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FACTORS ASSOCIATED WITH EARLY NEONATAL DEATH

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ABSTRACT

Introduction: Early neonatal death is classified as the death of a newborn (NB) from 0 to 6 days after birth. In Brazil, in the year 2019, data show that 52.14% of infant deaths were attributed to early neonatal death. In this epidemiological scenario, the contribution of deaths in this age group to the infant mortality rate is evident. Therefore, the assessment of this problem is essential to improve the health care of pregnant women and reduce mortality rates. **Methods:** In this observational, cross-sectional, quantitative, descriptive, and retrospective study, data were obtained from the medical records of 42 children who were born in the reference hospital for Pediatrics and Neonatology of the microregion of São João del-Rei (MG), Brazil, in the years 2018, 2019, and 2020. The sample comprised a group of newborns who died early and a surviving control group for comparison. The statistical analysis of the data was carried out through descriptive and inferential statistics. **Results:** Data analysis revealed that there was statistical significance for the variables weight at birth, gestational age, and APGAR<7 at the 5th minute of life. **Conclusion:** The analysis of the early neonatal mortality profile provides an adequate epidemiological basis that justifies effective and specific preventive measures in the area of maternal and child health.

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INTRODUCTION

In spite of the significant decrease in infant mortality in recent decades, neonatal mortality rates have not declined in the same proportion. Neonatal deaths constitute a significant part of deaths in children under 1 year of age (Pinstrupjoergensen, 2018). According to data from the United Nations (UN), namely the Global Health Observatory, the worldwide infant mortality rate in 2019 was28.2 per thousand live births. The neonatal mortality rate in the same period was 17.5, which represents more than 60% of the total deaths of children up to 1 year of age (WHO, 2019). The Infant Mortality Rate (IMR) is an epidemiological indicator used in healthcare that is characterized by the number of deaths for every 1,000 live births. Additionally, the neonatal period is considered as the first 28 days of an individual's life. When death occurs before 7 days of life, it is deemed early neonatal death. On the other hand, when death occurs after 7 days and before 28 days of life, it is called late neonatal death (Maletta, 2014). According to the Global Health Observatory, approximately 5.2 million deaths occurred in children under 5 years of age in 2019, the equivalent of nearly 14,000 children each day.

Among the 10 main causes of death in this age group, preterm birth complications lead in 1st place, followed by asphyxia at birth, in 3rd, and neonatal infections in 6th (WHO, 2019). In Brazil, the total number of infant deaths in 2019reached 35,293, of which 12,707 occurred in the Southeast region, with 2,942 deaths in the state of Minas Gerais alone (Ministério da Saúde, 2019). Regarding the number of neonatal deaths before 7 days of life, the national death rate reached 18,402 in the country and 1,576 in the state of Minas Gerais. As for the period between 7 and 27 days of life, there were a total of 6,102 and 510 deaths, respectively (Ministério da Saúde, 2019). The number of neonatal deaths is heterogeneously distributed throughout the globe. Sub-Saharan Africa and South Asia have the highest neonatal death rates, with an estimated 2.1 million deaths in 2015 (Goudar, 2020). This data is important since the objective of the United Nations' (UN) Sustainable Development Goals for 2030 is to reduce the preventable deaths of newborns and children under 5 years of age. It is expected that countries reduce neonatal mortality rates to at least 12 per 1,000 live births, and under-5 mortality to at least 25 per 1,000 live births (UNICEF, 2020). The infant mortality rate in the world has fallen significantly over the past 3 decades (nearly 59%), going from 93 deaths per 1,000 live births in 1990 to 38 deaths in

2019. Despite the improvement in the mortality rates, increasing the child survival rate is a major concern. The first 28 days of life are the most vulnerable for the newborn. In 2019, the global mortality rate in the neonatal period was 17 deaths per 1,000 live births. Approximately 2.4 million children died in the first month of life in the world in that year, totaling around 6,700 neonatal deaths every day; one-third of these deaths took place on the first day after birth, while nearly three-quarters occurred within the first week of life (UNICEF, 2020). In this epidemiological scenario, the contribution of neonatal death to the Infant Mortality Rate becomes evident, especially in the early neonatal period. In 2019, Brazilian data showed that 52.14% of infant deaths were allocated in the early neonatal period, a fact that highlights the importance of epidemiological studies (Ministério da Saúde, 2019). Understanding the factors associated with early neonatal mortality could assist in the detection of preventable causes for such deaths, helping to implement prevention and care strategies at the different levels of pre-, peri-, and postnatal health care.

