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Birth Asphyxia: A Major Cause of Early Neonatal Mortality in a Tanzanian Rural Hospital

WHAT'S KNOWN ON THIS SUBJECT: The presumed causes of neonatal deaths globally have remained unchanged over the past decade and include infections (~30%), prematurity (~30%), and asphyxia (~25%). Great uncertainty surrounds these estimates and, in addition, cases are likely misclassified as stillbirths.

WHAT THIS STUDY ADDS: These observational findings indicate that asphyxia accounts for a much higher percentage (60% of early deaths). Prematurity (18%), low birth weight (8%), and overt infection are much less common. The 5-minute Apgar score is an unreliable indicator of birth asphyxia.

abstract

OBJECTIVE: Early neonatal mortality within the first 24 hours contributes substantially to overall neonatal mortality rates. The definition of birth asphyxia (BA) is imprecise, and reliable cause-specific mortality data are limited; thus the estimated proportion of BA-related deaths globally remains questionable. The objective was to determine the presumed causes of neonatal death within the first 24 hours in a rural hospital in Northern Tanzania.

METHODS: This is a prospective descriptive observational study conducted in the delivery room and adjacent neonatal area. Research assistants were trained to observe and record events related to labor, neonatal resuscitation, and 24-hour postnatal course. BA was defined as failure to initiate spontaneous respirations and/or 5-minute Apgar score <7, prematurity as gestational age <36 weeks, and low birth weight (LBW) as birth weight <3rd centile for gestational age. Data were analyzed with χ^2 and Student's *t* tests.

RESULTS: Over 1 year, 4720 infants were born and evaluated. Of these, 256 were admitted to the neonatal area. Forty-nine infants died secondary to BA (61%), prematurity (18%), LBW (8%), infection (2%), congenital abnormalities (8%), and unclear reason (2%). The 5-minute Apgar score was ≥7 in 50% of the infants who died secondary to BA.

CONCLUSIONS: Most cases of early neonatal mortality were related to BA, and prematurity and LBW are additional important considerations. Reducing perinatal mortality requires a multifaceted approach with attention to issues related to BA, potential complications of prematurity, and LBW. The 5-minute Apgar score is a poor surrogate of BA. *Pediatrics* 2012;129:e1238–e1243

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KEY WORDS

millennium developmental goal 4, neonatal mortality, low-resource settings, causes of neonatal deaths

ABBREVIATIONS

BA—birth asphyxia
BMV—bag mask ventilation
BW—birth weight
FHR—fetal heart rate
GA—gestational age
LBW—low birth weight

Dr Ersdal had the idea for the study and is the guarantor (the contributor who accepts full responsibility for the finished article, had access to any data, and controlled the decision to publish); Drs Ersdal and Perlman performed the literature search and managed the research process, including study design, data collection, data analysis and interpretation, writing of the report, revision, and final approval of the version to be published; and Drs Mduma and Svensen participated in study design, data collection and analysis, revision of the report, and final approval of the version to be published. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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Neonatal mortality is defined as death before 1 month of age, and recent global estimates range from 2.9 to 3.6 million deaths per year.[1–4] Of these, ~50% occur within the first 24 hours. The presumed causes of neonatal deaths have remained unchanged over the past decade and include infections (~30%), preterm birth (~30%), and birth asphyxia (BA; ~25%).[2,5,6] However, uncertainty surrounds these estimates due to an almost complete lack of reliable vital registration systems from settings where mortality is highest.[3] Thus analyses are based on retrospective household surveys, and most cause specific data rely on verbal autopsy without consistent definitions and algorithms. Deaths within the first 24 hours are likely underreported or misclassified as stillbirths.[3,7] Nevertheless, early neonatal mortality, especially within the first day after birth, is thought to contribute substantially to the overall neonatal mortality rates.[3,7,8] Currently, neonatal deaths account for ~40% of the under 5 years child mortality. This proportion is steadily increasing due to the annual rate of decline in childhood mortality without a corresponding decrease in neonatal mortality.[1–4] Clearly, efforts to meet Millennium developmental goal 4 by 2015 have to focus on reducing neonatal deaths, in particular early deaths within the first 24 hours. Understanding the presumed causes of death, in settings with the highest burden, is critical before effective preventive strategies can be implemented. BA has for a long time been estimated to account for ~25% of neonatal mortality worldwide.[2,5,6,9,10] However, the definition is imprecise in part because the Apgar score, often used as an indicator to identify BA, is inaccurate or unreliable. Furthermore, many affected infants are likely not reported or misclassified as fresh stillbirths.[3,7] Therefore, considerable uncertainty surrounds the "true" estimated proportion of BA-related mortality. Finally, most cause-specific mortality data have been generated from studies in Asia,[9,11,12] whereas there is a paucity of data from sub-Saharan Africa, the region with the highest neonatal mortality rates and least reduction per year.[3,8]

