High risk pregnancies and factors associated with neonatal death*

Gestação de alto risco e fatores associados ao óbito neonatal

Gestación de alto riesgo y factores asociados con la defunción neonatal

Marcela de Oliveira Demitto[1], Angela Andréia França Gravena[1], Cátia Millene Dell'Agnolo[1], Marcos Benatti Antunes[1], Sandra Marisa Pelloso[1]

ABSTRACT

Objective: To identify the factors associated with intra-hospital neonatal mortality based on the individual characteristics of at-risk pregnant mothers, delivery and newborns. **Method:** This was a cross-sectional epidemiological study of live newborns delivered by women attended at the high-risk outpatient unit of a philanthropic hospital in Maringá, Paraná, Brazil between September 2012 and September 2013. **Results:** Six hundred and eighty-eight women participated in the study. The neonatal mortality coefficient found was 17.7/1,000 live births, most in the early neonatal phase. Premature labor, fetal malformation and multiple gestations were associated with neonatal death. Premature, very low birth weight newborns and those with an Apgar score of less than seven, five minutes after birth were at high risk of death. **Conclusion:** Identifying risk factors can help plan actions to consolidate the perinatal network. Specific programs should be incentivized in other countries, in the search for significant perinatal results such as reducing neonatal mortality.

DESCRIPTORS

Pregnancy, High-Risk; Infant mortality; Neonatal Nursing; Maternal-Child Nursing; Epidemiological Factors; Risk factors.

Corresponding author:
Marcela de Oliveira Demitto
Universidade Estadual de Maringá
Av. Colombo, 5790
CEP 87020-900 – Maringá, Paraná, Brazil
mar_demitto@hotmail.com

INTRODUCTION

Infant mortality has dropped significantly all over the world. In Brazil, infant mortality dropped from 51 deaths per thousand live births in 1990 to 15 per thousand in 2015[1]. Even in light of these advances, the infant mortality rate in Brazil is 19.88 deaths per 1,000 live births, ranking the country in 90th place out of 187 nations in the United Nations ranking, behind Cuba (5.25), Chile (6.48), Argentina (12.8), China (15.4) and Mexico (16.5)[2].

If we break down infant mortality by age, worldwide, neonatal (0 to 27 days) deaths account for 44% of all deaths among children under the age of five[3]. In Brazil this component is even larger, and can be as high as 70% in all regions[2], with 11.2 deaths per thousand live births between 2011 and 2012[4].

In the state of Paraná, neonatal deaths dropped from 2,426 in 1996 to 1,279 in 2014 (94.8% less). However, in spite of all the progress made, 71.8% of infant deaths in 2014 were in the neonatal period[5]. According to the Report on Levels and Trends in Infant Mortality (*Relatório de Níveis e Tendência em Mortalidade Infantil*), the main goal is to reduce mortality in the neonatal period, which is where most infant deaths occur[1].

To reduce maternal and infant mortality, and the high percentage of avoidable deaths, in 2012 a public policy for prenatal care and for the care of newborns at risk was created in Paraná. It focuses on early detection of pregnant women at risk, their prenatal care, risk stratification of mothers and infants, specialized ambulatory care for pregnant women and infants (under the age of one) at risk, and ensured delivery via a system that is linked to the hospital[6].

Numerous studies have attempted to analyze the causes of neonatal deaths. Studies show a strong link between neonatal deaths and maternal and infant life conditions and health, economic situation, and access to healthcare, and to biological conditions such as gestational age, weight at birth and Apgar index[7]. We also call attention to the risk in the current and previous pregnancy (prior stillbirth, premature or low birth weight infants), the movement of the pregnant woman to delivery and women giving birth to low-weight babies (< 1,500 grams) in hospitals not equipped with a Neonatal Intensive Care Unit (NICU)[4]. Studies show that among newborns in NICU, Cesarean birth, failure to use steroids, pre-eclampsia, oligohydramnios, <2,500 grams at birth, Apgar<7 in the fifth minute of life, endotracheal intubation and failure to use a surfactant are also associated with neonatal death[8].

