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ORIGINAL ARTICLE

Perinatal factors associated with early deaths of preterm infants born in Brazilian Network on Neonatal Research centers

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Abstract

Objective: To evaluate perinatal factors associated with early neonatal death in preterm infants with birth weights (BW) of 400-1,500 g.

Methods: A multicenter prospective cohort study of all infants with BW of 400-1,500 g and 23-33 weeks of gestational age (GA), without malformations, who were born alive at eight public university tertiary hospitals in Brazil between June of 2004 and May of 2005. Infants who died within their first 6 days of life were compared with those who did not regarding maternal and neonatal characteristics and morbidity during the first 72 hours of life. Variables associated with the early deaths were identified by stepwise logistic regression.

Results: A total of 579 live births met the inclusion criteria. Early deaths occurred in 92 (16%) cases, varying between centers from 5 to 31%, and these differences persisted after controlling for newborn illness severity and mortality risk score (SNAPPE-II). According to the multivariate analysis, the following factors were associated with early intrahospital neonatal deaths: gestational age of 23-27 weeks (odds ratio – OR = 5.0; 95%CI 2.7-9.4), absence of maternal hypertension (OR = 1.9; 95%CI 1.0-3.7), 5th minute Apgar 0-6 (OR = 2.8; 95%CI 1.4-5.4), presence of respiratory distress syndrome (OR = 3.1; 95%CI 1.4-6.6), and network center of birth.

Conclusion: Important perinatal factors that are associated with early neonatal deaths in very low birth weight preterm infants can be modified by interventions such as improving fetal vitality at birth and reducing the incidence and severity of respiratory distress syndrome. The heterogeneity of early neonatal rates across the different centers studied indicates that best clinical practices should be identified and disseminated throughout the country.

J Pediatr (Rio J). 2008;84(4):300-307: Neonatal mortality, infant, newborn, infant, preterm, infant, very low birth weight.

Introduction

The survival rates of preterm and very low weight newborn infants reflect the quality of antenatal care, of the care provided during labor and delivery and the infrastructure for the neonatal care in the different regions and countries of the world. It is expected that richer countries have lower rates of

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early and late neonatal mortality than countries where health-care is less robust. In contrast, the frequency of prematurity is higher in poorer countries exactly because of the less stable health conditions of the expectant mothers.[1] Premature delivery is the most important determinant of infant mortality in developed countries.[2] Among hospital deliveries in developing countries, prematurity is also the principal determinant of morbidity and neonatal mortality.[3]

In 2004, births prior to 24 weeks in the United States were 0.8% of total live births and were responsible for 46.3% of infant deaths.[2] Frequency of prematurity is increasing worldwide, with the possible exception of France and Finland.[4] In Brazil, in 2004, there were 3,026,548 births, of which 34,012 (1.1%) weighed < 1,500 g.[5] During the same year, 54,183 children died before 1 year of age, 15,560 (29%) of whom had birth weights < 1,500 g and 11,426 (73%) of these died before completing 7 days of life.[6]

In order to analyze early neonatal mortality rate of premature newborn infants in Brazil, it is necessary to consider the context in which the data were obtained, i.e. the quality of antenatal care, the quality of care provided during labor and delivery, the infrastructure in terms of physical, material and human resources, and the prevalence of the use of evidence-based interventions, in addition to family participation in neonatal intensive care.[7] To this end, epidemiological networks, which analyze together the morbidity and mortality data of a series of neonatal units, can provide two types of information. First, these networks can trace in real time the neonatal morbidity and mortality of centers with specific characteristics, and compare them with national and international data. Additionally, since the information obtained enables comparisons between different centers, it makes it possible to investigate the best strategies for reducing neonatal morbidity and mortality, based on processes for the improvement of the quality of perinatal care.[8,9] In this context, the objective of the present study is to evaluate perinatal factors associated with death before the 6th day of life in very low birth weight preterms infants treated at public university hospitals in the Brazilian states of São Paulo, Rio de Janeiro and Rio Grande do Sul, with emphasis on the different profiles of the patient populations treated at each hospital.