Haydom Lutheran Hospital is located in rural Northern Tanzania, 300 km from the nearest urban center, with a poor rural population in the area. It has an immediate catchment of ~500 000 people and serves as a referral hospital for ~2 million people.[13] The hospital provides comprehensive emergency obstetric and basic emergency newborn care. Midwives largely conduct deliveries with doctors on call 24 hours. After birth, infants requiring more than routine care are triaged to an adjacent neonatal area (a 10-m^2 room with 1 long bench, with the capability of providing intravenous fluids and antibiotics) and are intermittently cared for by family members and the labor staff. Most infants transition rapidly and are discharged; however, a subset dies for different reasons. Our objective for this study was to determine the presumed causes of death within the first 24 hours of birth in this scarcely resourced rural referral hospital.

METHODS

This is an ongoing descriptive observational study initiated in November of 2009 at Haydom Lutheran Hospital: a rural referral hospital in Northern Tanzania. Research assistants (observers) are continuously present in the labor ward to observe the routine practice of health care providers in the delivery room as well as postnatally in an adjacent neonatal area through the initial 24 postnatal hours. The observers work in 3 shifts over 24 hours. Three observers cover each shift; 2 are always located in the labor ward or in the theater, and 1 in the adjacent neonatal area. Altogether, 14 local women have been trained to observe the performance of the health care workers related to the deliveries and the newborns. Observations are timed by using a stop watch, and the findings are recorded on a data collection form immediately after the delivery (Table 1). The research assistants also review the partograms that are filled out by the birth attendants and the responsible midwives.

The following definitions were used. Gestational age (GA) was based on self-report of the last menstrual period and distance from symphysis pubis to the fundus. Normal term GA at Haydom Lutheran Hospital is routinely defined as 36 weeks. Thus prematurity was defined as a GA <36 weeks and low birth weight (LBW) as birth weight (BW) <3rd centile for GA.[14] BA was defined as a failure to initiate spontaneous respirations and/or 5-minute Apgar score <7: the most commonly used indicator to identify BA in resource limited settings. If a premature infant also had a history of suspected intrapartum related hypoxia (abnormal fetal heart rate [FHR], labor complication, no respiratory efforts, and/or 5-minute Apgar score <7), the primary cause of death was categorized as BA. Normal was defined as survival >24 hours without any detected difficulties. Fresh/intrapartum stillbirth was defined as an Apgar score of 0 at both 1 and 5 minutes with intact skin and suspected death during labor/delivery. Macerated/antepartum stillbirth was defined as an Apgar score of 0 at both 1 and 5 minutes with macerated skin and suspected death before start of labor.

Data Management at Haydom Lutheran Hospital

The research assistants are continuously supervised by the local research manager (Dr Mduma) who reviews the data collection forms on a daily basis for quality control issues including missing information or potential errors.

TABLE 1 Information Recorded on the Data Collection Form

Antenatal information	
Antenatal care	Yes or no
Pregnancy complications	Yes or no
Maternal infections	Non, uterine, malaria, HIV, sepsis, or other
Labor information	
Fetal presentation	Cephalic, breech, shoulder dystocia, transverse, or other
FHR	Normal: 120 –160 beats per min; Abnormal: <120 or >160 beats per min; Nondetected, or not measured
Mode of delivery	Spontaneous vaginal delivery, cesarean delivery, assisted breech delivery, and vacuum extraction
Labor complication	Prolonged labor, obstructed labor, preeclampsia, eclampsia, uterine rupture, hemorrhage, or cord prolapse
Neonatal information	
Transitional newborn adaption	Time intervals (s) from birth to initiation of spontaneous respirations and cord clamping
Gender	Boy or girl
BW	Grams
GA	Wk
Apgar scores	1 and 5 min
Interventions in the delivering room	Stimulation, suction ± BMV with a self-inflating bag, and time interval (s) to initiation of BMV
Specific observations	Newborn heart rate present or not; time interval (s) from initiation of BMV to the onset of spontaneous breathing or death
Indication for admission to the neonatal area	A specific reason for admission is written down on the data collection form
Perinatal outcome at 24 h postpartum	
Normal	Survival >24 h without any detected difficulties
Admitted	Designated neonatal area
Death	
Stillbirth	Macerated = antepartum or fresh = intrapartum

The data are double entered in EpiData 3.1 (EpiData Association, Odense, Denmark) by 2 different people. Random cross-checks of the entered data are undertaken intermittently, with double data extraction and data entry of all cases. If there is any discrepancy between the 2 entered databases, the data entering individuals recheck the original data (the source document) together and correct where necessary. For this report, the data collection is from November 2009 through October 2010.

