CLINICS

CLINICAL SCIENCE

Factors associated with the need for ventilation at birth of neonates weighing ⩾2,500 g

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OBJECTIVES: Approximately 20-40% of annual global neonatal deaths occur among infants with birthweights ⩾2,500 g, and most of these deaths are associated with intrapartum asphyxia in low- and middle-income countries. This study aims to evaluate the peripartum variables associated with the need for resuscitation at birth of neonates weighing ⩾2,500 g.

METHOD: This case-control retrospective study was performed on data from all public reference maternity units in the state of Ceará, Northeast Brazil, between March 2009 and March 2010. The subjects were singleton neonates without malformations weighing ⩾2,500 g, who required positive-pressure ventilation in the delivery room. The controls had a 1-minute Apgar score of ⩾8 and did not undergo resuscitation. Variables associated with positive-pressure ventilation in the delivery room were evaluated via conditional multivariate logistic regression.

RESULTS: Of the 2,233 live births with birth weights ⩾2,500 g, 1-minute Apgar scores ⩽7, and no malformations, 402 patients met the inclusion criteria, and they were paired with 402 controls. Risk variables for positive-pressure ventilation at birth were a gestational age <37 weeks (OR: 3.54; 95% CI: 1.14-10.92) and meconium-stained amniotic fluid (8.53; 4.17-17.47). Cervical examination at maternal admission (0.57; 0.38-0.84) and a written follow-up of the labor (0.68; 0.46-0.98) were identified as protective variables.

CONCLUSIONS: Significant flaws in obstetric care are associated with the need for positive-pressure ventilation at birth for neonates weighing ⩾2,500 g.

KEYWORDS: Newborn Infant; Positive-Pressure Ventilation; Resuscitation; Obstetric Labor Complications; Perinatal Care.

Sousa JR, Leite AJ, Sanudo A, Guinsburg R. Factors associated with the need for ventilation at birth of neonates weighing ⩾2,500 g. Clinics. 2016;71(7):381-386

Received for publication on January 27, 2016; **First review completed on** March 4, 2016; **Accepted for publication on** April 13, 2016

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INTRODUCTION

Each year, approximately 10 million infants require assistance to begin breathing at birth. Of these infants, six million need positive-pressure ventilation applied by mask and over one million require tracheal intubation, cardiac massage, drugs, or some combination of these procedures in the delivery room (1). Perinatal asphyxia is associated with approximately 717,000 (610,000-876,000) neonatal deaths per year and approximately one million survivors will have neurodevelopmental problems (2).

International estimates show that approximately 20-40% (740,000-1,480,000) of annual neonatal deaths occurs among "normal-weight" infants (⩾2,500 g) and in low- and middle-income countries, most of these deaths are associated with intrapartum asphyxia (3). The trends of neonatal mortality in low- and middle-income countries, including Brazil, show a concentration of deaths during the first week, particularly in the first day of life and a high percentage of normal-weight children (⩾2,500 g) contribute to these numbers (4-6). Brazilian regional statistics reveal that this problem is greater in the northern and northeastern regions (2,6,7). Research suggests that thorough obstetric care standards for these regions (e.g., skilled care givers attending the birth, emergency obstetric care and the potential for performing caesarean section if needed) would reduce the neonatal mortality rate related to childbirth by up to 85% (2). However, the effectiveness of these interventions is multifactorial and is most likely associated with each local situation (8). Therefore, identifying the risk factors associated with the mother and neonate is important, particularly those related to peripartum obstetric care (5,9).

The current study evaluated the peripartum factors associated with the necessity for neonatal resuscitation in the delivery room

No potential conflict of interest was reported.

DOI: 10.6061/clinics/2016(07)05

among newborn infants with birth weights ⩾2,500 g and without congenital malformations at all public referral maternity hospitals in the state of Ceará, Northeast Brazil.

METHOD

This study used a retrospective case-control design and was conducted based on data from all public tertiary referral maternity hospitals in Ceará in 2009-2010. Ceará, one of the 27 states of Brazil, is located in the northeastern part of the country on the Atlantic coast. It is the 8th largest Brazilian state by population and has a human development index of 0.682 (2013). In the year of the study, the following public hospitals were considered as referral hospitals for obstetric and neonatal care of high risk pregnancies in Ceará and accounted for 12% of all infants born alive in the state: General Hospital Dr. César Cals (HGCC; Fortaleza, Ceará), Fortaleza General Hospital (HG; Fortaleza, Ceará), Assis Chateaubriand Maternity School (MEAC; Fortaleza, Ceará), and São Lucas Hospital and Maternity Unit (HMSL; Juazeiro, Ceará). The ethics committees of those hospitals and the Federal University of São Paulo Ethics Committee on Research approved this study.

