clinical evolution (Leal et al., 2016).

Sepsis was one of the main factors limiting the survival of preterm infants in the study, similar to the study by Teixeira et al., who observed a high incidence of infections in Brazilian's NICU and the need to implement effective preventive measures (Li et al., 2021). Unlike Stoll et al., in the USA, where progress in prevention measures reduced infection rates in newborns at 28 weeks from 20 to 8% and increased survival in this group from 43 to 49% (Mactier et al., 2020).

Regarding the 28-week viability limit, it is worth mentioning the difficulty in direct comparison with other studies, due to the methodological differences used or restricted analysis for certain subgroups of GA or weight. Nor can we consider the regional and local inequalities related to obstetric and neonatal care of greater complexity in our country (Guimarães et al., 2017).

Regarding mortality, our results (55.9%) were comparable to those of prior Brazilian studies by Guinsburg et al. (53%) and Lima et al. (59.1%) (Guimarães et al., 2017; Manuck et al., 2016). However, they far exceeded those reported in other countries such as Portugal, China, and Australia, where mortality rates ranged from 21 to 37.5% (Barfield, 2018; Guimarães et al., 2017; Jung et al., 2019).

The underlying cause of death was difficult to determine in many cases. Among infants born at < 24 weeks, 100% of deaths were attributed to extreme prematurity and respiratory causes. This limitation is not exclusive to our study, as the cause of death in extreme prematurity is usually multifactorial (Lima et al., 2020). From the 25th week onwards, infectious causes represented 26.3% of deaths, reaching 60% in those born at 30 weeks, with sepsis as the leading late mortality cause.

The early mortality rate (77.1%) was higher than that of prior Brazilian reported by Carvalho et al. (2012 to 2017, 60%) and Guinsburg et al. (2012 to 2013, 53%), and extraordinarily high on comparison with other countries, such as Portugal (20.6%) (Guinsburg et al., 2016; Jung et al., 2019; Manuck et al., 2016). Actions aimed at improving care provided to pregnant women and childbirth, in addition to the use of evidence-based practices, are recommended prevention strategies to reduce these deaths (Guinsburg et al., 2016; Jung et al., 2019; Manuck et al., 2016).

Late mortality (22.8%), on the other hand, may have been related to increased NICU length of stay. However, Alleman et al., (2006 a 2009), point out that the differences in mortality between different units cannot be explained solely by neonatal characteristics diversity, but are also related to the use of survival predictive interventions, such as antenatal corticosteroids, maternal infections treatment, adequate assistance during childbirth, neonatal resuscitation, ventilatory support, nutrition, and hypothermia and infections prevention (Marques et al., 2019).

Present study limitations were secondary to incomplete data filling, since it was a retrospective evaluation. Additional research with death records and medical procedures joint investigation may help in this context, in addition to prospective development.

5. Conclusion

Through the methodology applied, it was possible to conclude that high mortality rate of 38.2% and viability limit of 28 weeks, in addition to fetal characteristics, such as extremely low gestational age (56.3%) and extremely low birth weight (39.8%), were influenced by a series of interventionable factors, such as asphysia (38.7%), respiratory distress syndrome (100%) and sepsis (40.6%).

Presented results allow us to observe alert conditions for monitoring neonatal mortality, showing that there is space for improvement and highlighting the need of changes in the organization and provided care quality. New studies may help define perinatal strategies and interventions to improve the extremely preterm infants prognosis.

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