METHODS

Sample characteristics: The present study is the result of an observational, cross-sectional, quantitative, descriptive, and retrospective research project. Cross-sectional studies are like photographs, since they collect information from a given population in a single moment. Thus, exposure and outcome are evaluated at the same time (Giolo, 2017). This type of study does not allow for the determination of cause-effect, but it does enable to determine the prevalence of a particular condition, as well as the relationships between the characteristics of interest (variables) analyzed (Oliveirafilho, 2015).

The sample was obtained from records pertaining to early neonatal deaths in the Neonatal Intensive Care Unit (NICU) of São João del-Rei (SJDR). This hospital unit provides assistance in the area of Pediatrics and Neonatology, both for public and private care. Thus, the study of deaths in this hospital unit reflects the reality of this municipality in the state of Minas Gerais, as it is the only reference unit in the region. Data were collected from medical records regarding early neonatal deaths in the years 2018, 2019, and 2020. The variables of interest included Maternal Age (MA), Sex of the Newborn (SNB), Birth Weight in grams (BW), Gestational Age in weeks (GA), Type of Delivery (Vaginal or Operative/Cesarean), Maternal Infection in the 3rd trimester (Yes or No), Asphyxia - APGAR <7 in the 5th minute of life (Yes or No), and comorbidities during pregnancy. The inclusion criteria comprised neonatal deaths that occurred in the municipality of São João del-Rei in the years 2018, 2019, and 2020. As for the exclusion criteria, newborns with congenital malformations were not considered. The sample constituted a group of neonates who had an early death and a control group. For each early neonatal death of a newborn, a live newborn that did not require admission to the ICU after delivery was considered. Medical records of 21 children in the ICU and 21 children who did not go to the ICU at birth were analyzed, totaling 20 NBs in 2018, 20 NBs in 2019, and 2 NBs in 2020.

Statistical analysis: The collected information was described by numerical synthesis (mean, median, standard deviation, minimum and maximum value, 5th percentile, and 95th percentile). The comparison of maternal age between the mothers of the live newborns and those that died was analyzed using the t-student test. Meanwhile, the comparison of median gestational age and birth weight was carried out using the Mann-Whitney test. The association of the type of delivery, maternal comorbidities, infection in the 3rd trimester, the occurrence of membrane rupture, and early neonatal death was determined using the Chi-square test, considering a significance level of 5%.

RESULTS

The frequency distribution for the evaluated variables was obtained using secondary data from 42 medical records, as shown in Table 1.

Table 1. Frequency distribution of the characteristics related to the pregnant mother and the NB

Co-variable		Status of the NB			*p* value
			Alive	Early Neonatal Death	
Type of Delivery	Vaginal	n	8	7	
		%	38.10%	33.30%	0.747
	Cesarean	n	13	14	
		%	61.90%	66.70%	
Comorbidities During Pregnancy	Absent	n	8	12	
		%	38.10%	57.10%	0.354
	Present	n	13	9	
		%	61.90%	42.90%	
Urinary Infection in the 3rd Trimester	Absent	n	17	18	
		%	81.00%	85.70%	0.679
	Present	n	4	3	
		%	19.00%	14.30%	
Rupture of Membranes	Less than 18h	n	20	17	
		%	95.20%	89.50%	0.596
	More than or equal to 18h	n	1	2	
		%	4.80%	10.50%	
Sex of the NB	Female	n	13	10	
		%	61.90%	47.60%	0.536
	Male	n	8	11	
		%	38.10%	52.40%	
Asphyxia Present	Yes	n	1	15	
		%	4.80%	83.30%	0.001*
	No	n	20	3	
		%	95.20%	16.70%	
APGAR greater than 7 at the 5th minute of life	Yes	n	20	9	
		%	95.20%	50.00%	0.002*
	No	n	1	9	
		%	4.80%	50.00%	

*p<0.005 indicates statistical significance.

