Survival at nine neonatal intensive care units in São Paulo, Brazil

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ABSTRACT *A collaborative effort to assess factors affecting newborn survival at neonatal intensive care units (NICUs) was made by studying 1 948 newborns admitted to nine NICUs in the city of São Paulo between 1 June and 30 November 1991. Data on the study subjects were obtained using a standardized form. This was the first activity undertaken by a network of neonatologists (the Paulista Collaborative Group on Neonatal Care) dedicated to jointly evaluating and improving neonatal care in that city. The study results showed an overall mortality of 59 deaths per 1 000 neonates, with survival improving as gestational age and birthweight rose. Other variables significantly affecting survival were a poor maternal obstetric history (a previous stillbirth or neonatal death, or two or more spontaneous abortions); birth asphyxia (Apgar at 5 minutes <7); respiratory distress syndrome; severe infections; and major malformations. However, multiple logistic regression analysis showed that the rates of neonatal survival in the nine NICUs differed even when these factors were considered. Potential sources of this variability included undetermined population differences in neonatal disease severity and medical care. These results suggest a need for greater efforts to identify and reduce risk factors associated with neonatal mortality, and to adequately evaluate the medical care provided in NICUs. Within this context, the collaborative network of neonatologists established in São Paulo provides a sound organizational structure for evaluating and improving the effectiveness of neonatal care.*

Over the past few decades, epidemiologic studies in the world's developed countries have found that survival of neonates with life-threatening conditions increased significantly when they were admitted to neonatal intensive care units (NICUs) (*1*). However, the cost of their care also increased (*2, 3*), as did the risk of overtreatment (*4*). For this reason among others, in the area of perinatal care considerable attention has been focused upon health technology assessment (*5, 6*), the adequacy of care utilization (*7*), the quality of care received (*8*), and the regional distribution of high-level services (*9, 10*).

It is a sad fact that 90% of the world's neonatal mortality still occurs

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in developing countries (*11*), where resources are meager and health technology assessment has different priorities—in terms of the level of care provided, the variables and risk factors involved, and the cultural acceptability of diverse infant care practices (*12–16*).

In Brazil, a country of contrasts with over 150 million inhabitants, it is estimated that perinatal mortality is 35 deaths per 1 000 births, one of the highest in the Latin America and Caribbean area, higher than perinatal mortality in a number of other countries with similar levels of development (*11*). This may be partly explained by the fact that the richest 20% of the population has roughly 26 times the income of the poorest 20%, one of the largest income gaps of this sort in the world (*17*). Within the health sector, this gap appears reflected in a virtual absence of tertiary public health care facilities and poorly equipped or nonexistent health centers (*18*).

Since perinatal care in Brazil has not been well documented (*19–21*), the present survey was planned at a time when national health care policies needed to be redefined (*18*). Like other groups of facilities that have undertaken perinatal research elsewhere (*22, 23*), the Paulista Collaborative Group on Neonatal Care is a voluntary network of neonatal intensive care units in São Paulo that was established to perform collaborative clinical research in this field. As a first step in organizing the network, each participating unit collected basic demographic and outcome information for infants admitted to the unit over a six-month period.

This report summarizes the results for high-risk babies admitted to the nine participating units and assesses the degree of association between survival and a number of potentially related clinical variables (*14, 24*), as well as the degree of association between survival and treatment at different units after adjusting for statistically significant factors. It is our impression that this collaborative initiative and the results obtained could help to provide a sound basis for systematically evaluating neonatal care and for planning research and other activities at São Paulo's NICUs.

METHODS

The study population included all hospital-delivered neonates in the nine participating level III NICUs (then staffed and equipped to provide intensive care, including respiratory support by mechanical ventilation) in the city of São Paulo (*25*) during the six-month period from 1 June through 30 November 1991. Three of the NICUs were in university hospitals, five were in university-affiliated hospitals, and one was in a general hospital. The NICUs, providing both intensive and intermediate care, had from 35 to 50 beds.