Methods

This was a prospective cohort study of all live births at gestational ages between 23 0/7 and 33 6/7, with birth weights of 400-1,500 g, delivered in eight public maternity units at tertiary university hospitals, located in five cities in three Brazilian states (Rio de Janeiro, Rio Grande do Sul and São Paulo), between June 2004 and May 2005. Patients were excluded if they were born with major congenital malformations or had been transferred from other institutions. All units are referral centers for high risk pregnancies, provide care almost exclusively for patients on the Brazilian National Health Service (Sistema Único de Saúde) and offer medical residency programs in pediatrics and neonatology. The project was approved by the Research Ethics Committees of all institutions. In order to maintain confidentiality, the institutions will be referred to as units A to H.

All eight units have delivery rooms with equipment for neonatal resuscitation and, altogether, they have a total of 282 intensive and intermediate care beds, varying from 20 to 48 beds per unit. In addition to the physical infrastructure necessary to care for high risk newborns, all units also have the material and human resources for intensive care, following Brazilian Ministry of Health and Brazilian Society of Pediatrics guidelines.[10]

At each unit, one or two neonatologists used a specially designed questionnaire to collect the following information on recently delivered mothers and their newborn infants:

Maternal characteristics: age and schooling in years; prenatal care, classified as present or absent (number of visits was not considered because this was a population whose pregnancies did not pass 34 weeks); single or multiple birth; hypertensive syndrome of any etiology and diabetes (present when diagnosed by the obstetrician); peripartum infection, defined as an infection of any etiology during the week prior to birth; prenatal corticosteroids (present if at least one dose of dexamethasone or betamethasone was given before delivery) and type of delivery.

Characteristics of the patient at birth: gestational age by the best obstetric estimate or by physical examination of the infant;[11] weight measured in a weight scale with 5 g precision; appropriateness of weight for gestational age, defining infants below the 10th percentile of the intrauterine growth curve as small for gestational age;[12] sex; 1st and 5th minute Apgar scores; resuscitation procedures according to the 2000 American Academy of Pediatrics recommendations[13] (positive pressure ventilation = ventilation with bag and mask or tracheal tube; advanced resuscitation = ventilation combined with cardiac massage and/or medication). Information on instillation of surfactant in the delivery room was also recorded.

Clinical progress during the first 72 hours of life: Score for Neonatal Acute Physiology, Perinatal Extension, Version II (SNAPPE-II), defining infants with score > 39 as having poor prognosis;[14] respiratory distress syndrome diagnosed by clinical and radiological criteria; persistent ductus arteriosus, defined according to clinical and/or echocardiographic findings; sepsis, defined by clinical criteria, with or without a positive blood culture; use of at least one dose of surfactant, irrespective of when or what type of surfactant was used; assisted ventilation (need of CPAP and/or mechanical ventilation). Deaths were classified according to time of occurrence.

Table 1 - Maternal demographic characteristics of the preterm infants born at the eight neonatal units assessed

	Unit A (n = 41)	Unit B (n = 68)	Unit C (n = 66)	Unit D (n = 85)	Unit E (n = 86)	Unit F (n = 41)	Unit G (n = 99)	Unit H (n = 93)	Total (n = 579)
Age (years)	26±7	27±8	25±8	28±7	27±7	27±7	27±7	26±7	27±7
Adolescents (%)	22	21	33	12	16	15	20	21	20
Education < 8 years (%)	20	42	6	-	28	34	44	38	32
Prenatal care present (%)	85	93	89	92	92	98	91	91	91
Multiple births (%)	27	21	14	18	14	7	16	15	16
Hypertensive syndrome (%)	39	41	35	44	42	68	46	37	43
Diabetes (%)	5	3	6	2	2	12	5	9	5
Peripartum infection (%)	34	18	52	23	31	39	29	30	31
Prenatal corticosteroids (%)	88	71	68	12	49	78	58	44	54
Caesarian delivery (%)	63	66	61	68	72	85	69	60	68

A descriptive analysis of all of the variables according to maternity unit of birth was made. Next, the characteristics of the newborn infants who died before 168 hours of life and those who survived beyond this point were compared by chi-square or Fisher's exact test for categorical variables and Student's *t* test or Mann-Whitney test for continuous variables. The next step was to compare the frequencies of early neonatal deaths among the eight units, controlled for SNAPPE-II. Finally, stepwise logistic regression was used in order to identify factors associated with early intrahospital death. The independent factors analyzed in the logistic regression were those that had $p < 0.20$ in the univariate analyses. Whenever possible covariables were detected, those with the greatest clinical relevance were selected. Therefore, the variable chosen to start the model was "gestational age," excluding "birth weight," as well as "5th minute Apgar score" instead of "positive pressure ventilation" and "advanced resuscitation," while the variable "respiratory distress syndrome" was preferred over "at least one dose of surfactant."

