Risk factors for mortality of very low birth weight newborns at a Neonatal Intensive Care Unit

Fatores de risco para a mortalidade de recém-nascidos de muito baixo peso em Unidade de Terapia Intensiva Neonatal

Factores de riesgo para la mortalidad de recién nacidos de muy bajo peso en Unidad de Terapia Intensiva Neonatal

Jair Almeida Carneiro[1], Magda Mendes Vieira[2], Tatiana Carvalho Reis[2], Antônio Prates Caldeira[3]

ABSTRACT

Objective: To identify variables associated with mortality among very low birth weight infants admitted to a Neonatal Intensive Care Unit in Minas Gerais, Southeastern Brazil.

Methods: Cross-sectional study based on chart data of a random sample of premature newborn infants admitted to a Neonatal Intensive Care Unit from January 2007 to June 2010. Inborn infants weighing less than 1500g were eligible for the study. Maternal demographic variables, variables related to health conditions during pregnancy and delivery and variables related to newborn infants were collected. The association between variables was measured by chi-square test and *Odds Ratio*. Variables associated up to the level of 25% ($p<0.25$) in the bivariate analysis were included in the multivariate analysis by logistic regression, assuming a significance level of 5% ($p<0.05$).

Results: Data of 184 patients were analyzed, and 44 (23.9%) of them died. The variables that remained statistically associated with death in very low birth weight infants after the multivariate analysis were: birth weight below 1000g (OR 7.29; 95%CI 3.19–16.63; $p<0.001$), Apgar Score at the 1st minute <7 (OR 3.57; 95%CI 1.53–8.32, $p=0.003$), and report of less than four prenatal visits (OR 2.72; 95%CI 1.19–6.23, $p=0.018$).

Conclusions: The results show gaps in prenatal care and the need for perinatal care improvement addressed to both mothers and infants.

Key-words: neonatal mortality; infant, very low birth weight; infant, premature; Intensive Care Units.

RESUMO

Objetivo: Identificar os fatores associados à mortalidade de recém-nascidos de muito baixo peso internados em uma Unidade de Terapia Intensiva Neonatal de referência no Norte de Minas Gerais, Brasil.

Métodos: Estudo transversal baseado na análise de prontuários de uma amostra aleatória de recém-nascidos admitidos em uma Unidade de Terapia Intensiva Neonatal de janeiro de 2007 a junho de 2010. Foram considerados elegíveis para o estudo recém-nascidos com peso inferior a 1500g, provenientes do bloco obstétrico da própria instituição. Foram identificadas variáveis demográficas maternas, variáveis relacionadas às condições de gestação e parto e variáveis do recém-nascido. A associação entre as variáveis foi aferida por meio do teste do qui-quadrado e *Odds Ratio*. As variáveis associadas até o nível de 25% ($p<0,25$) na análise bivariada foram inseridas na análise

Instituição: Centro de Ciências Biológicas e da Saúde da Universidade Estadual de Montes Claros (Unimontes), Montes Claros, MG, Brasil
[1]Estudante de Medicina da Unimontes, Montes Claros, MG, Brasil
[2]Estudante de Enfermagem da Unimontes, Montes Claros, MG, Brasil
[3]Doutor em Pediatria; Professor de Medicina e do Programa de Pós-Graduação em Ciências da Saúde da Unimontes, Montes Claros, MG, Brasil

Endereço para correspondência:
Antônio Prates Caldeira
Avenida Cula Mangabeira, 562 – Santo Expedito
CEP 39401-001 – Montes Claros/MG
E-mail: antonio.caldeira@unimontes.br

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múltipla por meio da regressão logística, assumindo-se o nível de significância de 5% (p<0,05).

Resultados: Foram selecionados e analisados os dados referentes a 184 prontuários, que registraram 44 óbitos (23,9%). As variáveis que se mantiveram estatisticamente associadas ao óbito de recém-nascidos de muito baixo peso, após análise multivariada, foram: peso de nascimento abaixo de 1000g (OR 7,29; IC95% 3,19–16,63; p<0,001), boletim de Apgar de 1º minuto menor do que sete (OR 3,57; IC95% 1,53–8,32; p=0,003) e realização de menos de quatro consultas de pré-natal (OR 2,72; IC95% 1,19–6,23; p=0,018).

