

Etiologies of NICU Deaths

Jack Jacob, MD, Michael Kamitsuka, MD, Reese H. Clark, MD, Amy S. Kelleher, MSHS, Alan R. Spitzer, MD

abstract

BACKGROUND AND OBJECTIVES: Infant mortality is an indicator of overall societal health, and a significant proportion of infant deaths occur in NICUs. The objectives were to identify causes of death and to define potentially preventable factors associated with death as areas for quality improvement efforts in the NICU.

METHODS: In a prospectively defined study, the principal investigator in 46 level III NICUs agreed to review health care records of infants who died. For each infant, the principal investigator reviewed the medical record to identify the primary cause of death and to look for preventable factors associated with the infant's death. Infants born at ≥ 22 weeks estimated gestational age who were born alive were included. Stillborn infants were excluded.

RESULTS: Data were collected on 641 infants who died. At lower gestational ages, mortality was most commonly due to extreme prematurity and the complications of premature birth (respiratory distress progressing to respiratory failure, intraventricular hemorrhage, necrotizing enterocolitis, and sepsis). With increasing gestational age, the etiology of mortality shifted to hypoxic-ischemic encephalopathy and genetic or structural anomalies. Reviewers of clinical care identified 197 (31%) infants with potentially modifiable factors that may have contributed to their deaths.

CONCLUSIONS: The factors associated with death in infants admitted for intensive care are multifactorial and diverse, and they change with gestational age. In 31% of the deaths, potentially modifiable factors were identified, and these factors suggest important targets for reducing infant mortality.

Pediatrics Medical Group, Center for Research and Education, Sunrise, Florida

Drs Jacob and Kamitsuka contributed to the conception and design of the study and provided extensive editorial input; Dr Clark contributed to the conception and design of the study, wrote the first draft, and edited the manuscript; Mrs Kelleher contributed to the drafting and revision of the article for important intellectual content; Dr Spitzer contributed to the conception and design of the study, analysis and interpretation of data, and critical revisions for important intellectual content; and all authors approved the final manuscript as submitted.

This trial has been registered at www.clinicaltrials.gov (identifier NCT00865150).

www.pediatrics.org/cgi/doi/10.1542/peds.2014-2967

DOI: 10.1542/peds.2014-2967

Accepted for publication Oct 22, 2014

Address correspondence to Reese H. Clark, MD, Pediatrics Medical Group, Inc, 1301 Concord Terrace, Sunrise, FL 33323-2825. E-mail: reese_clark@pediatrics.com

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2015 by the American Academy of Pediatrics

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: This work was supported by Pediatrics Medical Group. No outside honorarium, grant, or other form of payment was given to anyone to produce the manuscript.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

WHAT'S KNOWN ON THIS SUBJECT: Infant mortality is an important indicator of societal health, and approximately two-thirds of all infant deaths occur during the neonatal period and in neonatal intensive care units.

WHAT THIS STUDY ADDS: We report detailed information on the cause of death in infants admitted for intensive care. Factors associated with death are multifactorial, diverse, and change with gestational age. Potentially modifiable factors were identified in 31%.

Infant mortality is a sensitive indicator of overall societal health that is divided into 2 age periods: neonatal (birth–28 days) and postneonatal (29–364 days).¹ Approximately two-thirds of all infant deaths occur during the neonatal period and are caused by complications arising from preterm births, birth defects, maternal health conditions, complications of labor and delivery, and lack of access to appropriate care at the time of delivery.¹ A proportion of postneonatal deaths in NICUs can be attributed to factors arising from the neonatal period. Deaths occurring in NICUs have a major impact on infant mortality. Understanding the causes of death in NICUs and the modifiable factors associated with death has the potential to reduce infant mortality.

Public health policies to improve neonatal and infant survival rates must be informed by a thorough understanding of the factors contributing to neonatal and infant mortality rates.² Prematurity is a major cause of infant death, but standard ways of categorizing the cause of death do not fully capture modifiable factors that contribute to the death.^{3,4} Infants born prematurely, especially at earlier gestational ages, unless they are considered previsible and not offered care, may die of specific preventable diseases.

The goal of this study was to better understand the factors associated with mortality and identify potentially preventable causes of death in infants who die during NICU care. As a result, an improved classification system may help define strategies to decrease neonatal and infant mortality.

METHODS

Prospective Study

We included infants who were ≥ 22 weeks estimated gestational age (EGA) born alive and for whom health care was provided. Stillborn infants

were excluded. We included only infants who died before discharge from the hospital. Enrollment began in November 2010 and was completed in October 2012. The protocol was approved and a waiver of consent was obtained from each site's institutional review board. The study was conducted in compliance with the Health Information and Accountability Portability Act (HIPAA) Privacy Rule regarding the use of a decedent's health record.