Statistical Analysis

Analysis has been performed by using SPSS 17 (SPSS, Inc, Chicago, IL) and includes descriptive statistics, χ^2 calculations, Fisher's exact test, and independent-samples *t* tests. All data are presented as mean ± SD unless as otherwise stated.

Ethical Considerations

The Regional Committee for Medical and Health Research Ethics, Western Norway consider the project (reference number 2009/302) to be an evaluation program among certified health care workers. Formal approval from Norwegian ethical committee is thus not required. The National Institute for Research in Tanzania has approved this ongoing study as an evaluation of health care workers' performance with standardized anonymous collection of related routine data on patient outcomes. Informed consent was not obtained.

RESULTS

During the 12 months of observation, 4720 infants were born in the hospital and included in the study. Of these, 4595 (97.3%) were liveborn and 256 (5.6%) were admitted to the neonatal area (Fig 1). Perinatal outcomes at 24 hours' postpartum included the following: normal infants (n = 4529; 96.0%), still admitted in the neonatal area (n = 17; 0.4%), neonatal deaths (n = 49; 1.0%), fresh/intrapartum stillbirths (n = 75; 1.6%), and macerated/antepartum stillbirths (n = 50; 1.0%).

Infant characteristics, obstetric history including FHR recordings, and basic resuscitation provided as related to neonatal outcome are presented in Table 2. Infants who died were of lesser BW and GA as compared with normal infants ($P \leq .0005$). The proportion of premature and LBW infants was higher among infants who died than among normal infants ($P \leq .0005$).

Labor complications, delivery via cesarean delivery, abnormal FHR, and the need for basic resuscitation were more frequently recorded among those who died versus normal infants ($P \leq .0005$). There was a delay in time to initiation of bag mask ventilation (BMV) in infants who died versus those with normal outcome, that is, 100 ± 78 vs 82 ± 58 seconds (P = .045), respectively. In addition infants who died versus those with a normal outcome required a longer duration of BMV, that is, 16 ± 28 vs 5 ± 8 minutes (P = .01).

The timing and presumed causes of death in infants admitted to the neonatal area is as follows: 6 died within 15 minutes after birth due to severe BA; 41 died within 24 hours secondary to BA (n = 24), prematurity (n = 8), LBW (n = 4), infection (n = 1), and congenital abnormalities (n = 4; Fig 1). Two additional infants not admitted to the neonatal area died within 24 hours; 1 due to prematurity, and the other cause of death was unclear.

The characteristics of infants who died by presumed etiology, the obstetric history including FHR recordings, and resuscitation interventions are presented in Table 3. As anticipated, infants

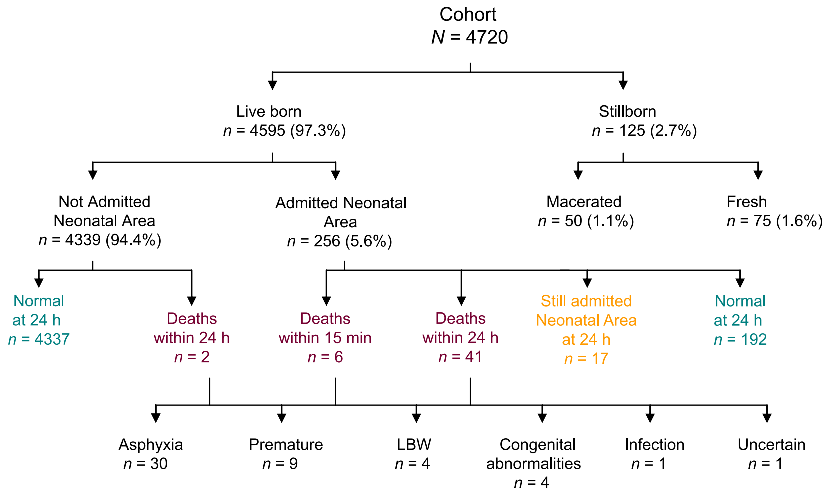

FIGURE 1
Overview of different pathways to perinatal outcome at 24 hours after birth.