Conclusões: Os resultados denotam falhas na assistência pré-natal e a necessidade de melhoria em relação aos cuidados perinatais ao binômio mãe e filho.

Palavras-chave: mortalidade neonatal; recém-nascido de muito baixo peso; prematuro; Unidades de Terapia Intensiva.

RESUMEN

Objetivo: Identificar los factores asociados a la mortalidad de recién nacidos de muy bajo peso, internados en una Unidad de Terapia Intensiva Neonatal de referencia en el Norte de Minas Gerais, Brasil.

Métodos: Estudio transversal, basado en el análisis de prontuarios de una muestra aleatoria de recién nacidos admitidos en una Unidad de Terapia Intensiva Neonatal desde enero de 2007 hasta junio de 2010. Fueron considerados elegibles para el estudio los recién nacidos con peso inferior a 1.500g, provenientes del bloque obstétrico de la propia institución. Fueron identificadas variables demográficas maternas, variables relacionadas a las condiciones de gestación y parto y variables del recién nacido. La asociación entre las variables fue verificada por medio de la prueba de chi cuadrado y *Odds Ratio*. Las variables asociadas hasta el nivel de 25% (p<0,25), en el análisis bivariado, fueron insertadas en el análisis múltiple por medio de la regresión logística, asumiéndose el nivel de significancia de 5% (p<0,05).

Resultados: Fueron seleccionados y analizados los datos referentes a 184 prontuarios, que registraron 44 óbitos (23,9%). Las variables que se mantuvieron estadísticamente asociadas al óbito de recién nacidos de muy bajo peso, después de análisis multivariado, fueron: peso de nacimiento inferior a 1.000g (OR 7,29; IC95% 3,19-16,63; p<0,001), boletín de Apgar de primer minuto inferior a siete (OR 3,57; IC95% 1,53-8,32; p=0,003) y realización de menos de cuatro consultas de prenatal (OR 2,72; IC95% 1,19-6,23; p=0,018).

Conclusiones: Los resultados denotan fallas en la asistencia prenatal y la necesidad de mejorías respecto a los cuidados perinatales al binomio madre e hijo.

Palabras clave: mortalidad neonatal; mortalidad infantil; recién nacidos de muy bajo peso; prematuro; Unidades de Terapia Intensiva.

Introduction

Infant mortality remains an important public health challenge in Brazil[1]. In particular, neonatal mortality, despite the reductions assigned to improved neonatal care, remains high when compared with the rates in other countries[1-3]. The importance of the neonatal component in infant mortality has motivated studies and research innovation to investigate the causes and determining factors of death in this age group[1,4-7].

In neonatal populations, premature and low birth weight newborns are the most vulnerable groups. Very low birth weight newborns (VLBW), that is, those that have a birth weight below 1500g, are the ones that contribute the most for high mortality rates in infancy.

VLBW infant survival has increased in several countries, even developing countries, but mortality remains a source of concern[8,9]. Lower rates have been assigned to improvements in perinatal care, such as the better access to life support technologies for neonates, seen in new neonatal intensive care units (NICU) and the use of exogenous surfactant, for example[9].

The study of the risk factors of neonatal death, indicators of the several aspects of mother and child healthcare, enable us to understand the links in the chain of determinant events that lead to death and to identify groups exposed to different risks. In the case of VLBW newborns, the study of factors associated with death may lead to the critical analysis of healthcare services and actions aimed at improving care for this group. Therefore, studies may help to identify the different healthcare needs and provide subsidies for interventions aimed at reducing infant death during the early prenatal period[10,11].

This study evaluated factors associated with the mortality of VLBW infants in a reference NICU in northern Minas Gerais, Brazil.