Death in this period reflects socioeconomic and reproductive conditions, and is also related to the quality of pre-natal care and care during delivery, revealing gaps in the healthcare network[9-10]. Given the significance of neonatal mortality as an indicator of maternal/infant health, this study aimed to identify the facts associated with intra-hospital neonatal mortality based on the individual characteristics of at-risk mothers, the delivery and the newborn.

METHOD

STUDY DESIGN AND POPULATION

This was a cross-sectional epidemiological study on newborns delivered by 688 women followed by the high-risk outpatient unit of a philanthropic hospital in Maringá, Paraná, Brazil, between September 2012 and September 2013. This period corresponds to the first year of the care program for high-risk pregnant women and newborns[7]. Stillbirths were not included in this study.

DATA GATHERING AND STUDY VARIABLES

The data were gathered by researchers between May and August 2014 and were taken from the pregnant woman's hospital records, which include a tool for evaluating gestation risk based on the following indicators: pre-existing clinical conditions (arterial hypertension, heart diseases, lung diseases, renal diseases, endocrine diseases, blood diseases, infectious illnesses and drug dependency), and obstetrical history (fetal and neonatal deaths, < 2,500 grams at birth, more than three Cesareans, placental accreta, bleeding in the second semester, pre-eclampsia, cervical cerclage, premature amniorrhexis, premature labor, premature delivery, repeated miscarriages), and clinical incidents (urinary tract infection, rubella, toxoplasmosis, gestational-specific hypertension, intrauterine growth limitations, premature labor, placenta previa, premature amniorrhexis, RhD alloimmunization, fetal malformation, concept macrosomia, multiple gestation)[5]. We also used birth records and newborn death certificates to complement the information in the file and check cause of death.

The dependent variable was death during the neonatal period. The independent variables were split into three groups: I – Maternal social, economic and demographic characteristics: race/skin color (white, brown or black), marital status (married, divorced, single or widowed), years of schooling (fewer than 8 years, 8 or more years), occupation (paid or non-paid), city of residence (Maringá or other cities and towns), religion (Catholic, other), age (19 or under, 20-34, 35 or older); II – Assessment of gestational risk: pre-existing clinical conditions, obstetrical history and clinical incidents in the current gestation; III – Overall delivery and newborn characteristics: type of gestation, type of delivery, parity, gestational age, newborn gender, weight at birth, Apgar index at one and five minutes. Cause of death was taken from the death certificate.

Missing (unknown) data is not included in the tables.

DATA ANALYSIS

The initial analysis showed a relationship between neonatal death and variables in all three groups. We used an Odds Ratio (OR) analysis of the gross data to analyze the association between risk factors and outcome using Epi Info 3.5.1, with a level of significance of 5%. After this, to assess the possible confusion variables in the bivariate analysis, we used logistics regression to select the variables with a level of significance of less than 0.20 ($p \leq 0.20$). We used Statistica 7.1 with significance level of of 5% and 95% Confidence Interval.

This study complies with National Health Board Standards and Guidelines Governing Research Involving Human Beings (CNS (*Conselho Nacional de Saúde*) Resolution 466/2012), and was approved with Opinion n. 681317/2014.

RESULTS

Six hundred and eighty-eight women and 732 live newborns were involved in the study, all coming from the high-risk outpatient unit. Among the births was one case of triplets and 42 women had twins. All medical files were reviewed, although there were gaps in the data. The neonatal mortality coefficient was 17.7 per thousand live births (1.8%), with a total of 13 neonatal deaths, 76.9% in the early neonatal period (0-6 days), and 23.1% in the late neonatal period (7-27 days).

Regarding the cause of the neonatal deaths, premature birth topped the list and accounted for 92.3%. This was followed by infection (46.1%), neonatal anoxia (46.1%), maternal factors (23.0%) and congenital malformations (15.3%). Other causes were present in smaller numbers, such as lung and gastric bleeding, cardiorespiratory arrest, acute renal failure and persistently patent arterial duct.