A total of 21 medical records of newborns who died in the early neonatal period were obtained, as were21 documents of newborns who were discharged from the hospital after birth (alive). Upon analyzing the characteristics related to the pregnant women, the mean maternal age in the live births group was 27.4 years, with a standard deviation of 6.6 years, and a minimum of 16 and a maximum of 37 years. As for the mothers of children who died, the mean age was slightly lower (25.8 ±5.2 years), with a minimum of 16 and a maximum of 36 years. There was no statistically significant

difference (*p* value=0.384) between the mean ages of the mothers. According to Table 2, the mode of delivery of the newborns who died was 33.3% (7) vaginal and 66.7% (14) cesarean section. In the non-death group, the number of vaginal deliveries was slightly higher (38.1%) (8), while the cesarean sections totaled 61.9% (13). No statistically significant difference (*p* value=0.747) was found between the type of delivery and the status of the NB.

neonatal death group. Meanwhile, in the term babies category, 86.4% (19 out of 22 children) remained alive and 13.6% (3 out of 22 children) died by the 6th day of life.These results are in agreement with the WHO, whose publications show that most deaths in children under 1 year of age are associated with premature birth [2]. The median gestational age of the newborns who died was 27 weeks, while in the control group, the median GA was 39 weeks.

Table 2. Frequency of live NBs and those who died early and the association of the status of the NB regarding the type of delivery, the presence of maternal comorbidities, and the occurrence of urinary infection in the 3rd trimester of pregnancy

Status of the NB	Type of Delivery				Comorbidities During Pregnancy				Urinary Infection in the 3rd Trimester			
	Vaginal		Cesarean		No		Yes		No		Yes	
	n	%	n	%	n	%	n	%	n	%	n	%
Alive	8	38.1	13	61.9	8	38.1	13	61.9	17	81.0	4	19.0
Early Neonatal Death	7	33.3	14	66.7	12	57.1	9	42.9	18	85.7	3	14.3
p value	0.747				0.354				0.679			

Table 3. Birth weight (grams) and gestational age (weeks). Comparison between the control group and the early neonatal death group

Statistics	Weight of the NB		Gestational Age	
	Control	Early Neonatal Death	Control	Early Neonatal Death
n	21	21	21	21
Mean	3197	1393	39	29
Standard Deviation	375	960	1	4
Median	3180	915	39	27
Minimum	2510	455	35	24
Maximum	3930	3520	40	39
5th Percentile	2600	535	36	24
95th Percentile	3785	3085	40	39

The common gestational history in both groups was urinary tract infection (UTI), systemic arterial hypertension (SAH), and Syphilis. In the control group, there was a record of gestational diabetes (GDM) and panic syndrome. Meanwhile, in the early neonatal death group, there were records of placental abruption, HELLP syndrome, oligohydramnios, drug use, and cases in which the pregnant women were unaware of their pregnancy. Urinary infection in the third trimester of pregnancy was reported in 85.7% (18) of the mothers of newborns who died. Among the pregnant women in the control group, the percentage was 81% (17). No statistically significant difference (*p*value=0.679) was observed between this maternal comorbidity and the status of the NB. Another variable that was investigated was the rupture of membranes after more than 18 hours of labor. We found that 95.2% (20) of the mothers of live NBs sustained membrane rupture in less than18h of labor. Meanwhile, for the mothers of children who died, the percentage was 89.5% (17). No significant difference (*p* value=0.596) was observed between this variable and the status of the NB. In the present study, among the NBs who sustained an early neonatal death, 52.4% (11) were male and 47.6% (10) were female. As for the live NBs, 61.9% (13) were female and 38.1% (8) were male. The sample consisted of a slightly larger number of female babies than male babies (23 and 21, respectively). There was no statistically significant difference (*p*value=0.536) between the sex and the status of the NBs. Birth weight is a highly relevant variable for death. The median birth weight of the newborns in the control group was 3,180g, while that of those who sustained early neonatal death was 915g. A statistically significant difference (*p* value=0.001) was found when comparing the median birth weightsof the two groups.