Method

This retrospective cross-sectional study included data from medical records of a random sample of newborns admitted to the NICU of the Clemente de Faria University Hospital (HUCF) of Universidade Estadual de Montes Claros (Unimontes) in Montes Claros, a town in the state of Minas Gerais, Brazil, from January 2007 to June 2010. The HUCF maternity is a reference for high-risk pregnant women in northern Minas Gerais, and has been evaluated as a safe maternity ward.

Inborn infants were eligible if they weighed less than 1500g at birth. During the study, 24,739 births were recorded in town, and 2,914 newborns (11.9%) weighed less than 2500g. Of those, 610 weighed less than 1500g, and 286 (46.9%) were born in the HUCF maternity ward and comprised the population for this study. The calculation of sample size showed that 181 medical records should be analyzed considering an estimated frequency of 50% of the event under analysis, a 5% error margin and a 95% confidence interval, with an addition of 10% to compensate for possible losses. The estimated frequency of the event was arbitrarily set at 50% because there were no previous local studies, and 50% was a conservative value that resulted in a larger sample size. Newborns with major malformations and genetic syndromes were excluded.

The following maternal data were collected: age; place of residence (town versus out of town); education; marital status (stable partnership versus other); parity (primipara versus not primipara); number of prenatal visits; smoking (any amount versus no smoking); gestational risk (normal versus high); hospitalization during pregnancy; use of antenatal corticosteroids; and type of delivery (vaginal versus cesarean). The following infant data were collected: sex; birth weight; multiple gestation; gestational age; Apgar score; resuscitation in delivery room; use of mechanical ventilation; use of surfactant. Clinical status and disorders detected in the newborn (sepsis, neonatal respiratory distress syndrome, necrotizing enterocolitis, etc.) were not evaluated in this study.

The dependent variable was outcome at discharge: survival or death. All collected data were analyzed using the Statistical Package for the Social Sciences (SPSS) 17.0 (SPSS for Windows, Chicago, IL). A chi-square test was used to evaluate the association between variables. To evaluate the magnitude of associations, odds ratio and 95% confidence intervals were calculated. The variables with a level of

Table 1 - Characteristics of mothers of very low birth weight infants admitted to a neonatal intensive care unit

	n	%
Mother's age		
14 to 19 years	42	22.8
20 to 29 years	99	53.8
30 to 47 years	43	23.4
Place of residence (same town)	66	35.9
Maternal schooling		
Illiterate	11	6.0
Incomplete elementary school	71	38.6
Complete elementary school	20	10.9
Incomplete secondary school	33	17.9
Complete secondary school	37	20.1
College	12	6.5
Marital status (stable partnership)	93	50.5
Primipara	81	44.0
Smoking	20	10.9
Gestational risk	152	82.6
Hospitalization during gestation	97	52.7
Use of antenatal corticosteroids	97	52.7
Vaginal delivery	70	38.0
Prenatal visits		
0 to 3	51	27.7
4 to 6	109	59.2
≥7	24	13.0

Table 2 - Characteristics of very low birth weight infants admitted to a neonatal intensive care unit

	n	%
Male sex	85	46.2
Multiple gestation	23	12.5
Gestational age (weeks)		
23 to 27	48	26.1
28 to 31	99	53.8
32 to 35	37	20.1
Birth weight <1000g	44	23.9
Apgar score at 1 minute		
0 to 4	44	23.9
5 to 7	71	38.6
8 to 10	69	37.5
Apgar score at 5 minutes		
0 to 4	4	2.2
5 to 7	48	26.1
8 to 10	132	71.7
Mechanical ventilation	139	75.5
Surfactant	69	37.5
Resuscitation in delivery room	49	26.6
Outcome at discharge		
Death	44	23.9
Survival	140	76.1

significance of up to 25% ($p<0.25$) in bivariate analysis were evaluated together using logistic regression, and the level of significance at this step was set at 5% ($p<0.05$).

This study was approved by the Ethics in Research Committee of the School of Medicine of Unimontes.