who died secondary to BA were of greater BW and GA as compared with infants who died of prematurity ($P \leq .0005$). In 1 premature infant, the primary cause of death was considered to be BA (Table 3). Among the premature infants who died, 2 were born of mothers with malaria. The rates of labor complications and cesarean deliveries were similar in the different groups. FHR abnormalities were more frequently detected among the infants who died secondary to BA versus prematurity, that is, 13/37 vs 1/9 ($P = .03$), respectively. Asphyxiated infants required BMV within the first 2 to 3 minutes after birth due to lack of spontaneous respirations more often than infants who died secondary to prematurity, that is, 29/30 vs 5/9 ($P = .006$), respectively. There was a strong association between need for BMV and asphyxia-related death, when adjusted for BW and GA (odds ratio = 386; 95% confidence interval: 52–2850, $P \leq .0005$). The time to onset of BMV was similar between the 2 groups, but the duration of BMV (until the onset of spontaneous breathing or death) was significantly longer in asphyxiated versus premature infants, that is, 19 ± 31 (median 9.5) vs 6 ± 5 (median 4) minutes ($P = .05$).

Of the asphyxiated infants, 14/30 (47%) had a 5-minute Apgar score <7 of whom 10 had FHR abnormalities, 5 were delivered via cesarean delivery, and 5 died within 15 minutes after birth. Conversely, the remaining 16 infants who died had a 5-minute Apgar score ≥7.

Of the premature infants who died, 5/9 (56%) received basic resuscitation and 1/9 (11%) remained with an Apgar score <7 at 5 minutes and died shortly after admission. All the LBW infants received basic resuscitative actions, and none were recorded to have a 5-minute Apgar score <7.

TABLE 2 Infant Characteristics Related to Normal or Dead Infants at 24 Hours

Characteristics	Normal[a] (*n* = 4529)	Dead (*n* = 49)	*P*
BW, g	3163 ± 475	2715 ± 765	≤.0005
GA, wk	36.6 ± 1.6	35.7 ± 2.4	≤.0005
Boy	2343 (52)	30 (61)	.184
Premature	88 (1.9)	12 (24.5)	≤.0005
LBW	53 (1.2)	5 (10.2)	≤.0005
Obstetric complications			
Pregnancy complication	36 (0.8)	2 (4.0)	.062
Maternal infection	86 (1.9)	3 (6.1)	.063
Labor complication	600 (13)	22 (45)	≤.0005
Cesarean delivery	502 (11)	18 (37)	≤.0005
FHR			
Normal (120–160)	4310 (96)	35 (71)	—
Abnormal	100 (2.2)	12 (25)	≤.0005
Nondetected	4 (0.1)	2 (4)	—
Not measured	82 (1.8)	0	—
Resuscitation	625 (14)	41 (84)	≤.0005
Stimulation	619 (13)	41 (84)	≤.0005
Suction	501 (11)	41 (84)	≤.0005
BMV	294 (6.5)	39 (80)	≤.0005
Time to start BMV, s	82 ± 58	100 ± 78	.045
Duration of BMV, s	319 ± 495	965 ± 1670	.012
Apgar score 1 min <7	3	33 (67)	≤.0005
Apgar score 5 min <7	1	17 (35)	≤.0005

Values given are *n* (%). *P*. deaths versus survival >24 h.
[a] Normal = survival >24 h without any detected difficulties.

DISCUSSION

These data for the first time provide prospective descriptive observational information on causes of early neonatal deaths in a rural hospital in a resource limited setting. The findings indicate that BA is the predominant cause accounting for 60% of deaths, with prematurity noted in 18% of cases, and LBW and congenital abnormalities are additional causes. Overt infection was a rare cause of early death. Approximately 50% of the "asphyxiated infants" were assigned a 5-minute Apgar score ≥7, which supports a long held notion that the Apgar score is an unreliable indicator of BA.