Primary Causes of Death

The site's principal investigator reviewed the medical record, completed a root cause analysis to identify the primary cause of death, and looked for potentially preventable factors associated with each infant's death. The investigators selected from a predefined list of potential causes and modifiable factors associated with death. Acquired bowel disease was defined as a subgroup of infants with necrotizing enterocolitis (NEC) or spontaneous intestinal perforation. Text input was allowed to report factors not provided on the lists and to provide details of events surrounding an infant's death. Those responses were reviewed and are summarized in the results.

Review of Pediatrix Clinical Data Warehouse

To evaluate the generalizability of our findings we retrospectively reviewed data on all deaths included in the Pediatrix Data Warehouse that occurred between 2010 and 2012 (the time our study was enrolling infants). This evaluation of outcome data were performed under a waiver from the Western Institutional Review Board for use of deidentified, HIPAA-compliant infant information within the Pediatrix Medical Group Clinical Data Warehouse (CDW). CDW data are captured prospectively from admission to discharge in daily progress notes generated by clinicians using a computer-assisted EMR.

Data Collection and Monitoring in the Prospective Study

An electronic system assigned unique study codes and collected deidentified data on each subject. Clinical research associates monitored each site for protocol adherence and data accuracy and ensured that the site's conduct was in accordance with the International Conference on Harmonization Good Clinical Practice Guidelines and HIPAA regulations. We determined data accuracy by reviewing data collected in the electronic case report form against the medical record.

Statistics and Sample Size Considerations

The project's unifying goal was to define potentially preventable causes of death in infants who received NICU care. Based on the assumption that 10% of neonatal deaths might be preventable and that 60 deaths due to preventable causes would provide an adequate sample to identify the most common causes of preventable death, we chose a sample size of 600 infants. This was a descriptive study, and we report our observations. No special statistics were needed.

RESULTS

Demographics

We identified 641 unique infants who were provided care in 46 different NICUs; all were level III NICUs (III, $n = 6$; IIIB, $n = 34$; and IIIC, $n = 6$). Infants who died were predominantly male and white; 36% of the infants were < 25 weeks' EGA (Fig 1); 59% died within 7 days of birth, and 85% died within 28 days after birth (Fig 2). Fifteen percent of the infants died in the postneonatal period. The 641 infants identified and included in our prospective study were also among 4418 infants that were reviewed using our CDW; the 2 groups were similar with respect to demographic characteristics, EGA distribution, and age at death (Figs 1 and 2 and Table 1).

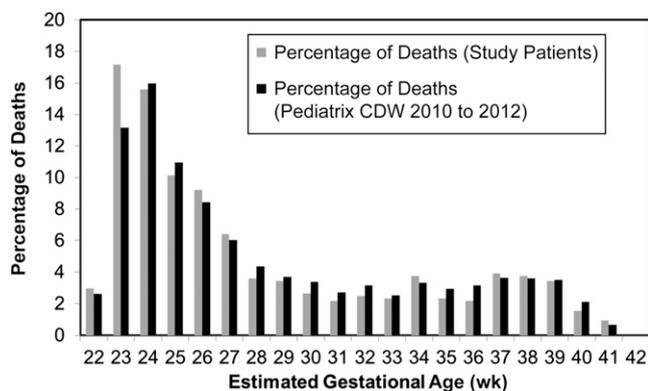


FIGURE 1
Percentage of deaths in the NICU by EGA.

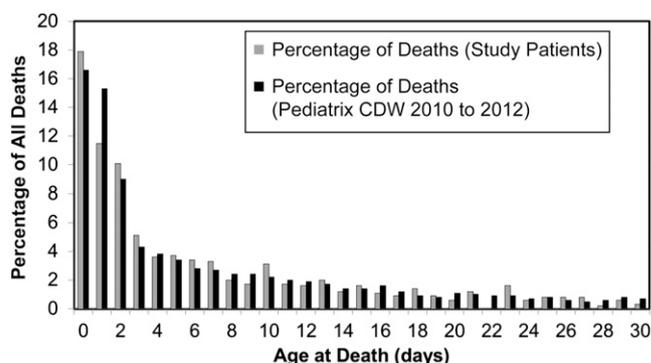


FIGURE 2
Percentage of deaths in the NICU by age at death up to 30 days.