Gestational age is used to classify newborns as term or premature. According to the WHO, children born at 37 weeks of age or older are considered full-term, whereas those born under 37 weeks are deemed preterm. The classification of preterm NBs encompasses four categories: extremely preterm (<28 weeks), very preterm (28 to<32 weeks), moderate preterm (32 to<37 weeks), and late preterm (34 to<37 weeks) [10]. The results found herein showed that 100% of the NBs classified as extremely preterm (12 NBs), very preterm (3 NBs), and moderate preterm (2 NBs) belonged to the early neonatal death group. Late preterm newborns represented 66.7% (2 out of 3 children) in the control group and 33.3% (1 out of 3 children) in the early

A significant difference (*p* value=0.001) was found between the medians of gestational age; there is evidence that the median gestational age of the newborns who died was lower. The statistical analysis for birth weight and gestational age is described in Table 3. Birth asphyxia was assessed by the 5-minute APGAR score. In the control group, asphyxia was present in only 4.8% (1) of the newborns. In the early neonatal death group, APGAR scores below 7 were found in the majority of the sample, 83.3% (15). There was a significant association (*p* value=0.001) between APGAR scores below 7 at the 5th minute of life and early neonatal death, indicating the presence of asphyxia at birth.

DISCUSSION

Early neonatal death is defined as the death of a newborn from zero to 6 days after birth and represents approximately 73% of the postnatal deaths worldwide. Deaths in this period of life are responsible for a large portion of the deaths of children under 5 years of age[11]. Understanding the factors associated with these deaths and knowing the context of each region are essential for improvements in care and to lower the number of deaths, thus reducing mortality rates. The present study revealed that the weight of newborns is a relevant variable in determining the risk of early neonatal death. In a study carried out in Angola in 2018, early neonatal death was more expressive among newborns born with less than 2,500g, similar to the findings obtained herein. Deaths in the late neonatal period (over 6 days) were more associated with prematurity [12]. This study showed that there was a significant difference in the median birth weight of children who died (*p* value=0.001, Mann-Whitney test) when compared to the group of children who survived (915g*vs*. 3,180g, respectively). These findings corroborate the association between low birth weight and early neonatal death. Low weight and prematurity have an intimate relationship, often occurring concomitantly. The Intergrowth-21st study showed that the presence of very low birth weight (VLBW) is associated with extreme prematurity since the 50th percentile of birth weight for fetuses aged 32 weeks is equal to 1,500g [13]. Despite the consistent epidemiological data already reported in the literature, one survey analyzed infant mortality and

low birth weight, comparing two cities in regions with distinct geographic and economic characteristics, the Brazilian Northeast and Southeast. The authors found a dissociation between low birth weight and infant mortality, which was considered an epidemiological paradox. The possible explanation would be the access to earlier medical interventions, a fact that could justify such discrepancy in the results (Da Silva, 2003). Preterm birth is a major public health problem and is the primary cause of mortality among children under age 5, with most of these deaths still occurring in the neonatal period (Walani, 2020). Data from the literature corroborate what was found in this study, where, among 21 children who had an early neonatal death, 18 were classified as preterm. Prematurity, in addition to being a risk factor for neonatal death, is associated with conditions such as hypoglycemia, hypotension, and neurological deficit, as well as long-term physical and mental development deficits, which makes it a condition of high morbidity (Field, 2008). The importance of prematurity as one of the leading causes of mortality in children under 1 year of age in Brazil has been evidenced by the WHO, as well as other factors, such as birth asphyxia and traumatic birth (WHO, 2019). It is imperative that the differences between the various countries and regions of the world be considered. In a study carried out in Ethiopia, while analyzing the survival status and predictors of mortality in NBs with low birth weight in a neonatal referral unit in the city of Bahir Dar, the authors also reported that the neonatal mortality rate did not follow the decrease in infant mortality (Woelile, 2021). Among the analyzed variables, birth weight (in grams) and gestational age (in weeks) were each stratified into three categories: <1,000g; 1,000-1,500g; 1,500-2,500g; 28-32w; 32-37w, and>37w. The weight range with the highest death rate was NBs born with less than 1,000g (82.9%), while the GA range with the highest percentage of deaths was between 28 and 32 weeks. In the Discussion section, the authors stated that the overall 28-day survival rate varied compared to other countries and regions in Africa. This fact could be explained by the care given by a more trained and specialized hospital staff, in addition to a more adequate physical environment, in places with better socioeconomic conditions (Woelile, 2021). The city of Pelotas (RS), located in southern Brazil, hosted an epidemiological study over the course of 33 years with the objective of identifying the risk factors associated with mortality in premature infants with very low birth weight. The authors showed that 61% of neonatal deaths occurred when the birth weight was below 1,500g (Victora, 2018). The association of low birth weight and prematurity with neonatal death was demonstrated in the presentassessment, corroborating the main results of the two aforementioned studies (Woelile, 2021 and Victora, 2020). The other variable that showed statistical relevance in this study was birth asphyxia, which was assessed by APGAR scores lower than 7 at the 5th minute of life.