Within each unit, the survey was conducted by the same individual(s) (one or more registered nurses or physicians) for the entire study period, using a pretested standardized data form and instructions agreed upon in advance by all participants. The center coordinating the survey reviewed the filled-out forms for completeness and internal consistency. A computer program was employed to validate the data's intrinsic consistency by cross-checking dates, diagnoses, and patient management.

Maternal and infant hospital records were reviewed for demographic data, medical and obstetric histories, the course of pregnancy and delivery, and complications occurring during hospitalization (*22*). For purposes of the study, a poor obstetric history was defined as one involving a stillbirth, a neonatal death, or two or more spontaneous abortions. Premature rupture of the membranes was defined as rupturing of the fetal membranes at least 24 hours before the onset of labor. Gestational age was estimated by the time of the mother's last menstrual period, ultrasound assessment of the fetus, or both, and was confirmed by clinical examination of the newborn. A small-for-gestational-age infant was defined as one having a birthweight below the 10th percentile for its gestational age and sex using the Denver reference curve. Birth asphyxia was assumed for any newborn with an Apgar score of less than 7 at 5 minutes. Respiratory distress syndrome was diagnosed on the basis of clinical signs and radiology, intraventricular hemorrhage by ultrasonography or autopsy, severe infections on the basis of positive cultures and clinical signs, and major (life-threatening) malformations by clinical signs or instrumentally.

Quantitative estimates of the effects of various covariables (such as gender, labor and delivery variables, and pathologic events) were obtained using odds ratios (OR) and 95% confidence intervals (CI). The test of statistical significance for contingency tables was based on the usual χ^2 value comparing observed with expected numbers of events.

Where appropriate, potential confounding effects were controlled for using stratification and the Mantel-Haenszel procedure. Data management and analyses were accomplished using the EPI Info 6 software package. Logistic regression analysis was done for neonatal survival outcome considering birthweight, gestational age, poor maternal obstetric history, birth asphyxia, respiratory distress syndrome, severe infections, and major malformations as predictor variables, using the SPSS software on a VAX 6 410 computer. Stepwise selection procedure and the log likelihood test were used to define the best model fitting the data. Rank order correlations between neonatal survival and the number of infants at each NICU were analyzed using the Spearman rank correlation coefficient.

RESULTS

Out of 10 135 newborns delivered at the study hospitals just before or during the survey period, a total of 1 948 weighing 500–5 620 g were admitted to the nine participating NICUs during this period. Demographic and clinical characteristics of these infants and their mothers are presented in Table 1.

TABLE 1. Maternal, delivery, and physical characteristics of the 1 948 study infants admitted to the nine participating neonatal intensive care units in São Paulo, Brazil, during the period 1 June–30 November 1991

		Neonatal intensive care unit								
	Total	1[a]	2[a]	3[a]	4[b]	5[a]	6[b]	7[b]	8[a]	9[c]
Infant data:										
No. of newborns delivered at the study hospitals	10 135	1 363	1 218	1 983	1 536	738	1 027	1 010	341	919
No. of newborns admitted to the nine participating NICUs	1 948	330	319	271	268	232	180	171	113	64
Mean birthweight in grams, ±1 SD[d]	2 682±845	3 010±745	2 710±855	2 650±750	2 720±865	2 570±830	2 950±800	2 300±840	2 120±860	2 500±765
No. of newborns with very low birthweight, <1 500 g	180	11	27	19	17	27	10	33	29	7
Mean gestational age in weeks, ±1 SD	37±3	38±3	37±3	37±3	37±3	37±3	38±3	36±3	35±3	37±3
Sex (M/F/unrecorded)	1 093/842/13	194/135/1	180/136/3	156/115/0	156/105/7	127/104/1	103/77/0	90/80/1	57/56/0	30/34/0
No. of newborns small for gestational age	280	23	55	28	40	35	17	39	32	11
No. of newborns with birth asphyxia (Apgar score at 5 min <7)	242	25	58	33	35	37	8	20	19	7
No. of neonatal deaths	124	7	22	9	18	19	11	19	11	8
Maternal data:										
Mean age in years, ±1 SD	27±6.5	28±6	26±7	27±6	25±6	28±6	28±6	27±7	27±6	28±7
No. of mothers with disease during pregnancy[e]	1 280	90	266	259	121	212	82	115	97	38
No. of mothers with poor obstetric histories	141	14	16	15	21	17	13	16	25	4
Delivery data:										
Vaginal delivery/ cesarean section	1 569/379	234/96	240/79	208/63	241/27	183/49	154/26	152/19	106/7	51/13
Multiple births	118	14	17	15	22	18	2	12	16	2
Preterm, <37 weeks	696	66	105	102	95	91	43	93	74	27
Premature rupture of membranes, ≥24 hours	172	13	26	42	27	12	6	28	14	4