The sample size calculation took into consideration the need of 10 to 15 patients for each of the 20 independent variables to be analyzed in the logistic regression model. Therefore, at least 300 newborn infants should be enrolled on the study.

Throughout the analyses, the statistician was blind to the identity of the maternity units. The software employed was SPSS 12.0 and significance was set at $p < 0.05$.

Results

Between June 1, 2004 and May 31, 2005, 17,219 children were born live at the eight units, 579 (3%) of these were preterm infants with gestational ages between 23 0/7 and 33 6/7 weeks, birth weight of 400-1,500 g and free from major congenital malformations. The characteristics of the mothers, births and clinical progress during the first 72 hours were heterogeneous across the eight units.

Regarding maternal characteristics (Table 1), the maximum and minimum percentages of each variable at units A-H were: adolescent mothers 12-33%, less than 8 years' education 6-44%, prenatal care present 85-98%, multiple births 7-27%, hypertensive syndrome 35-68%, diabetes 2-12%, peripartum infection 18-52%, antenatal corticosteroids 12-88% and caesarian delivery 60-85%.

Regarding characteristics of the patients at birth (Table 2), the maximum and minimum percentages of each variable at units A-H were: gestational age from 23 to 27 weeks 22-37%, weight < 1,000 g 32-55%, small for gestational age 24-55%, male sex 41-59%, positive pressure ventilation 61-77%, advanced resuscitation 0-26%, 5 minute Apgar less than seven 5-26%, and surfactant in the delivery room (0-60%).

Regarding the clinical progress of the newborn infants during their first 72 hours of life (Table 3), the maximum and minimum percentages of each variable at units A-H were: SNAPPE-II ≥ 40 in 9-29%, respiratory distress syndrome 53-77%, patent ductus arteriosus 28-49%, sepsis 3-51%, at least one dose of surfactant 32-68%, and assisted ventilation 70-95%.

Ninety-two newborn infants died before 168 hours of life, of whom 44 (48%) died before 24 hours, 19 of these in the delivery room. Fourteen of the 19 infants born at 23 weeks died in the first 6 days of life. The same happened to 17 of the

Table 2 - Characteristics of the patients at birth at each of the eight neonatal units studied

	Unit A (n = 41)	Unit B (n = 68)	Unit C (n = 66)	Unit D (n = 85)	Unit E (n = 86)	Unit F (n = 41)	Unit G (n = 99)	Unit H (n = 93)	Total (n = 579)
GA (weeks)	29.6±2.6	28.4±2.5	28.7±2.4	29.2±2.9	29.0±2.6	28.6±2.6	28.9±2.8	28.6±3.2	28.9±2.9
GA 23-27 weeks (%)	22	37	35	25	28	32	32	33	31
BW (g)	1,083±292	1,017±217	1,091±267	994±281	1,019±293	989±294	1,016±298	965±311	1,017±291
BW 400-999 g (%)	32	47	38	47	47	44	50	55	46
Small for GA (%)	51	35	24	55	53	39	46	48	45
Male sex (%)	44	57	55	47	43	41	46	59	50
Ventilation in DR (%)	61	49	77	73	72	71	59	72	67
Advanced resuscitation (%)	2	0	5	14	6	22	17	26	13
5 minute Apgar score	8±1	8±1	8±2	5±3	7±2	8±2	8±3	8±3	8±2
5 minute Apgar < 7 (%)	5	10	15	26	26	7	20	19	18
Surfactant in DR (%)	2	60	0	0	40	0	0	1	13
Death in DR	0	0	0	4 (5%)	0	1 (2%)	5 (5%)	9 (10%)	19 (3%)

BW = birth weight; DR = delivery room; GA = gestational age.