This scale was designed by the American anesthesiologist Virginia Apgar in the mid-1950s (Apgar, 1957). Since then, this scoring system has been used universally as an indicator of vitality at birth. The APGAR score consists of 5 components: heart rate, breathing, tonus, presence of reflexes, and color. Each category ranges from 0 to 2 points, totaling 10 points. When evaluated at the 5th minute of life, the APGAR scale proved to be a predictor of neonatal survival (Cnattingius, 2017). Only1 out of 20 children in the control group had a 5-min APGAR score <7. Among the NBs who died, the majority (15) had an APGAR<7, indicating an association between the APGAR score and early neonatal death. As previously reported by the WHO (2019), asphyxia and prematurity are some of the primary causes of mortality in children under 1 year of age. One cross-sectional study, conducted in the city of Maringá (PR), Brazil, that analyzed pregnant women in an outpatient clinic for high-risk prenatal care, showed that most neonatal deaths occurred early. According to the authors, the main factors associated with such deaths were low birth weight and 5-min APGAR <7 (Demitto, 2017). These results were similar to those found herein, evidencing the relevance of adequate neonatal care in the delivery room. The number of prenatal consultations is extremely important in the context of maternal and fetal health. In the present study, the incomplete recording of such data rendered the analysis of associations with early neonatal death impossible. The Prenatal Care and Birth Humanization Program (PHPN), instituted by the Brazilian Ministry of Health in 2000, aims to standardize care for pregnant women to improve health care for this population, reducing maternal and neonatal mortality. Some of the recommendations proposed in the program include: accommodation, recruitment of pregnant women at the end of the 1st trimester, active search for absentee pregnant mothers, carrying out a minimum of 6 consultations, complementary exams, educational actions, encouraging normal delivery, bonding with the birth location, and proper registration in the pregnant woman's health card[22]. Recording information on the pregnant woman's prenatal care in the medical records can provide important data for the conduct of care and prevention during childbirth. The Brazilian Neonatal Research Network (RBPN) has 20 associated centers, and its records show that the lower the gestational age, the higher the death rate. Currently, the limit of viability in public university centers of reference is between 25 and 26 weeks (Rede Brasileira de Pesquisas Neonatais, 2021). Thus, neonatal mortality, particularly of premature infants, also depends on the place of birth and the conditions of access to adequately qualified health services. The present study included pregnant women whose deliveries took place in 2018, 2019, and 2020. The year 2020 culminated with the pandemic of the new Coronavirus, SARS-CoV-2, a disease known as COVID-19. In this study, none of the mothers had suggestive clinical presentation or positivity to the disease. However, mass testing only began in 2021, a fact that hinders ruling out asymptomatic cases. According to the COES MINAS COVID-19 technical note No. 18, of April 1, 2020, the high demand for tests and the difficulty in acquiring inputs made COVID-19 testing unfeasible at that time as a strategy for mass tracking of the disease[24]. Therefore, the absence of COVID-19 tests in the medical records of the pregnant women in this sample may be associated with the norms in force in that period.

CONCLUSION

Early neonatal mortality is an extremely important subject in neonatology studies. The relevance lies mainly in the fact that these deaths represent a large part of the avoidable losses of children under five years of age. The UN's Sustainable Development Goals represent a milestone in the fight to reduce infant and child mortality rates around the world. Reducing these indices is essential for sustainable development and the health and balance of future generations. The analysis of data obtained from the medical records of the reference health service in the microregion of São João del-Rei indicated three factors as the most important for early neonatal death: birth weight, gestational age, and APGAR<7 at the 5th minute of life. The analysis of these data is important for understanding the factors that have the greatest impact on death and, thus, to provide guidance for planning care and health promotion actions for pregnant women and newborns. Efforts to reduce mortality rates must not be interrupted.

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