[a] University hospital.
[b] University-affiliated hospital.
[c] General hospital.
[d] SD = standard deviation.
[e] Both preexisting maternal diseases (i.e., hypertension, renal disease, epilepsy, diabetes mellitus) and diseases arising during pregnancy (i.e., severe infections).

Of all the 1 948 infants, 1 824 (94%) were discharged alive from the NICU and 124 (6%) died. Of the 124 who died, 92 perished within the first week after birth (early neonatal mortality), 23 died between 8 and 27 days after birth (late neonatal mortality), and 9 died after surviving 28 days or more (postneonatal mortality). Neonatal survival at individual intensive care units ranged from 88% to 98%, the differences between individual units being significant ($\chi^2 = 31.4$, $P < 0.0005$).

As expected, there was a clear trend toward reduced neonatal mortality as birthweight increased and also as gestational age increased (a contingency table is available from the authors on request). From the χ^2 associated with stepwise introduction of the independent variables in the logistic regression analysis, a model in which gestational age was the only independent variable could be improved by the addition of birthweight as the second independent variable, although gestational age was a better predictor of neonatal survival than birthweight. A combination of gestational age <32 weeks and birthweight <700 g was uniformly fatal (for seven newborns) whereas 97% (1 725/1 773) of the study infants born at ≥37 weeks or with birthweights ≥1 500 g survived.

For purposes of analysis, the study infants were classified into two groups according to birthweight and gestational age: those considered premature infants with very low birthweights (born at <37 weeks of gestation with a birthweight <1 500 g) and all of the other study infants (those born at ≥37 weeks of gestation or with a birthweight ≥1 500 g). These two groups were used in univariate analyses

(Table 2) to assess relationships between neonatal survival and a number of variables reportedly associated with survival of NICU populations. A significant inverse association was found between study infant survival and a poor maternal obstetric history; however, no significant associations were found between survival and hypertension during pregnancy or any of several labor and delivery variables (premature rupture of the fetal membranes, multiple gestation, or cesarean versus vaginal delivery). Regarding newborn-related variables, no significant associations were found between survival and sex, size for gestational age, or intraventricular hemorrhage; but significant inverse associations were found between survival and babies with respiratory distress syndrome or severe infections; and even stronger inverse associations were found between survival and birth asphyxia or major malformations.

The combined effects of gestational age, birthweight, poor obstetric history, birth asphyxia, respiratory distress syndrome, severe infection, and major malformation were evaluated in a multiple logistic regression model that adequately fit the data ($P < 0.001$). With the exception of respiratory distress syndrome, all the variables were jointly significant in the directions expected (Table 3).

The probability of survival at 28 days of life was estimated for each infant, and these probabilities were summed for all of the study infants in each of the nine participating NICUs. The percentage differences found between the observed and expected number of survivors in each unit (Table 4) indicate that survival rates varied by as much as 10% (–7.0% to +3.0%) from one NICU to another and that these differences were not due to the possible confounding effects of gestational age, birthweight, poor obstetric history, birth asphyxia, severe infections, or major malformations.