Table 3 - Clinical progress of the newborn infants at each of the eight neonatal units studied (excluding the 19 deaths in the delivery room)

	Unit A (n = 41)	Unit B (n = 68)	Unit C (n = 66)	Unit D (n = 81)	Unit E (n = 86)	Unit F (n = 40)	Unit G (n = 94)	Unit H (n = 84)	Total (n = 560)
SNAPPE-II ≥ 40 (%)	10	16	14	9	29	24	19	27	19
RDS (%)	56	66	77	42	49	68	53	60	58
PDA (%)	49	41	44	28	34	32	32	31	37
Sepsis before 72 h (%)	44	3	37	51	49	35	18	19	31
Surfactant ≥ 1 dose (%)	54	68	48	32	64	63	39	42	49
Assisted ventilation (%)	90	84	95	89	94	92	70	93	88
Death < 168 h	2/41 (5%)	5/68 (7%)	5/66 (8%)	11/85 (13%)	12/86 (14%)	6/41 (15%)	22/99 (22%)	29/93 (31%)	92/579 (16%)
Death < 24 h	0	0	0	9	6	3	13	13	44

PDA = persistent ductus arteriosus; RDS = respiratory distress syndrome; SNAPPE II = Score for Neonatal Acute Physiology, Perinatal Extension, Version II.

25 infants born at 24 weeks, 16 of the 37 neonates born at 25 weeks, nine of the 43 born at 26 weeks and 11 of the 54 patients born at 27 weeks' gestational age. A total of 401 children were born at 28 to 33 weeks, of whom 25 (6%) died during the first week of life. Early neonatal death rates varied from 5% at unit A to 31% at unit H (Table 3).

Comparison of the 92 neonates who died before 168 hours with those who survived beyond this point demonstrated that the following variables were more frequent among the patients who died: multiple births, gestational age 23-27 weeks, birth weight < 1,000 g, need for ventilation and advanced resuscitation in the delivery room, 5th minute Apgar

Table 4 - Characteristics of the premature infants who died before 168 hours compared to those who survived beyond that point

	Hospital death before 168 hours		
	Yes (n = 92)	**No (n = 487)**	**p**
Maternal age (years)	26.7±7.0	26.8±7.2	0.919
Prenatal care present	81 (88%)	445 (91%)	0.394
Multiple birth	23 (25%)	71 (15%)	0.013
Hypertensive syndrome	21 (23%)	226 (46%)	< 0.001
Diabetes	5 (5%)	25 (5%)	0.801
Peripartum infection	29 (32%)	149 (31%)	0.918
Antenatal corticosteroids	34 (37%)	274 (56%)	< 0.001
Caesarian delivery	42 (46%)	349 (72%)	< 0.001
GA 23-27 weeks	67 (73%)	146 (30%)	< 0.001
Birth weight < 1,000 g	77 (84%)	192 (39%)	< 0.001
Small for GA	30 (33%)	231 (47%)	0.009
Male sex	49 (53%)	239 (49%)	0.462
PPV in delivery room	80 (87%)	308 (63%)	< 0.001
Advanced resuscitation	36 (39%)	37 (8%)	< 0.001
5 minute Apgar < 7	48 (52%)	56 (11%)	< 0.001
SNAPPE-II ≥ 40	41/69 (59%)	64/481 (13%)	< 0.001
RDS	64 (70%)	263 (54%)	< 0.001
PDA	15 (16%)	190 (39%)	0.001
Sepsis before de 72 h	29 (32%)	144 (30%)	0.131
Surfactant ≥ 1 dose	55 (60%)	231 (47%)	0.030

GA = gestational age; PDA = persistent ductus arteriosus; PPV = positive pressure in delivery room; RDS = respiratory distress syndrome; SNAPPE-II = Score for Neonatal Acute Physiology, Perinatal Extension, Version II, given for the total number of patients for whom data are available.

< 7, SNAPPE-II > 39, presence of respiratory distress syndrome and use of surfactant. On the other hand, infants who died before 168 hours had a lower frequency of maternal hypertensive syndrome, use of antenatal corticosteroids, caesarian delivery, small for gestational age and patent ductus arteriosus (Table 4).

The frequency of deaths before 168 hours by unit of birth was controlled for the clinical severity of the patients during the first 12 hours of life, i.e., the SNAPPE-II scores: for every extra point on the score, the chance of death increased by 7% (95%CI 5-8) for the 550 (95%) newborn infants for whom the information was available. In order to analyze mortality at the eight units controlled for SNAPPE-II scores, the reference was chosen among those units with the lowest absolute mortality (units A, B and C, Table 3), on the basis of the shortest confidence interval, i.e., unit B. Therefore, early mortality controlled for SNAPPE-II scores were: odds ratio (OR) = 1.1 (95%CI 0.2-6.9) for A vs. B; OR = 1.2 (95%CI 0.3-5.2) for C vs. B; OR = 1.0 (95%CI 0.2-4.2) for D vs. B; OR = 0.8 (95%CI 0.2-3.2) for E vs. B; OR = 1.4 (95%CI 0.3-6.4) for F vs. B; OR = 2.4 (95%CI 0.7-8.3) for G vs. B; and OR = 3.8 (95%CI 1.1 to 12.8) for H vs. B.