Results

Data from 184 medical records of VLBW neonates were collected and analyzed during the study. Table 1 shows the main sociodemographic characteristics of the mothers in the group. There was a high percentage of teenage mothers (22.8%), with no stable marital life (49.5%), who did not finish secondary school (55.5%) and who had fewer than four prenatal visits (27.7%).

The characteristics of the newborns evaluated are shown in Table 2. Birth weight ranged from 450g to 1400g, and mean weight was 1110±253g. Gestational age ranged from 23 to 35 weeks. Multiple gestations accounted for 12.5% of the premature infants, and there was a slight predominance of female sex (53.8%). About one fourth of the newborns had an Apgar score at 1 minute below five. Mechanical ventilation was used in 75.0% of the infants, and the use of surfactant was recorded for 37.5% of the VLBW newborns.

There were 44 deaths in the sample under study (23.9%). NICU hospitalization lasted from one to 158 days, and

Table 3 - Association between maternal variables and death of very low birth weight infants admitted to a neonatal intensive care unit

	Death		Survival		*p*-value	OR (95%CI)
	n	%	n	%		
Maternal age (years)					0.311	
<20	13	29.5	29	20.7		1.61 (0.70–3.68)
≥20	31	70.5	111	79.3		1.0
Place of residence					0.327	
Other towns	25	56.8	93	66.4		0.66 (0.31–1.41)
Same town	19	43.2	47	33.6		1.0
Maternal schooling					0.100	
<8 years	13	29.5	63	45.0		0.51 (0.23–1.12)
≥8 years	31	70.5	77	55.0		1.0
Marital status					0.548	
Single/others	24	54.5	67	47.9		1.31(0.63–2.73)
Stable partnership	20	45.5	73	52.1		1.0
Parity					0.458	
Primipara	22	50.0	59	42.1		1.37 (0.66–2.86)
Other than primipara	22	50.0	81	57.9		1.0
Smoking					0,414	
Yes	3	6.8	17	12.1		0.53 (0.12–2.06)
No	41	93.2	123	87.9		1.0
Gestational risk					0.399	
High risk	34	77.3	118	84.3		0.63 (0.25–1.60)
Usual risk	10	22.7	22	15.7		1.0
Prenatal visits					0.021	
<4	24	54.5	47	33.6		2.37 (1.13–5.01)
≥4	20	45.5	93	66.4		1.0
Hospitalization during gestation					0.809	
Yes	22	50.0	75	53.6		0.87 (0.42–1.80)
No	22	50.0	65	46.4		1.0
Use of antenatal corticosteroids					0.201	
No	25	56.8	62	44.3		1.66 (0.79–3.47)
Yes	19	43.2	78	55.7		1.0
Delivery					0.181	
Vaginal	21	47.7	49	35.0		1.70 (0.81–3.56)
Caesarean	23	52.3	91	65.0		1.0

median stay was 15 days; 76% of the premature infants were dismissed from the NICU before the 30th day of life.

Table 3 shows the associations between maternal variables and the outcome death. Table 4 shows the same analysis for the neonate variables. The variables with an association of up to 25% were evaluated together using logistic regression. The variables that remained statistically associated with VLBW neonate death after logistic regression were: birth weight below 1000g (OR 7.29; 95%CI 3.19-16.63; $p<0.001$), Apgar score at 1 minute below seven (OR 3.57; 95%CI 1.53-8.32; $p=0.003$) and fewer than four prenatal visits (OR 2.72; 95%CI 1.19-6.23; $p=0.018$).

Discussion

This study collected data about survival of VLBW neonates admitted to a reference NICU in northern Minas Gerais, Brazil, and findings revealed a high percentage of deaths, although close to what has already been recorded in other hospitals in Brazil. The mortality rate for VLBW neonates in towns other than the capital city of the state of Sao Paulo changed from 36.2 to 29.5% between 1995 and 2000[12]. In Rio de Janeiro, the percentage of deaths for the same type of patients ranged from 10 to 37% in four maternity wards[13]. In Fortaleza, in the state of Ceará, that percentage was much higher: 51.2% for newborns weighing less than 1500g[14]. International studies also found similar results in developed countries[7,8], but some studies revealed better indices[15,16].