Primary Causes of Death

The most common cause of death was extreme prematurity or low birth weight ($n = 89$, 14% of studied infants) (Fig 3). The second and third most common causes of death were sepsis (79, 12%) and acquired bowel disease (70, 11%). Other primary causes of death (n , %) in descending order of occurrence included lung hypoplasia (61, 9.5%), intraventricular hemorrhage (IVH) or intracranial hemorrhage (60, 9.4%), respiratory distress syndrome (RDS) (51, 8.0%), lethal anomaly (49, 7.6%), hypoxic-ischemic encephalopathy (HIE) (39, 6.1%), genetic syndrome (32, 5.0%), major heart defects (22, 3.4%), bronchopulmonary dysplasia (18, 2.8%), hemorrhagic shock or profound anemia (14, 2.2%), pulmonary hemorrhage (13, 2.0%), renal failure (13, 2.0%), congenital diaphragmatic hernia (11, 1.7%), air

leak syndrome (4, 0.6%), and pulmonary hypertension (4, 0.6%).

At lower gestational ages, mortality was most commonly caused by extreme prematurity and the complications of premature birth (RDS, IVH, NEC, and sepsis). With increasing gestational age, the etiology of mortality shifted to HIE and genetic or structural anomalies (Table 2).

Confounding Factors Associated With Death

The 89 infants with extreme prematurity or low birth weight were either <25 weeks (79 out of 89, 89%) or <750 g (85 out of 89, 96%) at birth. Nineteen (21%), all of whom were born alive, were considered nonviable and offered comfort care alone. Ten (11%) of the 89 infants were born at level II or lower units; 3 (3.4%) were unplanned deliveries that occurred at home. Six (6.7%) of

the 89 mothers who delivered extremely preterm infants had received no prenatal care, and only 50 (56%) mothers had a previous consultation with a maternal-fetal medicine specialist. Thirteen (15%) were conceived using artificial reproductive technology, 8 from in vitro fertilization. Fifty (56%) died within 24 hours, and 79 (89%) died within 7 days of birth.

Sepsis as a cause of death occurred after 7 days of life (48 out of 641, 7.5%) more commonly than sepsis causing death on or before day 7 (31 out of 641, 4.8%). Thirty-nine percent of infants who died of sepsis were born at <25 weeks' gestational age. The 2 most commonly acquired gastrointestinal causes of death were NEC (63, 9.8%) and spontaneous intestinal perforation (7, 1.1%). Of the 63 infants with NEC, 21 (33%) had total bowel necrosis, 19 (30%) were born at <25 weeks' gestation, and 3 (4.8%) had major anomalies (gastroschisis, atrioventricular canal, and tracheoesophageal fistula).

In 61 infants with lung hypoplasia, the most common causes for hypoplasia were major renal anomalies ($n = 23$, 38%), prolonged rupture of membranes ($n = 20$, 33%), and hydrops ($n = 7$, 11%). Although lung hypoplasia was considered the primary cause of death in infants with renal anomalies, we suspect that the renal anomalies (renal agenesis or Potter syndrome, $n = 7$; polycystic kidney disease, $n = 5$; posterior urethral valves or obstructive uropathy, $n = 4$; multicystic dysplastic kidney, $n = 2$; hydronephrosis or other, $n = 5$) were important contributing factors.

Fifty-one infants died of progressive respiratory failure from RDS; 25 (49%) were <25 weeks' and 6 (12%) were ≥ 34 weeks' EGA. All 51 infants were ventilated, 47 (92%) were treated with surfactant, and 19 (37%) received inhaled nitric oxide.

Of 49 infants with lethal anomalies, 22 (45%) had brain anomalies,

TABLE 1 Demographic Characteristics for Infants in Study and Infants Reviewed in CDW

	Identified for Study	CDW 2010–2012
Number of infants ^a	641	4418
Male, %	55	57
Race or ethnicity		
Black or African American, %	28	26
Hispanic, %	15	23
Other, %	7	9
White, %	50	42
Outborn, %	22	22
Cesarean delivery, %	70	68
Report of major anomaly, %	28	33
Trisomy reported, %	4.4	3.7
Maternal age	27 (19–36)	27 (19–37)
Teen mother (<20 y), %	11	12
Multiple (twin, triplet, quadruplet), %	19	17
EGA, median (10–90th percentile)	26 (23–38)	26 (23–37)
Birth wt (g), median (10–90th percentile)	800 (480–2881)	850 (510–2810)
Apgar @ 1 min, median (10–90th percentile)	3 (1–7)	3 (1–7)
Apgar @ 5 min, median (10–90th percentile)	5 (1–8)	6 (1–9)
Apgar @ 10 min, median (10–90th percentile)	6 (1–8)	6 (1–8)
Age at death (d), median (10–90th percentile)	5 (0–40)	5 (0–40)

^a The 641 infants identified and included in our prospective study were also among 4418 infants from our CDW.