Newborn infants were pre-selected from the Live Births Information System database from March 1, 2009 to March 31, 2010 to identify those with a birth weight ⩾2,500 g and a 1-minute Apgar score ⩽7 and/or a 5-minute Apgar score <7 at the chosen hospitals and those born over the same period in the same maternity hospitals with 1-minute Apgar scores of >7. After identifying the pre-selected records in the hospital archives, patients and controls were chosen according to criteria described below. The selected cases were singleton infants with birth weights of ⩾2,500 g who required positive-pressure ventilation immediately after birth. Neonates for whom resuscitation procedures at birth were not reported in the medical records but whose 5-minute Apgar scores were <7 were also included in the case group. Patients born without signs of life and those with congenital malformations reported on their birth certificates or in the hospital records were excluded from the case group. In each maternity unit where a patient was born, a neonate control was selected from within same survey period. Control infants were singletons with 1-minute Apgar scores of >7 who had not undergone any type of resuscitation. These controls were matched for sex, birth weight (±100 g), gestational age (±7 days) and birth time (the closest possible match), in that order. Neonates with congenital malformations reported on their birth certificates or in their medical records were also excluded from the control group.

Given the necessity of performing a logistic regression, the sample size was estimated at 15 cases per independent variable (10,11). Because the initial design sought to analyze 23 variables, the estimated sample size was therefore 345 cases. The sample size was increased by 15% to account for possible data loss; therefore, the total study population required was calculated to be 400 case-control pairs.

The data were collected from the medical records of the newborns and their mothers. The diagnoses and procedures performed that were noted in the records relating to maternal or fetal diseases or complications were considered in relation to the relevant variables. The duration of labor was defined as the time between the first examination of cervical dilation and the delivery. The following variables associated with in-hospital and childbirth care were collected: type of delivery, weekend delivery (i.e., between 7 pm on Friday and 7 am on Monday), workload over a 12-hour period in the maternity unit (⩾7 births, >30% of caesareans, or both) (12,13), monitoring of delivery/intrapartum period (defined based on the presence of regular vaginal examination notes and notes on fetal heart rate or the use of a partograph preceding birth and during the intrapartum period) and notes on the presence of uterine activity. In addition, the following information on newborns was collected: gestational age (determined based on the following ranked criteria: 1st) first trimester ultrasound examination, 2nd) last menstrual period, 3rd) neonatal physical exam) (14); birth weight as measured in the four hospitals on scales accurate to within 10 g; sex; 1- and 5-minute Apgar scores as evaluated by a health professional who attended the patient in the delivery room; and resuscitation procedures performed according to the notes made in the delivery room, which were classified as positive-pressure ventilation (ventilation with a resuscitation bag and mask or endotracheal tube) or advanced resuscitation (ventilation accompanied by chest compressions, medication, or both).

Paired t-tests or a Wilcoxon signed-rank test were used to compare the patients and controls with regard to the variables. The associations among the categorical variables were tested using McNemar's chi-square test. Odds ratios (ORs) and their respective 95% confidence intervals (95% CIs) were calculated for the univariate analysis. For the multivariate analysis, a conditional logistic regression model was fitted in which all variables in the univariate analysis with p-values <0.20 were initially included. Variables that were not significant were then individually removed from the model. All analyses were performed using STATA/SE 12.1 software (StataCorp. 2011. College Station, TX, USA).

RESULTS

During the study period, 16,292 live births were reported at the four public hospitals included in the study, representing 11.5% of all births in the state. Of these births, 12,883 (79%) newborns weighed ⩾2,500 g, 12,617 of whom had no congenital malformations. Of the latter group, 2,223 (18%) had 1-minute Apgar scores of ⩽7, 5-minute Apgar scores of <7, or both.

Out of the 2,233 live births weighing ⩾2,500 g with 1-minute Apgar scores of ⩽7 and/or 5-minute Apgar scores of <7, or both, without congenital malformation across the four hospitals, 394 received positive-pressure ventilation, eight required advanced resuscitation positive-pressure ventilation, eight required advanced resuscitation and 33 had no notes in their medical record regarding whether they received resuscitation. Thus, 402 infants met the inclusion criteria and were allocated to the patient group and a control infant was matched with each patient.

The distribution of births across the four referral hospitals is shown in Table 1. Three referral hospitals were located in the state capital (MEAC, HGF, and HGCC) and one was located in the interior (HMSL). Table 2 shows their general characteristics.