Lower mortality rates for VLBW newborns in developed countries suggest that rates may be reduced in Brazilian hospitals. Protocols, as well as the resources available in the NICU, should be standardized. A Brazilian multicenter study pointed to significant differences between the units

Table 4 - Association between infant variables and death of very low birth weight infants admitted to a neonatal intensive care unit

Variable	Death		Survival		*p*-value	OR (95%CI)
	n	%	n	%		
Apgar score at 1 minute					<0.001	
<7	33	75.0	51	36.4		5.24 (2.30–12.11)
≥7	11	25.0	89	63.6		1.0
Apgar score at 5 minutes					<0.001	
<7	14	31.8	13	9.3		4.56 (1.79–11.65)
≥7	30	68.2	127	90.7		1.0
Multiple gestation					0.295	
Yes	3	6.8	20	14.3		0.44 (0.10–1.68)
No	41	93.2	120	85.7		1.0
Surfactant					<0.001	
No	18	40.9	97	69.3		0.31 (0.14–0.65)
Yes	26	59.1	43	60.7		1.0
Mechanical ventilation					0.086	
Yes	38	86.4	101	72.1		2.45 (0.90–7.01)
No	6	13.6	39	27.9		1.0
Resuscitation					0.932	
Yes	12	27.3	37	26.4		1.04 (0.45–2.38)
No	32	72.7	103	73.6		1.0
Sex					0.073	
Male	26	59.1	59	42.1		1.98 (0.94–4.18)
Female	18	40.9	81	57.9		1.0
Birth weight					<0.001	
<1000g	30	68.2	27	19.3		8.97 (3.94–20.70)
≥1000g	14	31.8	113	80.7		1.0
Gestational age					<0.001	
<29 weeks	28	63.6	46	32.9		3.58 (1.67–7.73)
≥29 weeks	16	36.4	94	67.1		1.0

evaluated for percentages of neonatal deaths among VLBW premature infants even after controlling for clinical severity of their condition and other factors that indicate perinatal risk of death[17]

Of the variables that remained associated with mortality of VLBW newborns after multivariate analysis, birth weight below 1000g and number of prenatal visits below 4 may be seen as a summary measure of neonatal biological vulnerability and of low quality of prenatal care. To a certain point, the third variable identified in multivariate analysis (Apgar at 1 minute below seven) may also be seen as a sign of perinatal care, which includes obstetric and pediatric healthcare.

Low birth weight has been classically associated with neonatal death, and several recent studies have corroborated that[1,5,6,18]. Even when a specific population of neonates with birth weight below 1500g is analyzed, the lower the birth weight, the greater the risk of death[7,8,13,14,19].

The smaller the newborns, the more vulnerable they are. Such vulnerability, the result of organ and system immaturity, demands more interventions, which increases the risk of negative outcomes. Therefore, measures to reduce the number of premature deliveries should be taken, such as ensuring that mothers receive adequate prenatal follow-up. Better neonatal intensive care resources should be available, as well as better clinical practices, because there are limits to scientific advances that may reduce rates of low birth weight[20,21].

In agreement with other studies, Apgar scores were associated with greater risk of neonatal death. Apgar scores may represent the interface between obstetric and neonatal care and denote the scarcity of measures available to reduce perinatal hypoxia[23]. Therefore, infants in more critical conditions to adapt to the external environment run greater risks of negative outcomes, including death.

Also associated with greater risk of death in the group under study was the reduced number of prenatal visits (fewer than four). A higher number of prenatal visits does not necessarily mean high quality healthcare. However, a small number of visits points, invariably, to difficulties in access or delayed care, which reflects the low quality of prenatal care[23]. Future studies should analyze this factor, because the mere increase in the number of medical visits may not have a direct favorable impact on mortality. However, our results undoubtedly raise questions about the organization of local services to provide care to pregnant women.