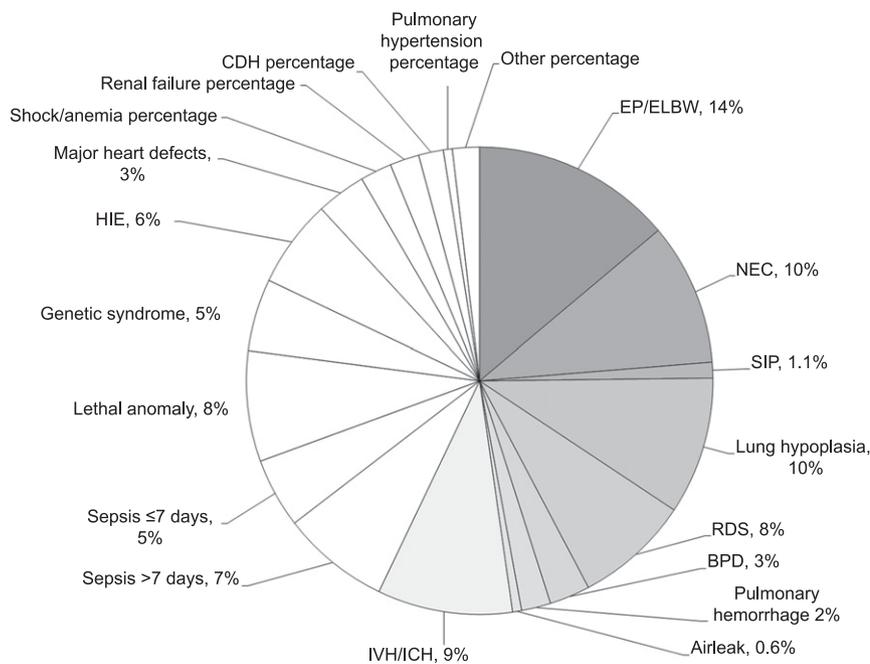


FIGURE 3

Causes of death in the NICU ordered in subgroups and then by most common to least common. BPD, bronchopulmonary dysplasia; CDH, congenital diaphragmatic hernia; EP/ELBW, extreme prematurity or extremely low birth weight; ICH, intracranial hemorrhage; SIP, spontaneous intestinal perforation.

7 (14%) had renal agenesis and profound renal failure but not severe lung hypoplasia, 4 (8.2%) had thanatophoric dwarfism, and 8 (16%) had multiple anomalies but no defined syndrome or genetic disorder. The most common brain anomalies were anencephaly ($n = 8$) and severe

hydrocephalus ($n = 5$). Other lethal anomalies were a large sacroccygeal teratoma associated with severe hydrops, severe craniofacial banding and airway anomalies, lethal skeletal dysplasia, Pierre Robin anomaly with profound hypotonia and significant airway

problems, scimitar syndrome, sirenomelia, surfactant protein B deficiency, and VACTERL association.

Of the 39 infants with HIE, 15 (38%) were born at <35 weeks' EGA and did not receive hypothermia. Of the 24 infants born at ≥35 weeks' EGA, 4 (17%) were not treated with hypothermia. Fifty-nine percent of infants with HIE were born at a level III center, 90% were intubated at birth, 62% had a neonatologist or a neonatal nurse practitioner in attendance, 72% received chest compressions, and 62% received epinephrine at delivery.

Thirty-two infants died of major genetic syndromes: trisomy 18 ($n = 13$, 41%), trisomy 13 ($n = 5$, 16%), Wolf-Hirschhorn syndrome ($n = 2$, 6.3%), and 1 each of trisomy 4, trisomy 20, 4P-, 12q24.21–q24.22, 22Q deletion, chromosome 15 deletion, congenital central hypoventilation syndrome, Klinefelter syndrome, myotonia congenita, myotonic dystrophy type 1, myotubular myopathy, Smith-Lemli-Opitz syndrome, and Zellweger syndrome. In 3 infants with trisomy 21, the deaths were not attributed to their genetic defect.

The 22 major heart defects were congenital cardiomyopathy ($n = 6$), hypoplastic left heart ($n = 5$), transposition ($n = 3$), complex cyanotic congenital heart defects ($n = 3$), critical aortic stenosis ($n = 2$), and 1 each of tetralogy, truncus arteriosus, and double outlet right ventricle or mitral valve atresia. Of the infants with major heart defects, 20 (91%) were born at level III centers.