No significant rank order correlations were found between infant survival and the number of infants in the NICU.

TABLE 2. Study infants in two groups (those 175 born after less than 37 weeks of gestation with birthweights under 1 500 grams and all of the other study infants) showing the influence of 11 variables upon survival. For each variable listed, the first line shows the percentage surviving (number surviving/total) with that variable; the second line shows the percentage surviving without it; the third line shows the odds ratio (OR); and the fourth line shows the 95% confidence interval (95% CI)

Variable	Infants born at <37 weeks with birthweight <1 500 g	Infants born at ≥37 weeks or with ≥1 500 g birthweight	Total
Poor obstetric history (χ^2 = 6.61; *P* = 0.01):[a]			
Yes	59% (10/17)	92% (114/124)	88% (124/141)
No	63% (100/158)	98% (1 609/1 649)	95% (1 709/1 807)
OR[b]	0.83	0.28	0.45
95% CI	0.27–2.60	0.13–0.63	0.22–0.84
Hypertension during pregnancy:			
Yes	65% (32/49)	98% (286/292)	93% (318/341)
No	62% (78/126)	97% (1 437/1 481)	94% (1 515/1 607)
OR	1.16	1.46	1.28
95% CI	0.55–2.46	0.59–3.88	0.73–2.28
Premature rupture of membranes:			
Yes	67% (32/48)	96% (119/124)	88% (151/172)
No	61% (78/127)	97% (1 604/1 649)	95% (1 682/1 776)
OR	1.26	0.67	1.03
95% CI	0.59–2.68	0.25–1.95	0.55–1.94
Multiple births:			
Yes	63% (12/19)	95% (94/99)	90% (106/118)
No	63% (98/156)	97% (1 629/1 674)	94% (1 727/1 830)
OR	1.01	0.52	0.75
95% CI	0.95–3.04	0.19–1.53	0.34–1.62
Mode of delivery:			
Cesarean	33% (1/3)	98% (368/376)	97% (369/379)
Vaginal	63% (109/172)	97% (1 355/1 397)	93% (1 464/1 569)
OR	0.29	1.43	1.23
95% CI	0.01–4.17	0.64–2.32	0.59–2.64
Sex:[c]			
Male	64% (57/89)	97% (976/1 004)	95% (1 033/1 093)
Female	61% (52/85)	98% (739/757)	94% (791/842)
OR	1.64	0.85	1.15
95% CI	0.81–3.35	0.45–1.60	0.72–1.81
Small for gestational age:			
Yes	61% (59/97)	96% (175/183)	84% (234/280)
No	65% (51/78)	97% (1 548/1 590)	96% (1 599/1 668)
OR	0.82	0.59	0.73
95% CI	0.42–1.60	0.26–1.39	0.43–1.23
Birth asphyxia (χ^2 = 78.29; *P* < 0.001):[a]			
Yes	44% (32/72)	85% (145/170)	73% (177/242)
No	76% (78/103)	98% (1 575/1 603)	97% (1 653/1 706)
OR	0.25	0.09	0.16
95% CI	0.12–0.50	0.05–0.17	0.09–0.23
Respiratory distress syndrome (χ^2 = 22.17; *P* < 0.001):[a]			
Yes	55% (44/80)	87% (102/117)	74% (146/197)
No	69% (66/95)	98% (1 621/1 656)	96% (1 687/1 751)
OR	0.54	0.16	0.35
95% CI	0.28–1.05	0.08–0.31	0.18–0.51
Severe infections (χ^2 = 16.88; *P* < 0.001):[a]			
Yes	57% (36/63)	88% (109/124)	78% (145/187)
No	66% (74/112)	98% (1 614/1 649)	96% (1 688/1 761)
OR	0.68	0.16	0.40
95% CI	0.35–1.36	0.08–0.31	0.21–0.59