While we found more neonatal deaths among the children of white women who were married, gainfully employed, catholic, aged 20 to 34 with more years of schooling, we found no statistical association between these variables and neonatal death (Table 1).

Table 1 – Social, economic and demographic characteristics of pregnant women followed by the high-risk outpatient clinic, according to neonatal death – Group I – Maringá, Paraná, Brazil, 2014.

| Variables | Neonatal Death | | | | p |
| | Yes* | | No* | | |
	n	%	n	%	
Age					
19 or younger	2	2.8	69	97.2	
20-34	9	1.9	460	98.1	0.75
≥ 35	2	1.4	146	98.6	
Years of schooling					
8 or less	2	1.3	156	98.7	
≥ 8	11	2.1	519	97.9	0.39
Race/Color					
White (Caucasian)	9	2.1	415	97.9	
Brown	4	1.7	228	98.3	0.67
Black	-	-	32	100.0	
City of Residence					
Maringá	8	2.6	301	97.4	
Other locations	5	1.3	374	98.7	0.17
Marital status					
Married	10	2.5	394	97.5	
Divorced	0	0	11	100	
Single	3	1.1	263	98.9	0.59
Windowed	-	-	5	100.0	
Religion					
Catholic	9	2.1	410	97.9	
Other	4	1.5	265	98.5	0.37
Occupation					
Paid	7	1.7	395	98.3	
Unpaid	6	2.1	278	97.9	0.72

*Unknown data was excluded.

Among the overall delivery characteristics (type of gestation, type of delivery, parity, gestational age) and of the newborn (gender, weight at birth, Apgar at minute one and five), in both the bivariate analysis as well as logistics regression neonatal death was associated with premature birth, very low birth weight and Apgar lower than seven in the fifth minute of life (Table 2).

In terms of gestational risk, we found no relationship between pre-existing conditions and neonatal death. In terms of clinical incidents during the current gestation,

after a logistic regression analysis, women who went into premature labor and birth, fetal malformations and multiple gestations presented high risk for an outcome of neonatal death (Table 3).

Table 2 – Overall characteristics of the delivery and newborn of women followed by the high-risk outpatient unit, according to neonatal death – Group III – Maringá, Paraná, Brazil, 2014.

Variables	Neonatal Deaths					
	Yes* n (%)	No* (n%)	Gross OR (CI 95%)	p	OR Adjusted (CI 95%)	p
Gestational Age (weeks)						
< 28	5 (55.6)	4 (44.4)	69.37 (54.00-203.39)	<0.001	682.47 (64.31-7241.65)	<0.001
28-31	4 (28.6)	10 (71.4)	22.00 (2.05-740.98)	<0.001	260.61 (25.24-2690.63)	<0.001
32-36	2 (1.8)	107 (98.2)	10.37 (0.73-29.41)	0.07	11.30 (1.01-127.07)	0.04
≥ 37	1 (0.2)	555 (99.8)	1.0			
Parity						
Primiparous	4 (2.1)	190 (97.9)	1.26 (0.32-4.66)	0.74		
Multiparous	8 (1.6)	478 (98.4)	1.0			
Type of Delivery						
Cesarean	9 (1.8)	500 (98.2)	0.78 (0.22-3.06)	0.74		
Normal	4 (2.2)	174 (97.8)	1.0			
Type of Gestation						
Single	10 (1.6)	632 (98.4)	1.0			
Multiple	2 (4.7)	41 (95.3)	3.08 (0.01-15.73)	0.17	0.49 (0.04-5.28)	0.56
Gender						
Female	5 (1.4)	344 (98.6)	0.77 (0.21-2.74)	0.66		
Male	7 (1.8)	373 (98.2)	1.0			
5-minute Apgar						
< 7	7 (35.0)	13 (65.0)	75.82 (18.37-326.86)	<0.001	36.36 (5.35-247.13)	<0.001
≥ 7	5 (0.7)	704 (99.3)	1.0			
Weight at birth (grams)						
< 1500	9 (36.0)	16 (64.0)	34.13 (8.90-475.92)	< 0.001	217.73 (22.18-2137.08)	<0.001
1500-2499	2 (1.9)	105 (98.1)	11.31 (0.80-317.90)	0.06	7.46 (0.61-90.73)	0.11
≥ 2500	1 (0.2)	594 (99.8)	1.0			