Twelve infants did not fit into any predefined category. Their causes of death included gastroschisis or cardiac tamponade due to Broviac complication; complications of surgery for Hirschsprung disease; congenital airway abnormalities that prevented intubation; omphalocele; severe perinatal depression but no hypoxic-ischemic encephalopathy; ureaplasma pneumonia;

TABLE 2 Causes of Death by EGA Group

Cause of Death Group	Preterm <25 wk	Preterm 25–28 wk	Preterm 29–33 wk	Late Preterm 34–36 wk	Term >36 wk
Total	229	188	84	53	87
Percentage of all deaths	36%	29%	13%	8%	14%
Extreme prematurity or extremely low birth wt	79 (34.5) ^a	10 (5.3) ^a	0 (0)	0 (0)	0 (0)
IVH or intracranial hemorrhage	33 (14.4) ^a	23 (12.2) ^a	2 (2.4)	1 (1.9)	1 (1.1)
RDS	25 (10.9) ^a	16 (8.5) ^a	4 (4.8)	2 (3.8)	4 (4.6)
NEC	19 (8.3) ^a	31 (16.5) ^a	10 (11.9) ^a	2 (3.8)	1 (1.1)
Sepsis >7 d	19 (8.3) ^a	22 (11.7) ^a	5 (6) ^a	1 (1.9)	1 (1.1)
Sepsis ≤7 d	12 (5.2) ^a	12 (6.4) ^a	5 (6) ^a	1 (1.9)	1 (1.1)
Lung hypoplasia	7 (3.1)	22 (11.7) ^a	13 (15.5) ^a	12 (22.6) ^a	7 (8) ^a
Genetic syndrome	0 (0)	5 (2.7)	7 (8.3) ^a	9 (17) ^a	11 (12.6) ^a
HIE	1 (0.4)	3 (1.6)	8 (9.5) ^a	7 (13.2) ^a	20 (23) ^a
Lethal anomaly	1 (0.4)	5 (2.7)	13 (15.5) ^a	11 (20.8) ^a	19 (21.8) ^a
Major heart defects	2 (0.9)	5 (2.7)	5 (6) ^a	2 (3.8)	8 (9.2) ^a
Congenital diaphragmatic hernia	0 (0)	3 (1.6)	1 (1.2)	1 (1.9)	6 (6.9) ^a
Airleak	3 (1.3)	1 (0.5)	0 (0)	0 (0)	0 (0)
Bronchopulmonary dysplasia	7 (3.1)	9 (4.8)	2 (2.4)	0 (0)	0 (0)
Renal failure	7 (3.1)	4 (2.1)	2 (2.4)	0 (0)	0 (0)
Spontaneous intestinal perforation	6 (2.6)	0 (0)	0 (0)	0 (0)	1 (1.1)
Pulmonary hemorrhage	4 (1.7)	8 (4.3)	1 (1.2)	0 (0)	0 (0)
Pulmonary hypertension	1 (0.4)	0 (0)	0 (0)	1 (1.9)	2 (2.3)
Hemorrhagic shock or profound anemia	2 (0.9)	5 (2.7)	3 (3.6)	2 (3.8)	2 (2.3)
Other	1 (0.4)	4 (2.1)	3 (3.6)	1 (1.9)	3 (3.4)

^a Indicates etiologies that occur in ≥5% of the infants in any subgroup.

tracheoesophageal fistula with intractable respiratory failure; and bladder outlet obstruction, hydronephrosis, or respiratory syncytial viral pneumonia. Two infants died of unexplained shock, and 2 infants died in the delivery room with no identifiable cause.

An autopsy was performed in 74 out of 641 (11%) infants, and in 53 out of 74 (72%) an important finding was noted. The most common findings were identification of an organism associated with sepsis or identification or confirmation of an anomaly.

Comparison of Death Certificate to Research-Reported Primary Cause of Death

A total of 507 death certificates could be reviewed. In 9 (1.8%) the primary cause of death on the case report form was not listed on the death certificate, in 326 (64%) there was agreement between line 1 of the death certificate and the study primary cause of death, and in 172 (34%) the primary cause of death was listed on the death certificate but was not listed on line 1 of the death certificate. In 134 infants

(21%), the death certificate was completed and sent out of the NICU before it could be reviewed.

Most death certificates include the following statement: “The immediate cause does not mean the mechanism of death or terminal event (for example, cardiac arrest or respiratory arrest). The mechanism of death (for example, cardiac or respiratory arrest) should not be reported as the immediate cause of death as it is a statement not specifically related to the disease process, and it merely attests to the fact of death.” Despite this instruction, 131 out of 507 (26%) reviewed death certificates contained nonspecific data (Table 3).