The multivariate analysis for the outcome "early intra-hospital neonatal death" showed associations with the following independent factors: gestational age 23-27 weeks (OR = 5.0; 95%CI 2.7-9.4), absence of hypertensive syndrome (OR = 1.9; 95%CI 1.0-3.7), 5th minute Apgar score of 0-6 (OR = 2.8; 95%CI 1.4-5.4), respiratory distress syndrome (OR = 3.1; 95%CI 1.4-6.6) and neonatal unit. Infants born at unit H had a 7.84 (95%CI 1.57-39.17) times greater risk of early death than those born at unit A, controlling the other variables in the model. The final fit of the model was adequate (Hosmer & Lemeshow test; p = 0.629).

Discussion

This multicenter study has shown important differences between the units studied in terms of early neonatal mortality among infants born at 23 to 33 weeks' gestational age weighing from 400 to 1,500g and free from major congenital malformations. These differences still remain after controlling the data for the clinical severity of the patients and for other perinatal risk factors associated with death.

The population assessed includes newborn infants at the extreme limit of fetal viability. The decision to include neonates born at 23 to 25 weeks was based on the fact that such infants can survive, as demonstrated in studies carried out by epidemiological networks in developed countries,[8,15,16] although there is a great deal of discussion with respect to their viability, their future quality of life and the cost of care.[17] Indeed, of the 92 early neonatal deaths analyzed, 47 were of patients born at 23 to 25 weeks, setting fetal viability at the studied units around 26 weeks of gestational age. Also, it was decided to exclude late premature births because they constitute a group of patients with specific patterns of morbidity and mortality, distinct from those born up to 33 weeks.[18,19] Patients suffering from major congenital anomalies were excluded since the presence of malformation in itself increases the risk of death.[2] Finally, only inborn infants were included, since it is known that mortality of outborn preterm infants is significantly higher.[20]

Results here presented describe university hospitals that are referral centers for high risk pregnancies and which belong to the Brazilian National Health Service. It is interesting to note that the profile of neonatal deaths in Brazil can change depending on the institutional status of the hospital. In Belo Horizonte, a population based investigation detected three distinct neonatal death profiles: at private hospitals the deaths were unlikely to be preventable (malformations and extreme prematurity); at hospitals contracted to the Brazilian National Health Service, the majority of deaths were preventable (newborn infants with birth weight > 2,500 g, who died from hypoxic insults and infections); whereas at hospitals belonging to the Brazilian National Health Service, the profile of deaths was mixed.[21]

Before analyzing early neonatal mortality overall, it is necessary to look at the characteristics of the mothers and newborn infants cared for at the different units, since many reports of epidemiological networks have found evidence that significant differences in neonatal characteristics, morbidity and clinical practices can influence the outcomes.[22-24] This study has confirmed these differences. In terms of clinical practices, the use of antenatal corticosteroids varied from 12% at unit D (although 92% of expectant mothers received prenatal care) up to 88% at unit A. At birth, advanced resuscitation procedures were not used at unit B, but they were needed in 26% of the patients at unit H, even though gestational age and birth weight were similar at both units. It was also observed that only units B and E administered surfactant during the first minutes of life, in the delivery room, and that the use of at least one dose of surfactant varied from 32% at unit D to 68% at unit B. Finally, with respect to assisted ventilation, variation was also noted, although of less significance compared to the other practices. Therefore, it is not surprising that the percentage of deaths varied across the eight units, even when controlled for the SNAPPE-II clinical severity index. In order to reduce the early neonatal mortality rate and the variation between the units, it is necessary to implement improvement programs focused on the quality of neonatal care and based on four key points: being open to change; becoming used to apply evidence-based practices; systematically and uniformly evaluating the results obtained; and learning to work in a cooperative manner both within each unit and between units.[25]