The assignment of BA as a proximate cause of death in this report was strict. It included a complicated obstetric

TABLE 3 Infant Characteristics Related to Dead Infants (Within 24 Hours) by Etiology

Characteristics	BA (n = 30)	Prematurity (n = 9)	P	LBW (n = 4)	Abnormalities (n = 4)
BW, g	3013 ± 536	1621 ± 247	≤.0005	1440 ± 381	2477 ± 1004
GA, wk	36.4 ± 1.2	29.8 ± 2.1	≤.0005	36.5 ± 0.6	34.5 ± 1.9
Boy	21 (70)	5 (56)	.42	1 (25)	2 (50)
Premature	1 (3.3)	9 (100)	—	0	2 (50)
LBW	0	0	—	4 (100)	1 (25)
Obstetric complications					
Pregnancy complication	1 (3.3)	1 (11)	.35	0	0
Maternal infection	0	2 (22)	.06	0	1 (25)
Labor complication	15 (50)	4 (44)	.77	2 (50)	0
Cesarean delivery	12 (40)	3 (33)	.72	2 (50)	0
FHR					
Normal (120–160)	17 (56)	8 (89)	.03	4 (100)	4 (100)
Abnormal	11 (37)	1 (11)	.03	0	0
Nondetected	2 (7)	0	—	0	0
Not measured	0	0	—	0	0
Resuscitation	29 (97)	5 (56)	.001	4 (100)	3 (75)
BMV	29 (97)	4 (44)	.001	3	3
Time to start BMV, s	88 ± 70	103 ± 125	.71	107 ± 30	190 ± 88
Duration of BMV, s	1130 ± 1907	345 ± 300	.05	230 ± 94	932 ± 1102
Apgar 5 min <7	14 (47)	1 (11)	.05	0	2 (50)

Values given are n (%). P: BA versus prematurity outcome.

history with abnormal FHR measurement in 50%, a consistent failure of infants to initiate spontaneous respirations coupled with the requirement for basic resuscitative actions including BMV, and the absence of overt signs of infection. The finding of a 60% early mortality rate attributed to BA is consistent with findings from rural Ghana and Bangladesh.[8,12] However, this observation is not consistent with the global estimates of BA-related neonatal mortality of ~25% within 1 month.[2,6] We speculate that this striking discrepancy is in part due to underreporting of early neonatal deaths, misclassification of asphyxiated infants as stillbirths (the nonbreathing nonresuscitated infant), and an unreliable "high" 5-minute Apgar score.

A basic tenet of the Helping Babies Breathe program[15,16] is that initiation of BMV within the Golden first minute after delivery in nonbreathing infants has the great potential to reduce early neonatal deaths and "fresh stillbirths" (the nonbreathing nonresuscitated infant) dramatically. This is a critically important concept because it makes the assumption that most nonbreathing infants are in primary apnea and will respond to the early initiation of BMV. We have previously reported that in the same population ~83% of infants spontaneously initiated breathing within the first minute after delivery, ~8% responded to stimulation and suctioning by initiating breathing, and the majority of the remaining infants responded to BMV by initiating breathing within 4 to 5 minutes.[17] The time to initiation of BMV as well as the duration of BMV were significantly longer among infants who died compared with infants with normal outcome. Specifically, the risk for death increased 16% for every 30 seconds' delay in initiating BMV up to 6 minutes and 6% for every minute of applied BMV.[17] In this report, infants with a diagnosis of BA-related deaths were significantly more likely to receive BMV when corrected for BW and GA. Many of these infants presented with obstetrical complications and FHR abnormalities. Analysis of the same population (and reported separately) reveals that FHR abnormalities intermittently detected with the fetoscope identifies fetal compromise, and the risk for early neonatal deaths and fresh stillbirths.[18] Thus, FHR monitoring and anticipation of the potential need for BMV before delivery should become an important teaching point of the Helping Babies Breathe program.[15]

The data also indicate that a multifaceted approach beyond BMV is necessary to achieve the greatest impact of reducing early neonatal mortality. Thus premature and LBW infants did not require much resuscitation in the delivery room suggesting that other potential factors may have contributed to death including temperature instability, hypoglycemia, and unrecognized or unanticipated infection. In the hospital setting in this report, the initial management of the neonate was by family members and labor staff with no specific education in appropriate care and treatment of newborns. This raises the need for simple neonatal protocols to observe and manage the "seemingly stable" premature or LBW infant. The lack of basic monitoring equipment and blood tests in this population might have contributed to an underestimation of early infection as a causative factor of death.

CONCLUSIONS

The majority of early neonatal deaths are related to BA and failure to initiate spontaneous respirations. The 5-minute Apgar score is a poor surrogate of BA. In general, the deaths of premature and LBW newborns do not appear to be related to cardio-respiratory depression but presumably to known complications such as temperature instability. Reducing early neonatal mortality requires a multifaceted approach with attention related to FHR monitoring and obstetric care, basic neonatal resuscitation including BMV, and potential complications of prematurity and LBW.

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