Potentially Modifiable Factors Associated With Death

Of the 641 infant deaths, the study reviewer identified 197 (31%) infants with potentially modifiable factors that may have contributed to the death; 75 out of 197 (38%) infants had >1 factor. The most common modifiable factor associated with mortality was delivery at a center without an appropriate level of support ($n = 67$, 10%) for the infant’s needs; 13 (2.0%) were born at home.

One hundred forty-one (23%) infants needed transport. In 6 infants, transport was delayed, 2 each for weather, inadequate resources, and delay in consultation. Eight (1%) infants were difficult to intubate; 4 of these infants were born in hospitals without NICUs, and 4 were born in hospitals with NICUs and an attending neonatologist at the delivery.

Limited or no prenatal care ($n = 57$, 8.9%) was the second most common modifiable factor associated with mortality. In 35 out of 641 (5.5%) infants, the mother had no prenatal care, and in 22 out of 641 (3.4%) prenatal care was limited (≤2 visits). Other perinatal modifiable risk

TABLE 3 Nonspecific Causes of Death Listed on Line 1 of Death Certificate

Line 1 of Death Certificate	Count
Respiratory failure	61
Cardiorespiratory failure	32
Cardiopulmonary failure	12
Cardiac arrest	8
Cardiorespiratory arrest	5
Cardiopulmonary arrest	4
Progressive respiratory failure	3
Cardiovascular collapse	3
Cardiorespiratory collapse	3

factors included the following: 101 (16%) mothers smoked tobacco during pregnancy, 47 (7.3%) used nonprescription drugs, and 28 (4%) had a history of alcohol abuse. Drug screens were positive in 41 (6.4%) mothers or their infants. Two mothers who used drugs left the hospital against medical advice, only to return and deliver precipitously. Sixty-nine (11%) mothers were <20 years old.

One hundred thirty-seven (27%) mothers of 501 infants born at <34 weeks' EGA did not receive antenatal glucocorticoids. The most common reason provided was the urgent need for delivery or no prenatal care ($n = 97$ out of 501, 20%); however, in 40 out of 501 (8.0%) preterm infants there were no contraindications to maternal antenatal steroids, yet they were not given.

Hospital-acquired infections were reported in 31 (4.8%) infants. There were 22 (3.4%) infants with a report of an adverse event, and although most were not the immediate cause of death, the associated complication may have contributed to the death. In 5 infants, the diagnosis and treatment of sepsis was delayed: 3 died within 7 days after birth (2 had *Escherichia coli*, and 1 had *Haemophilus parainfluenzae*), and 2 died after 7 days (1 had congenital herpes, and 1 had methicillin-resistant *Staphylococcus aureus*). Intubation was difficult and delayed in 5 infants. Three preterm infants had profound hypothermia (<34°C); in 2, hypothermia developed before transport at level I hospitals, and in 1 the infant was hypothermic after returning from the operating room. In 3 infants, NICU-specific feeding protocols were not followed and were considered to have contributed to NEC. In 2 infants, the diagnosis of pericardial effusion associated with indwelling central lines was delayed; in 1 case (infant with gastroschisis), the associated tamponade was thought to be the cause of death. In

the other case, the pericardial effusion was treated successfully with pericardiocentesis, and the death was attributed to hypoplastic left heart syndrome. One infant died of surgical complications for Hirschsprung disease, and 1 infant died after placement of a gastrostomy tube from complications of peritonitis. An infant with hypoplastic left heart died during cardiac catheterization. There was a delay in providing blood for 1 infant with profound anemia due to fetomaternal hemorrhage.

DISCUSSION

The factors associated with death in infants admitted for NICU care are multifactorial and diverse, and they change with EGA. At lower gestational ages, mortality is most commonly caused by extreme prematurity and its complications, namely RDS, IVH, NEC, and sepsis. With increasing EGA, the etiology of mortality shifts to HIE and genetic and structural anomalies. Efforts to decrease NICU mortality in premature infants should therefore focus on preventing or delaying preterm birth and optimizing therapies that may decrease IVH, NEC, RDS, and sepsis. In more mature infants, targets should include preventing and managing HIE and defining optimal management strategies for infants with nonlethal anomalies.