*Unknown data was excluded.

Table 3 – Stratification of gestational risk, preexisting clinical conditions, obstetrical history and clinical incidents during the current gestation of women seen at the high-risk outpatient unit, according to neonatal death – Group II – Maringá, Paraná, Brazil, 2014.

Risk stratification	Neonatal Death					
	Yes* n (%)	No* (n%)	Gross OR (CI 95%)	p	OR Adjusted (CI 95%)	p
Obstetrical history						
Fetal and neonatal death	4 (7.4)	50 (92.6)	5.56 (1.38-20.69)	0.001	3.60 (0.93-13.89)	0.06
Low birth weight	3 (6,7)	42 (93.3)	4.52 (0.95-18.77)	0.04	1.74 (0.27-11.11)	0.55
Premature labor	3 (6.3)	45 (93.8)	6.22 (1.54-23.29)	0.01	3.58 (0.65-19.53)	0.13
Premature labor	3 (6.0)	47 (94.0)	4.01 (0.84-16.64)	0.06	0.85 (0.11-6.31)	0.87
Clinical incidents during the current gestation						
Premature labor	3 (10.7)	25 (89.3)	7.80 (1.59-33.58)	0.01	11.43 (2.70-48.27)	< 0.001
Fetal malformation	2 (6.9)	27 (93.1)	4.36 (0.01-22.50)	0.10	7.92 (1.50-41.67)	0.01
Multiple gestations	3 (6.0)	47 (94.0)	4.01 (0.84-16.54)	0.06	6.01 (1.45-24.87)	0.01

*Unknown data was excluded.

DISCUSSION

This is the first Brazilian study aimed at analyzing the factors associated with mortality during the neonatal period, based on a public healthcare policy focused on high-risk pregnancies, identifying health conditions of the mother and newborn that increase the risk of death during the neonatal period.

The neonatal mortality coefficient in this study (17.7 deaths/1,000 live births) is below the 2012 world average (21/1,000 live births)[3], but far above that found in other parts of Brazil, such as the south, southeast, middle-west and northeast, at 6.1, 8.0, 8.4 and 14.5 deaths per 1,000 live births respectively[4]. One should use caution when comparing these numbers however, as this study was based on women with high-risk pregnancies.

The higher percent of deaths in the early neonatal phase corroborates data in the literature showing that this period is the main component of infant death worldwide, with many (25%) of the deaths happening in the first 24 hours[11].

In this study, an Apgar below seven was statistically associated with neonatal death. A recent study of 1,029,207 live births in Salvador showed that an Apgar of less than seven in the fifth minute of life was associated with a higher risk of neonatal death. This association was even stronger at Apgars between 0 and 3, showing the importance of this assessment in contemporary practice[12].

An Apgar of less than seven in the fifth minute of life shows a need for immediate care to minimize the consequences of poor brain oxygenation[13]. A high risk of neonatal death in cases of asphyxia/hypoxia may be related to poorly trained professionals and the absence of suitable technological resources. This is thus a sensitive indicator of the quality of the care provided during labor and delivery[14].

This study showed that only very low birth weight newborns (<1,500 grams) were at risk of death during the neonatal period (OR = 217.73), which may be explained by the fact that these infants required long periods in the NICU to gain weight, exposing them to infections and other complications[15].

Low birth weight is an important characteristic of the newborn, and is the main isolated predictor of neonatal death, with evidence of higher risk of death as birth-weight goes down[4,16].