Among the risk factors that were independently associated with early neonatal mortality, the most important was the neonatal unit where the birth took place, as well as low gestational age, absence of maternal hypertensive syndrome and presence of perinatal asphyxia. Fetal maturity has always been a predictive variable that dominates any model of risk factors associated with neonatal death.[26] Several international studies prove that the lower the gestational age, the greater the risk of death. In the United Kingdom, Belgium and France, studies undertaken in the 1990s of 1,976 births at gestational age ≤ 26 weeks showed that intrahospital neonatal mortality was 91% at 23 weeks, 73% at 24 weeks, 53% at 25 weeks and 46% at 26 weeks. Before 24 weeks, 68% died in the delivery room.[27] In Brazil, in 2004, 56% of the 10,846 infants born at 22 to 27 weeks died by 6 days of life,[6] while, in this study, 38% of the 178 infants born between 23 and 27 weeks died before 168 hours. Thus, even though the early neonatal mortality observed among these preterms born between 23 and 27 weeks was below the national rate, being born within this gestational age range increased the chance of early neonatal mortality by five times. It is important to note that the frequency of early neonatal deaths among those infants born at 28 to 33 weeks in this study was 6%, below the 20% found for infants born between 28 and 31 weeks in Brazil.[6]

One protective factor against early neonatal mortality was the presence of hypertensive syndrome during pregnancy. Other studies have indicated the same finding. Evans et al.[26] analyzed 11,498 very low birth weight infants born between 25 and 32 weeks in Australia and New Zealand, between 1998 and 2001. Maternal hypertension was an independent protective factor with relation to intrahospital death, reducing it to around half (OR = 0.46; 95%CI 0.36-0.50). Another multicenter investigation in small for gestational age newborn infants with 24-42 weeks of gestation admitted to 17 Canadian intensive care units showed that maternal hypertension is associated with increased survival. One possible explanation for these findings is related to differences between normotensive and hypertense mothers in terms of placental nutrition and oxygen transfer. It is possible that hypertension during gestation leads to reduction in autoregulation of arterial flow in the intervillous space, with a consequent increase in perfusion and in mother-fetus transfer of nutrients and oxygen. It is probable that there is a point at which this loss of autoregulation of intervillous flow becomes pathological, increasing maternal and neonatal mortality.[28] In this context, the increased frequency of small for gestational age infants among those who survived for at least 1 week is of note.

The fact that respiratory distress syndrome continues to be an independent risk factor for death during the first week of life indicates failures at several levels of perinatal care. The low frequency of antenatal corticosteroids use is associated with an increased incidence of respiratory distress syndrome and neonatal mortality. Just 54% of the patients born before 34 weeks studied here were given the medication, whereas, in the United States, for more than 10 years, 79% of expectant mothers have received the medication.[9] During the immediate neonatal period, there was a relatively low frequency of surfactant use, which can avoid or attenuate the severity of respiratory distress syndrome: 49% of the analyzed preterm infants were given at least one dose of surfactant. In the Vermont-Oxford Network, 62% of the 26,007 patients born in 1999 with weights from 501 to 1,500 g were given surfactant.[8] Finally, the fact that respiratory distress syndrome has an influence on neonatal mortality indicates that it is necessary to improve the care given to critically ill newborns at the units analyzed.

With relation to perinatal asphyxia, the 5th minute Apgar score between 0 and 6 was strongly associated with early neonatal mortality. This finding has been confirmed by other studies. Casey et al. evaluated 13,399 single pregnancy births born at 26 to 36 weeks at a single American center from 1988 to 1998. The risk of neonatal death was 59 times greater when the 5 minute Apgar score was 0-3 and 13 times greater for values from 4-6, using scores from 7-10 as reference. The 1st minute Apgar score was not useful for predicting the risk of death.[29]

It can be concluded that the university units studied here, which are reference centers for the care of critically ill preterm patients, showed high rates of early neonatal mortality in comparison with developed countries standards, although these rates are much lower than average Brazilian data. A significant proportion of the risk factors associated with early neonatal mortality can be modified by interventions such as improving fetal vitality at birth and reducing the incidence and/or severity of respiratory distress syndrome by optimizing the use of antenatal corticosteroids and postnatal surfactant. Furthermore, the differences observed between the mortality rates at the eight units indicates that there is a need to identify possible best practices and adopt them uniformly throughout our country.

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