Eighty-six percent of infants who died were <37 weeks' EGA at birth, and 36% were <25 weeks. The most common modifiable factor associated with mortality was the delivery of an infant at a center without appropriate support (10%). For prematurely born infants, administration of antenatal steroids and management by maternal-fetal specialists increase survival.^{5,6} A substantial percentage of extremely premature infants were offered care but died despite intensive care. Recent studies demonstrate variability in the prenatal care offered to such infants^{7,8} and suggest that

improvements can be made. Respiratory failure, sepsis, IVH, and NEC are often the cause of death and are modifiable events (eg, through use of antenatal steroids). Addressing public health, organizational, and medical care issues in the perinatal period, ensuring good access to prenatal care, promoting delivery of at-risk infants at centers with appropriate neonatal care, and consulting with high-risk maternal-fetal specialists could reduce mortality in prematurely born infants. Our findings emphasize the importance of close collaboration between obstetrics and neonatology to decrease NICU mortality from prematurity.

The primary cause of death on the death certificate was commonly misleading. Although the most common causes of death were related to complications of prematurity, its classification as a cause of death has limited our ability to modify preventable causes of death. It is often difficult to assign a single event as the cause of death, and many infants have confounding factors associated with their death. Also, the accuracy of death certificates is hampered by the requirement that they be completed shortly after death. There is no mechanism to improve the accuracy of the death certificate through revision after return of additional pertinent information or autopsy results. Having accurate information on causes of death is essential for evaluating potential solutions.⁹

Our study has limitations. A root cause analysis may not identify all the factors associated with an infant's death. Only 74 infants had an autopsy performed, and in 53 out of 74 (72%) an important finding was noted. It is likely we missed some important factors, such as the expertise of the health care providers providing care, underlying family beliefs and health care decisions about comfort care, and missed diagnoses.

The findings in this study have implications for how NICUs should

conduct quality improvement efforts related to mortality. The development of a mortality database for NICUs that focuses on the issue of preventability and modifiable factors (public health, organizational, and medical) affecting mortality may advance our understanding of causes of death in the NICU.

ACKNOWLEDGMENTS

Principal investigators were Kaashif Ahmad, MD, Methodist Children's Hospital, North Central Baptist Hospital, St. Luke's Baptist Hospital (San Antonio, TX); Laura Basile, MD, St Mary's Medical Center (West Palm Beach, FL); Rosaire Josie Belizaire, MD, Women's & Children's Hospital Lafayette (Lafayette, LA); Edward Co, MD, Integris Baptist Medical Center (Oklahoma City, OK); Sally Downey, MD, Memorial Hermann Southwest Hospital (Dallas, TX); Padmaja Itikala, MD, Presbyterian Hospital (Albuquerque, NM); Jack Jacob, MD, Providence Alaska Medical Center (Anchorage, AK); Susanne Jane Johnson, NNP, Swedish Medical Center (Seattle, WA); Erzsebet Jung, MD, Mercy Hospital (St Louis, MO); Sharon Lundstrom, APRN/NP, St Luke's Hospital (Kansas City, MO); Eric Scott Palmer, MD, Women's Hospital at Centennial (Nashville, TN); Mitchell Rodriguez, MD, Medical Center of Central Georgia (Macon, GA); Jayesh B. Shah, MD, Charleston Area Medical Center (Charleston, WV); Whit Walker, MD, Greenville Memorial Hospital (Greenville, SC); and Robert White, MD, Memorial Hospital South Bend (South Bend, IN).

Contributors were Mehrdad Asadifar, MD, Summerlin Hospital, Spring Valley Hospital, Valley Hospital (Las Vegas, NV); Marc Belcastro, MD, Miami Valley Hospital (Dayton, OH); James Berger, MD, Ogden Regional Medical Center (Ogden, UT); Arpitha Chirivola, MD, Baylor University Medical Center (Austin, TX); Tommy Cox, MD, McLeod Regional Medical

Center (Florence, SC); Michelle David-Hugues, MD, Pinnacle Health (Harrisburg, PA); Joseph Harlan, MD, McLeod Regional Medical Center (Florence, SC); Victor Iskersky, MD, Palmetto Health Richland (Columbia, SC); Michael Kamitsuka, MD, Swedish Medical Center (Seattle, WA); Mary Laird, MD, Memorial Hospital for Children (Colorado Springs, CO); Sue Ann Mackey, NPS, Miami Valley Hospital (Dayton, OH); Gregory Martin, MD, Banner Good Samaritan Medical Center, Banner Desert Medical Center, Phoenix Children's Hospital (Phoenix, AZ); Laura Miller, NNP, Women's & Children's Hospital Lafayette (Lafayette, LA); Khawar Mohsini, MD, Covenant Medical Center (Saginaw, MI); Mashelle Monhaut, NNP, Memorial Hospital South Bend (South Bend, IN); Heather Morgan, MD, Stormont Vail Hospital (Topeka, KS); Randy Nederhoff, MD, Presbyterian Hospital (Albuquerque, NM); Julie Reid, ARNP, Integris Baptist Medical Center (Oklahoma City, OK); David Riley, MD, Cook Children's Medical Center (Dallas, TX); Nan O'Donnell, Long Beach Memorial Medical Center (Long Beach, CA); Todd Scharnberg, MD, Dell Children's Medical Center, Seton Medical Center, University Center at Brackenridge (Austin, TX); Christopher Slocum, MD, Carillion Clinic Children's Hospital (Roanoke, VA); Bharath Srivasta, MD, Northside Hospital (Atlanta, GA); Arthur Strauss, MD, Long Beach Memorial Medical Center (Long Beach, CA); Christine Wade, RNC, BSN, Banner Good Samaritan Medical Center, Banner Desert Medical Center, Phoenix Children's Hospital (Phoenix, AZ); and Stephanie Willis, RN, BSN, Memorial Hermann Southwest Hospital (Houston, TX). We also acknowledge Dan Ellsbury for reviewing the manuscript and offering important edits and Melissa McLennon, Lisa Camacho, Larrissa Otero, and Vernice Vixamar for their administrative support with the study.