The existence of clinical incidents during gestation may predict adverse perinatal results that may have as an outcome neonatal death[17]. In this study, fetal malformation, multiple gestations and premature labor were shown to be important risk factors for neonatal death, corroborating the *Nascer no Brasil* (Birth in Brazil) Survey[4].

A study of neonatal infant mortality among the offspring of high-risk pregnant women in Brazil shows that, of the newborn who died, 20.8% had congenital malformations like hydrocephaly, emphalocelle and renal malformation[18]. In a cohort study performed in Brazil, congenital malformation increased the risk of neonatal death 15.5-fold[18], suggesting the need to invest in early diagnosis, clinical and surgical treatment, and primary prevention to improve the evolution of these cases[19].

This survey included 42 gemellar and one triplet pregnancy. Regarding the type of gestation, it is known that newborns of multiple pregnancies are at higher risk of being premature and have low birth weight. Because of this, gemellarity is also considered a maternal factor associated with neonatal death[16].

Newborns of women with premature labor are 11 times more likely to die in the neonatal period. It is known that in these cases ante-natal corticosteroids and surfactants after birth are care practices that can minimize respiratory failure resulting from pulmonary immaturity of the newborn, with a positive impact on neonatal mortality[20].

Of the 13 neonatal deaths in this study, 12 were premature infants. A survey of premature and very low birth weight newborns found that those receiving a corticosteroid in the antenatal period were 3 times less likely to die in the neonatal period, and required 2.4 times less resuscitation, compared to those not receiving a corticosteroid[21].

Worldwide, 34% of neonatal deaths are due to the complications of premature birth[3]. In this survey, premature birth was present in almost all cases of neonatal death, followed by health problems that are likely related to this, such as infection and anoxia, which alerts to the need for measures focused on prevention, starting with early identification of the factors of pre-natal risk.

The variables indicating increased severity of newborns are statistically associated with neonatal death. These include premature birth, very low birth weight and Apgar less than seven in the fifth minute of life, factors also found in other studies[15,22-23].

Premature birth and neonatal mortality are inversely related. In other words, the smaller the gestational age of the newborn, the higher the risk of death, leading to a global concern with premature birth rates. In 2010, more than one in ten live births were premature, or about 15 million (11.1%), over a million of whom died because they were premature[24]. It is the main cause of neonatal morbidity and mortality[25-26], and a major challenge for public health.

In a recent study, adolescents, tobacco users, those with a diagnosis of diabetes or hypertension, multiple pregnancies, a history of gestational diabetes, fetal anomaly and miscarriages were associated with a higher incidence of prematurity[27]. In Porto Alegre, low birth weight (< 2,500 grams), inadequate prenatal care, 5-minute Apgar between 0 and 3, Cesarean delivery, multiple pregnancies, mothers below the age of 19 or above 34, and inadequate maternal education were also associated with prematurity[28]. Because it is one of the main causes of neonatal death, investigating prematurity and the associated factors may reveal indirect risk factors that must be taken into consideration for prevention. Our research shows that many of the risk factors for prematurity, such as multiple gestations, fetal anomalies and low birth weight were associated with fetal death.

This shows that investment is required in measures to prevent avoidable prematurity, such as focusing on pre-natal care, in particular high-risk pregnancies, and prevention of iatrogenic prematurity, related with unnecessary pregnancy interruption, such as inadequately indicated Cesareans[29].

In light of the characteristics of gestational risk of the women in this study, and the results found, we stress the importance of quality service that can handle highly complex deliveries and newborns. Some studies have shown that infants transferred to other facilities due to the absence of the conditions required to safely care for the mothers and newborns in serious condition have a high probability of death during the neonatal period[4]. Furthermore, infants born of women who do not get suitable pre-natal care, who are born at home and have no post-natal care are also at higher risk of death before they are 28 days old[30].