The mean age of the mothers of the 804 patients analyzed was 25±7 years and 176 (22%) were adolescents, 307 (38%) had fewer than eight years of education, only 19 (2%) had no prenatal visits, 356 (44%) were primiparous, 54 (7%) had prenatal diabetes, 185 (23%) had hypertensive syndrome and

499 (62%) had a caesarean delivery. The neonates in the case group had an average weight of 3,282 ± 366 g. Their gestational age was 39 ± 2 weeks and 120 (30%) were between 2,500 and 2,999 g, whereas 28 (7%) were ⩾4,000 g. Forty-eight (12%) were born between 32 and <37 weeks, whereas 42 (10%) were born at ⩾41 weeks. Of these infants, 233 (58%) were male. Among the controls, the mean weight was 3,275 ± 358 g and the mean gestational age was 39 ± 2 weeks. The distributions of weight, gestational age and sex were identical to those of the patient group. The median 1-minute Apgar score of the case group was 4 ± 2, and the median 5-minute score was 8 ± 2, while 55 (14%) infants had 1-minute Apgar scores of <3 and 82 (20%) infants had 5-minute Apgar scores of <7. Of the 402 patients, 394 (98%) received positive-pressure ventilation and eight (2%) received advanced resuscitation in the delivery room. Among the controls, the mean Apgar score at both 1 and 5 minutes was 9 ± 0.

Table 3 shows the distribution of newborn pairs in the patient and control groups based on maternal and neonatal characteristics. The univariate ORs and their 95% CIs were calculated based on a comparison of the occurrence of a specific variable only in the case group of each pair *versus* its occurrence only in the control patients. The conditional univariate analysis results regarding complications during the intrapartum period and the markers of obstetric care quality during labor and birth are shown in Table 4. The results of the conditional logistic multivariate analysis are presented in Table 5.

Table 1 - Distribution of the infants included in the study among the 4 reference maternity hospitals.

Hospital	Cases	Controls	Live-born infants ⩾2,500 g
MEAC	158 (39.3%)	158 (39.3%)	4317 (33.5%)
HGF	57 (14.2%)	57 (14.2%)	1280 (9.9%)
HGCC	102 (25.4%)	102 (25.4%)	3189 (24.8%)
HMSL	85 (21.1%)	85 (21.1%)	4097 (31.8%)
Total	402 (100%)	402 (100%)	12.883[1] (100%)

MEAC: Maternidade Escola Assis Chateaubriand; HGF: Hospital Geral de Fortaleza;
HGCC: Hospital Geral Dr. Cesar Cals; HMSL: Hospital e Maternidade São Lucas.
[1] Live-born infants with birth weights ⩾2500 g in the four maternity hospitals.

DISCUSSION

The results of this multicenter study based on data from referral hospitals in Ceará, northeastern Brazil, revealed that the factors related to access to care and monitoring during labor and delivery influence the necessity for delivery-room resuscitation of neonates born weighing ⩾2,500 g.

The newborns without malformations who received positive-pressure ventilation or advanced resuscitation in the delivery room (402 patients) represented 2.5% of all live births and 3.1% of the infants weighing ⩾2,500 g in the

Table 2 - Characteristics of the hospitals included in the study during 2009.

	MEAC	HGF	HGCC	HMSL
Live-born infants during the study period	5328	1640	4834	4490
Average number of live-born infants per month	409	126	372	345
Percentage of infants with birthweights ⩾2500 g	81%	78%	66%	91%
Number of obstetricians in the ER and OR per shift	04	03	04	02
Number of neonatologists in the DR per shift	02	02	02	01
Number of nurses in the ER and OR per shift	02	02	02	01
Number of anesthesiologists in the DR per shift	02	01	02	01
Number of obstetric residents in the DR per shift	02	02	02	-
Number of neonatal fellows in the DR per shift	01	01	01	-
Beds in the neonatal intensive care unit	21	12	21	08
Beds in intermediate neonatal care unit	30	13	37	14
Presence of ultrasonographic equipment	yes	yes	yes	Yes
Presence of a fetal heart monitor	yes	yes	yes	No

MEAC: Maternidade Escola Assis Chateaubriand; HGF: Hospital Geral de Fortaleza; HGCC: Hospital Geral Dr. Cesar Cals; HMSL: Hospital e Maternidade São Lucas; OR: Operating Room; ER: Emergency Room; DR: Delivery Room.

Table 3 - Maternal and neonatal characteristics.