REFERENCES

1. Grand Rounds CDC; Centers for Disease Control and Prevention (CDC). CDC Grand Rounds: public health approaches to reducing U.S. infant mortality. *MMWR Morb Mortal Wkly Rep.* 2013;62(31):625–628
2. Lasswell SM, Barfield WD, Rochat RW, Blackmon L. Perinatal regionalization for very low-birth-weight and very preterm infants: a meta-analysis. *JAMA.* 2010; 304(9):992–1000
3. Callaghan WM, MacDorman MF, Rasmussen SA, Qin C, Lackritz EM. The contribution of preterm birth to infant mortality rates in the United States. *Pediatrics.* 2006;118(4):1566–1573
4. Mathews TJ, MacDorman MF. Infant mortality statistics from the 2004 period linked birth/infant death data set. *Natl Vital Stat Rep.* 2007;55(14):1–32
5. Carlo WA, McDonald SA, Fanaroff AA, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Association of antenatal corticosteroids with mortality and neurodevelopmental outcomes among infants born at 22 to 25 weeks' gestation. *JAMA.* 2011;306(21): 2348–2358
6. Bottoms SF, Paul RH, Iams JD, et al; National Institute of Child Health and Human Development Network of Maternal–Fetal Medicine Units. Obstetric determinants of neonatal survival: influence of willingness to perform cesarean delivery on survival of extremely low-birth-weight infants. *Am J Obstet Gynecol.* 1997;176(5):960–966
7. Alleman BW, Bell EF, Li L, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Individual and center-level factors affecting mortality among extremely low birth weight infants. *Pediatrics.* 2013;132(1). Available at: www.pediatrics.org/cgi/content/full/132/1/e175
8. Smith PB, Ambalavanan N, Li L, et al. Approach to infants born at 22 to 24 weeks' gestation: relationship to outcomes of more-mature infants. *Pediatrics.* 2012; 129(6). Available at: www.pediatrics.org/cgi/content/full/129/2/e1508
9. Barfield WD; Committee on Fetus and Newborn. Standard terminology for fetal, infant, and perinatal deaths. *Pediatrics.* 2011;128(1):177–181

Etiologies of NICU Deaths

Jack Jacob, Michael Kamitsuka, Reese H. Clark, Amy S. Kelleher and Alan R. Spitzer
Pediatrics 2015;135:e59

DOI: 10.1542/peds.2014-2967 originally published online December 8, 2014;

Updated Information & Services	including high resolution figures, can be found at: http://pediatrics.aappublications.org/content/135/1/e59
References	This article cites 8 articles, 3 of which you can access for free at: http://pediatrics.aappublications.org/content/135/1/e59#BIBL
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): Administration/Practice Management http://www.aappublications.org/cgi/collection/administration:practice_management_sub Quality Improvement http://www.aappublications.org/cgi/collection/quality_improvement_sub Fetus/Newborn Infant http://www.aappublications.org/cgi/collection/fetus:newborn_infant_sub Neonatology http://www.aappublications.org/cgi/collection/neonatology_sub
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://www.aappublications.org/site/misc/Permissions.xhtml
Reprints	Information about ordering reprints can be found online: http://www.aappublications.org/site/misc/reprints.xhtml

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Etiologies of NICU Deaths

Jack Jacob, Michael Kamitsuka, Reese H. Clark, Amy S. Kelleher and Alan R. Spitzer

Pediatrics 2015;135:e59

DOI: 10.1542/peds.2014-2967 originally published online December 8, 2014;

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://pediatrics.aappublications.org/content/135/1/e59>

Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2015 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 1073-0397.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