TABLE 2. ***(Continued)***

Variable	Infants born at <37 weeks with birthweight <1 500 g	Infants born at ≥37 weeks or with ≥1 500 g birthweight	Total
Major malformations (χ^2 = 56.15; P < 0.0001):[a]			
Yes	50% (2/4)	81% (62/77)	79% (64/81)
No	63% (108/171)	98% (1 661/1 696)	95% (1 769/1 867)
OR	0.58	0.09	0.13
95% CI	0.06–5.97	0.04–0.18	0.05–0.21
Intraventricular hemorrhage:			
Yes	61% (27/44)	88% (15/17)	69% (42/61)
No	63% (83/131)	97% (1 708/1 756)	95% (1 791/1 887)
OR	0.92	0.21	0.78
95% CI	0.43–1.97	0.04–1.37	0.37–1.60

[a] Mantel-Haenszel summary χ^2.
[b] The odds ratios for the first two columns are crude, while those for the last column (both groups combined) are weighted.
[c] Infants whose sex was not recorded are not reflected in these data.

TABLE 3. Multiple logistic regression model for the study infants that treats gestational age (23–45 weeks) and birthweight (500–5 620 g) as continuous variables and all other variables as dichotomous, taking the value of 1 if the condition is present and 0 otherwise; log likelihood test for goodness of fit: *P* < 0.001

Variable	β coefficient	Standard error	Odds ratio	95% confidence interval
Gestational age	0.1218	0.0313		
Birthweight	0.0003	0.0001		
Poor maternal obstetric history	–0.5359	0.1810	1.70	1.20–2.43
Birth asphyxia	–0.8687	0.1262	2.38	1.86–3.05
Respiratory distress syndrome	–0.1952	0.1414	1.21	0.92–1.60
Severe infection	–0.4787	0.1374	1.61	1.23–2.11
Major malformation	–1.2570	0.1898	3.51	2.42–5.09

TABLE 4. Survival rates of study infants at 28 days of life in each participating NICU, showing the expected versus actual numbers and percentages surviving and the percentage departure from the expected survival figure in each unit—"expected" survival being calculated by logistic regression for prediction of neonatal survival, taking into account gestational age, birthweight, poor obstetric history, birth asphyxia, severe infections, and major malformations; the percentage difference = (observed − expected)/expected

Unit No.	No. of infants	No. surviving		% surviving		% difference
		Observed	Expected	Observed	Expected	
1	330	324	318.5	98.2	96.5	1.8
2	319	299	298.7	93.7	93.6	0.1
3	271	264	258.5	97.4	95.4	2.1
4	268	250	252.2	93.3	94.1	–0.9
5	232	216	215.6	93.1	92.9	0.2
6	180	169	174.1	93.9	96.7	–2.9
7	171	153	157.0	89.5	91.8	–2.5
8	113	102	99.1	90.3	87.7	3.0
9	64	56	60.2	87.5	94.1	–7.0
Total	1 948	1 833	1 833	94.1	94.1	0

DISCUSSION

In the face of methodologic and epidemiologic difficulties that similar studies from countries with more advanced organization of perinatal care have long made apparent, this report on neonatal survival of babies admitted to NICUs in São Paulo is the first attempt to construct a survival profile for a representative sample of the neonatal intensive care population in that city. The observed mortality rate of 59 deaths per 1 000 live-born infants admitted to participating NICUs in this study compares favorably with that reported by similar surveys in other countries (*26*).

It has been previously noted, both in Brazil (*27*) and in other countries (*22, 28–30*), that neonatal survival tends to increase with gestational age and birthweight, and that the importance of these variables as well as the close relationship between them is particularly evident for infants with very low birthweights. Likewise, it has been widely found outside Brazil that infant survival is unfavorably influenced by poor maternal obstetric history, major malformations, birth asphyxia, or respiratory distress syndrome (*1, 14, 16, 22, 26*).

In the present study, neonatal survival was found to vary significantly among the participating NICUs, even after accounting for significant associated variables (particularly major malformations and birth asphyxia). Thus, previously noted variability in newborn survival at different NICUs (*31, 32*) was corroborated by our findings.