	Pairs with data	Present only in cases	Present only in controls	Odds ratio (95% CI)
Adolescent mother	402	59 (14.7)	74 (18.4)	0.80 (0.56; 1.14)
<8 years of school	381	95 (24.9)	88 (23.1)	1.08 (0.80; 1.46)
>6 prenatal visits	390	94 (24.1)	90 (23.1)	1.04 (0.77; 1.41)
First delivery	402	111 (27.6)	94 (23.4)	1.18 (0.89; 1.57)
Previous C-section	390	84 (21.5)	49 (12.6)	1.71 (1.19; 2.49)
Previous fetal death	401	17 (4.2)	17 (4.2)	1.00 (0.48; 2.09)
Diabetes	402	26 (6.5)	18 (4.5)	1.44 (0.76; 2.80)
Hypertension	402	82 (20.4)	52 (12.9)	1.58 (1.10; 2.28)
Placental abruption	402	20 (5.0)	2 (0.5)	10.00 (2.43; 88.24)
Oligohydramnios	401	14 (3.5)	10 (2.5)	1.40 (0.58; 3.52)
Birthweight <3000 g	402	8 (2.0)	4 (1.0)	2.00 (0.53; 9.07)
Gestational age <37 wk	402	17 (4.2)	4 (1.0)	4.25 (1.39; 17.36)

CI: confidence interval, wk: weeks.

Table 4 - Characteristics related to the labor and delivery.

	Pairs with data	Present only in cases	Present only in controls	Odds ratio (95% CI)
Cesarean section	402	157 (39.0)	51 (12.7)	3.08 (2.23; 4.31)
Dystocia	402	73 (18.1)	29 (7.2)	2.52 (1.62; 4.01)
Meconium-stained AF	402	67 (16.7)	9 (2.2)	7.44 (3.70; 16.98)
Uterine activity present	278	5 (1.8)	28 (10.1)	0.18 (0.05; 0.47)
Cervical exam at admission	389	58 (14.9)	113 (29.0)	0.51 (0.37; 0.71)
Ruptured membranes >12 h	402	12 (3.0)	27 (6.7)	0.44 (0.20; 0.91)
Induction of labor	402	65 (16.2)	64 (15.9)	1.01 (0.71; 1.46)
Monitoring of labor	402	65 (16.2)	120 (29.8)	0.54 (0.39; 0.74)
Fetal rate heart monitored	394	80 (20.3)	61 (15.5)	1.31 (0.93; 1.86)
△ 1st exam-delivery >12 h	123	22 (17.9)	13 (10.6)	1.69 (0.81; 3.66)
△ last exam-delivery >2 h	121	23 (19.0)	24 (19.8)	0.96 (0.52; 1.77)
△ admission-delivery >6 h	401	107 (26.7)	80 (19.9)	1.34 (0.99; 1.81)
Woman transferred	402	43 (10.7)	26 (6.5)	1.65 (0.99; 2.80)
Delivery at night	402	93 (23.1)	90 (22.4)	1.03 (0.76; 1.40)
Delivery on weekend	402	100 (24.9)	78 (19.4)	1.28 (0.94; 1.75)
⩾7 deliveries/shift	402	70 (17.4)	84 (20.9)	0.83 (0.60; 1.16)
>30% of C-sections/shift	402	86 (21.4)	34 (8.4)	2.53 (1.68; 3.88)

CI: confidence interval; AF: amniotic fluid; Woman transferred: pregnant woman transferred from another hospital.

Table 5 - Variables associated with the use of positive-pressure ventilation.

	Odds ratio	95% Confidence interval	*p*-value
Meconium-stained amniotic fluid	8.53	(4.17; 17.47)	<0.001
Cervical examination at admission	0.57	(0.38; 0.84)	0.005
Written follow-up of labor and delivery	0.68	(0.46; 0.98)	0.041
Gestational age <37 weeks	3.54	(1.14; 10.92)	0.028

four hospitals. These values are similar to those of a Brazilian study of 6,945 infants with gestational ages between 34 and 41 weeks without congenital malformations who were born vaginally or via non-emergency caesarean section across 35 maternity referral hospitals in 20 Brazilian capitals in September 2003. Of these infants, 277 (4.0%) required positive-pressure ventilation at birth and 10 (0.1%) required advanced resuscitation (15). Research conducted at a rural referral hospital in Tanzania in 2009 showed that 6.5% of infants needed mask ventilation at birth, regardless of weight (16). Global estimates, regardless of the birth weight or type of unit where the birth occurred, indicate that 3.0-6.2% of neonates need basic or advanced resuscitation (1).