In this regard, we highlight one of the pillars of care for high-risk pregnant women in the region, which is ensure delivery in hospitals with NICUs[6], which guarantees better results in terms of the risk of neonatal death[4].

One of the limitations of this study was the use of file data and birth and death records, thus depending on the quality with which they were filled out by professionals, as we often found missing (unknown) data not included in the tables. We do not know how gestational age was estimated, if ultrasound or the date of the last menstrual period, something that could affect the classification of premature birth.

CONCLUSION

This study found risk factors for neonatal death among women with high-risk pregnancies, early labor, fetal malformation and multiple current gestation. In addition to prematurity, very low birth weight and an Apgar of less than seven in the fifth minute of life.

Identifying risk factors can help plan actions to consolidate the perinatal network, restructuring and qualifying pre-natal care for high-risk pregnancies, delivery and care of the newborn.

Specific programs that focus on high-risk pregnancies, ensuring delivery in a hospital capable of handling highly complex cases, must be encouraged in other developing countries, and even in other regions of Brazil, in the search for significant perinatal results, such as lower neonatal mortality.

RESUMO

Objetivo: Identificar os fatores associados à mortalidade neonatal intra-hospitalar com base nas características individuais de gestantes de risco, do parto e do recém-nascido. **Método:** Estudo epidemiológico do tipo transversal, realizado com crianças nascidas vivas de partos hospitalares de mulheres acompanhadas pelo ambulatório de alto risco de um hospital filantrópico de Maringá, Paraná, Brasil, no período de setembro de 2012 a setembro de 2013. **Resultados:** Fizeram parte da pesquisa 688 mulheres. O coeficiente de mortalidade neonatal foi de 17,7 óbitos/1.000 nascidos vivos, sendo sua maioria no período neonatal precoce. Trabalho de parto prematuro, malformação fetal e gestação múltipla foram as intercorrências associadas ao óbito neonatal. Recém-nascidos prematuros, com muito baixo peso ao nascer e Índice de Apgar menor que sete no quinto minuto de vida apresentaram risco elevado de morte. **Conclusão:** A identificação de fatores de risco pode auxiliar no planejamento de ações para consolidação da rede perinatal. Programas específicos devem ser incentivados em outros países, na busca de resultados perinatais expressivos, como a redução da mortalidade neonatal.

DESCRITORES

Gravidez de Alto Risco; Mortalidade Infantil; Enfermagem Neonatal; Enfermagem Materno-Infantil; Fatores Epidemiológicos; Fatores de Risco.

RESUMEN

Objetivo: Identificar los factores asociados con la mortalidad neonatal intrahospitalaria con base en las características individuales de gestantes de riesgo, del parto y del recién nacido. **Método:** Estudio epidemiológico del tipo transversal, realizado con niños nacidos vivos de partos hospitalarios de mujeres seguidas en el ambulatorio de alto riesgo de un hospital filantrópico de Maringá, Paraná, Brasil, en el período de septiembre de 2012 a septiembre de 2013. **Resultados:** Hicieron parte de la investigación 688 mujeres. El coeficiente de mortalidad neonatal fue de 7,7 defunciones/1.000 nacidos vivos, siendo su mayoría en el período neonatal precoz. Trabajo de parto prematuro, malformación fetal y gestación múltiple fueron los sucesos asociados con la defunción neonatal. Recién nacidos prematuros, con muy bajo peso al nacer e Índice de Apgar menor que siete el quinto minuto de vida presentaron riesgo elevado de muerte. **Conclusión:** La identificación de factores de riesgo puede auxiliar la planificación de acciones para consolidación de la red perinatal. Se deben incentivar programas específicos en otros países, en la búsqueda por resultados perinatales considerables, como la reducción de la mortalidad neonatal.

DESCRIPTORES

Embarazo de Alto Riesgo; Mortalidad Infantil; Enfermería Neonatal; Enfermería Materno-Infantil; Factores Epidemiológicos; Factores de Riesgo.

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