Some of the factors associated with neonatal death according to other studies in the literature did not appear in the final model of multivariate analysis in our study. Gestational age, for example, classically and inversely associated with greater risk of neonatal death[7,17,24], did not remain significantly associated after data were analyzed together. Gestational age is not a precise measure and may be affected by the method used to define it: ultrasound, chronological criterion according to date of last menstruation, or clinical and neurological evaluation of the infant at birth. Therefore, the lack of standardization may have compromised the assessment of this variable.

Other studies that analyzed the combined effect of several factors on neonatal death also failed to find an effect of gestational age[1,8,13,18]. According to some authors, the difficulty in measuring gestational age accurately may generate similar results[7,13]. In a study conducted with VLBW infants in South Africa, the authors argued that, although gestational age may be an accurate measure and closely associated with risk of death, the methods used to define it, either late gestation ultrasound or clinical evaluation conducted by physicians with little experience, compromise its generalized use[7].

The variables associated with neonatal care, such as mechanical ventilation and use of corticosteroids or surfactant, were also not associated with greater mortality among VLBW infants. Medical technologies and the care provided to premature and low birth weight infants are known to have an impact on survival in this population[3,9,17]. However, the lack of standardized procedures precludes more rigorous analyses, and results should be interpreted in the context in which the study was conducted, considering, among other factors, the limitations discussed below.

In an analysis of similar and apparently paradoxical results of factors associated with neonatal mortality, Duarte and Mendonça reported that the use of surfactant was not associated with death of VLBW infants and that the risks were greater for neonates that received mechanical ventilation than for those that did not[21]. These results indicate the complexity of analysis of such interventions in the definition of explanatory models for death of VLBW newborns. If, on the one hand, interventions reflect the care provided, they may also be signs of disease severity.

The use of antenatal corticosteroids has been shown to be an important protective factor for premature infants[25]. However, some authors did not find any differences in the survival of VLBW neonates when these drugs were used[24]. A study conducted in towns other than the capital city in the state of São Paulo found a reduction in the mortality of

VLBW infants from 1995 to 2000. In the same time interval, the use of antenatal corticosteroids and surfactant increased in the hospital under analysis, but these variables were not included in the final explanatory model, and findings showed that neonatal sepsis was a more important factor[12]. In our study, the effect of neonatal sepsis was not evaluated, because the criteria for its diagnosis are not precise, and the use of antimicrobial drugs was common in the group under analysis.

The clinical variables associated with neonatal death may vary widely according to the characteristics of the population under study, the medical care practices adopted, the study methods used and the time interval under analysis, as pointed out by other authors[8,12].

The interpretation of the results of our study should take into consideration some study factors and limitations:

- This was a retrospective study with data collected from medical records and conducted in a single hospital.
- No criteria were included to define severity of neonatal clinical conditions in the evaluation of the variables associated with death.
- The group of neonates under analysis included only those that were admitted to the NICU, that is, those that had already survived the critical conditions of delivery and were classified as potential survivors still in the delivery room. However, it should be taken into consideration that it is not always possible to use a prospective design for similar analyses, particularly in less developed areas of Brazil. The continental dimensions of Brazil and the diversity of social and cultural characteristics in the different states of the country justify the need to conduct regional studies, such as the one presented here, so that more accurate knowledge of the Brazilian reality may be obtained.

The northern region of Minas Gerais, a place of well-known socioeconomic needs and that has a population of over 1.5 million inhabitants, has only 28 beds in the pediatric ICU, including the beds for premature infants. This study generated data about the factors associated with the mortality of VLBW infants hospitalized in a NICU in this region. These findings should be analyzed and taken into consideration by governmental officials, and should subsidize measures to restructure the maternal and neonatal care networks, focusing on the reduction of neonatal mortality. Moreover, these data should be carefully analyzed by healthcare personnel working in the NICUs in the region, and partnerships should be established. The building of NICU networks has been pointed out as an important tool to improve medical care quality and safety for premature neonates and their families[26].

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