The factors associated with the need for resuscitation among the patients analyzed in the current study include the biological variables related to the mother-fetus dyad and those related to the quality of obstetric care received. With regard to the biological variables, despite the fact that gestational age was a pairing criteria in the study and it presented a similar distribution between cases and controls, a gestational age of <37 weeks correlated with an approximately 4-fold increase in the chance that neonates weighing ⩾2,500 g would need resuscitation in the delivery room even after adjusting for other risk factors. Recent research has also demonstrated that preterm infants, including those weighing ⩾2,500 g, have a higher risk of morbimortality than those of a similar weight but who are born at term (17-19).

With regard to complications during pregnancy, the presence of meconium in the amniotic fluid is associated with adverse neonatal outcomes, including sepsis, seizures and cerebral palsy. In addition, meconium aspiration syndrome (MAS) is responsible for approximately 3-5% of all perinatal deaths (20-22). A national survey that examined early neonatal mortality in Brazil between 2005 and 2009 found an early neonatal mortality rate due to MAS of 0.30 per thousand live births and the rate ranged from 0.32 to 0.41 per 1,000 live births per year in the northeastern states (22). These rates are high compared with other countries and are approximately 30 times higher than those in Australia and New Zealand from 1990-2000, as well as 15 times higher than those in France in the 2000s (22,23).

Of the factors related to the quality of obstetrical care, after adjusting for the other variables in the conditional logistic regression, the results show that receiving a more detailed physical examination at admission (including a vaginal examination and the monitoring of labor and childbirth using a partograph or medical records) was a protective factor against the need for resuscitation. It must be stressed that these measures are affordable and accessible at any hospital. Thus, this finding reveals serious deficiencies in the labor-associated care provided by the analyzed units, particularly in regard to inadequate monitoring during labor and delivery. Moreover, of the 428 patients who had partographs or notes regarding the development of examinations during labor, 51% were examined less than once every two hours on average. This falls short of the World Health Organization's recommendations concerning the intrapartum monitoring of "low-risk women" (24), which call for the periodic evaluation of the fetal heart rate every 60 minutes during the latent phase of labor and every 30 minutes at the beginning of the active phase. In fact, although the quality of intrapartum care is critical for neonatal health, the literature regarding periodic evaluations during labor is scarce (25). However, it is clear that the time interval between examinations is an important factor for the early detection of changes in intrapartum fetal health (26). One hypothesis to explain the lower levels of obstetric vaginal examinations and the lack of documentation regarding monitoring the progress of labor and childbirth refers to the concept of "relative neglect" in basic intrapartum care. This concept is characterized by the fact that a greater emphasis is placed on monitoring high-risk pregnant women

at the expense of neglecting the majority of women with a lower intrapartum risk.

The use of secondary data from medical records and the retrospective nature of the case-control methodology represent limitations of this study because they preclude determining the causal direction of the variables analyzed with any certainty. It should also be noted that the four reference hospitals for high risk pregnancies in the State of Ceará were heterogeneous regarding human resources and equipment for supporting women and providing neonatal care, but we did not evaluate the impact of these differences on the need for resuscitation procedures at birth in the study population. In addition, the data were collected in 2009 and 2010 and may not reflect recent obstetric care practices, although early neonatal deaths of infants with birth weight ⩾2500 g remained approximately 2.0 per thousand live births in Northeast Brazil during the 5-year period since the study was performed (27) and the persistence of problems in the organization of the Brazilian perinatal care system have been recently reported (28). Finally, this study did not attempt to evaluate factors associated with perinatal asphyxia and/or hypoxic-ischemic encephalopathy, but it did evaluate the factors associated with the need for resuscitation procedures in the delivery room that indicate that the infant's transition to the extrauterine environment required intervention, which is critically dependent on the availability of skilled health professionals at the birth. It is important to highlight that the present study provides the most thorough Brazilian study to date examining the influence of the quality of obstetric care on the need for the resuscitation of neonates who would otherwise be expected to be healthy and to transition to the extrauterine environment with minimal complications.

The present study is a reminder that, for newborns with adequate birth weight, the requirement for resuscitation in the delivery room can be minimized using accessible, low-tech and inexpensive techniques that require a basic level of organization of the care provided to women in labor. Furthermore, health professionals should be educated with regard to the need for constant monitoring of fetal well-being.

AUTHOR CONTRIBUTIONS

Sousa JR participated in designing the study, collecting, analyzing and interpreting the data, and manuscript writing. Leite AJ participated in designing the study, interpreting the data and manuscript writing. Sanudo A participated in the statistical analysis, interpreting the data, revising the edited manuscript and approved the final version of the manuscript as submitted. Guinsburg R participated in designing the study, analyzing and interpreting the data and manuscript writing. All authors participated in the conception and design of the study, the analysis and interpretation of the data, in the drafting or revision of the manuscript and have approved the final version of the manuscript.

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