Obviously, we have only accounted for the effects of a few variables (although more than the number tested in some similar studies), and other potentially confounding variables (such as the study infants' severity of illness) could have played a significant role. However, evaluation of such other variables was not part of the present survey, which was conceived as only the first stage of a more ambitious collaborative project. Future efforts of the Paulista Collaborative Group on Neonatal Care may focus on identifying causes of the differences in survival outcomes of patients at the various NICUs—including each baby's physiologic status and disease severity profile, as well as prevailing practices at the different NICUs.

Obviously, a wide range of factors affect the admission, management, and mortality of high-risk babies worldwide (*24*). However, even when priorities differ, common goals include sound care assessment, improved planning of interventions, and optimal deployment of resources (*33*). In the NICUs of developed countries, use of prognostic scoring systems (*26, 34, 35*) combined with obstetric ultrasound scans (*36*) has been recommended for assessing the risks of neonatal morbidity and mortality (*34*). However, much remains to be done to develop and assess scientifically appropriate technology in developing countries (*33, 37*), particularly in areas where scarce financial, planning, and teaching resources demand low-cost approaches (*38*). Therefore, from a Brazilian perspective the appraisal of neonatal intensive care appears as both a national and an international challenge (*1*). Within this context, creation of a permanent multicenter collaborative network for the continuing assessment of neonatal care in São Paulo and other regional settings would seem appropriate, cost-effective, and worthwhile.

Acknowledgments. The authors and other team members extend their thanks to the staff members of the participating units for their cooperation. They also wish to thank Dr. João Yunes of the Pan American Health Organization in Washington, D.C., whose kind interest and availability rendered the study feasible, and also Daniela Miglio for secretarial assistance and Judy Baggott for help in editing the manuscript.

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Manuscript received on 13 November 1995. Revised version accepted for publication on 5 February 1997.

RESUMEN

La supervivencia en nueve unidades de cuidados intensivos neonatales en São Paulo, Brasil

Una iniciativa colectiva para evaluar los factores que inciden en la supervivencia de los recién nacidos en unidades de cuidados intensivos neonatales (UCIN) se llevó a cabo mediante el estudio de 1 948 neonatos ingresados en nueve UCIN de la ciudad de São Paulo entre el 1 de junio y el 30 de noviembre de 1991. Se usó un formulario estandarizado para recoger información sobre los niños estudiados. Fue la primera actividad emprendida por una red de neonatólogos (Grupo Colaborador Paulista para la Atención Neonatal) dedicada a evaluar y mejorar, mediante un esfuerzo colectivo, la atención neonatal en la ciudad. Los resultados del estudio revelaron una mortalidad general de 59 defunciones por 1 000 recién nacidos y una mayor supervivencia mientras mayores fueran la edad gestacional y el peso al nacer. Otras variables que tuvieron un efecto significativo en la supervivencia fueron la presencia de antecedentes obstétricos maternos desfavorables (hijos mortinatos o muertes neonatales previas, o dos o más abortos espontáneos); asfixia al nacer (Apgar <7 a los 5 minutos); síndrome de insuficiencia respiratoria; infecciones graves; y malformaciones importantes. No obstante, un análisis de regresión logística múltiple reveló diferencias en las tasas de supervivencia neonatal de las nueve UCIN, aun después de tener en cuenta estos factores. Entre las posibles causas de esta variabilidad figuran algunas diferencias indeterminadas en cuanto a la gravedad de las enfermedades neonatales y la atención médica en cada población. Estos resultados sugieren la necesidad de hacer un mayor esfuerzo por identificar y reducir los factores de riesgo que se asocian con la mortalidad neonatal y de evaluar adecuadamente la atención médica brindada en las UCIN. En este contexto, la red colaboradora de neonatólogos establecida en São Paulo proporciona una sólida estructura organizacional para evaluar y mejorar la efectividad de la atención del recién nacido.