CLINICAL ARTICLE

Incidence and risk factors for early neonatal mortality in newborns with severe perinatal morbidity in Uganda

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A R T I C L E   I N F O

A B S T R A C T

Objective: To determine the incidence and risk factors for early neonatal death among newborns with severe perinatal morbidity. *Methods:* A prospective cohort study was performed of 341 newborns with severe perinatal morbidity admitted to the neonatal intensive care unit of Mulago Hospital, Uganda. All newborns were followed up for 7 days or until time of death. Information surrounding the mother's obstetric history and pregnancy, the birth, and the neonatal history was collected using an interviewer-administered questionnaire and by review of relevant records. Multivariate logistic regression analysis was performed to assess factors independently associated with early neonatal death. *Results:* A total of 37 (10.9%) neonates died within 7 days, giving an incidence of early neonatal death of 109 deaths per 1000 live births (3 per 100 person-days). In multivariate analysis, respiratory distress (adjusted risk ratio [aRR] 31.29; 95% CI, 4.17–234.20; P = 0.001) and inadequate fetal heart monitoring during labor (aRR 6.0; 95% CI 1.40–25.67; P = 0.016) were significantly associated with an increased risk of early neonatal death. *Conclusion:* Approximately one in 10 neonates with severe perinatal morbidity died within 7 days of birth. Respiratory distress and poor monitoring of labor were risk factors for early neonatal death.

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1. Introduction

Early neonatal death is the death of a neonate within 7 days of birth, and accounts for three-quarters of all neonatal deaths [1]. Its major causes include birth asphyxia, neonatal infections, birth trauma, and complications of prematurity. Assessment of maternal near-miss morbidity is recommended as a measure of the quality of maternal health care [2–4]. As a related concept, a neonatal near-miss case refers to a neonate who presents with severe life-threatening complications but survives the neonatal period [5,6], while a perinatal near miss may refer to a neonate who survives severe life-threatening perinatal complications. Neonatal near-miss cases can be identified in several ways [7,8]: by clinical features (such as lethargy, failure to suckle, prematurity, low birth weight, respiratory complications, or hypothermia at birth); using organ-system dysfunction (metabolic, respiratory, neurological, or cardiovascular dysfunction such as hypoglycemia, jaundice,

encephalopathy, sepsis, electrolyte imbalance, or thrombocytopenia); and from interventions used in the management of complications (such as tracheal intubation or blood transfusion).

Assessment of stillbirths, neonatal morbidity, and neonatal mortality can generate useful data for establishing targeted interventions to address these problems [9]. The aim of the present study was to determine the incidence and risk factors for early neonatal death among neonates with severe perinatal morbidity.

2. Materials and methods

The present study was conducted in the labor ward and the neonatal intensive care unit (NICU) of Mulago Hospital, Kampala, Uganda. On average, 2500 mothers are admitted to the labor ward and 300 newborns to the NICU every month, and the neonatal mortality rate is 26%–29% (Mulago hospital records 2012). A prospective cohort study of newborns admitted to the NICU with severe perinatal morbidity was undertaken from February 1 to March 31, 2013. The inclusion criteria were delivery in Mulago Hospital, a diagnosis of severe perinatal morbidity, a gestational age of 28 weeks or more, birth weight of at least 800 g, admission to the NICU within 24 hours of birth, and mothers'

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informed consent for newborns to participate in the study. Severe perinatal morbidity was defined as birth asphyxia (5-minute Apgar score <7) with or without fetal distress (defined as intrapartum bradycardia, tachycardia, or irregular fetal heartbeat, fetal skull molding, or meconium-stained liquor), respiratory distress, or meconium aspiration. Ethical approval for the study was granted by the Research and Ethics Committee of Mulago Hospital, the Ethics and Research committee of the Makerere University School of Medicine, and the Uganda National Council for Science and Technology.

Consecutive sampling was used, whereby all neonates meeting the inclusion criteria were recruited until the sample size of 341 was achieved. This sample size was calculated from an estimated incidence of early neonatal mortality of 33.3% in the NICU for neonates with low Apgar scores (unpublished data from Mulago NICU records 2012), with an acceptable error of 5%, a power of 80%, and a 95% significance level.

All newborns were followed up for 7 days or until time of death. Data were obtained from review of maternal and neonatal records (antenatal, laboratory, and delivery records) for newborn or obstetric complications and subsequent care. For neonates, data collected included breastfeeding, appearance, temperature, pallor, cyanosis, jaundice, results of investigations, and management provided. An interviewer-administered questionnaire was used to assess mothers' sociodemographic characteristics (maternal age, level of education, occupation, marital status, and urban/rural residence), prenatal and prior obstetric history (parity, pregnancy, or childbirth complications such hypertensive disease, hemorrhage, cesarean delivery, and postpartum complications), childbirth complications, newborn care (neonatal resuscitation, cord care, immunization, eye care, and antibiotic treatment), and neonatal complications (convulsions, hyperthermia, hypothermia, hypoglycemia, septicemia, hyperbilirubinemia, and anemia) and their management. Neonates who died in the 7 days constituted the early neonatal deaths, and survivors constituted the neonatal near-miss cases.

Data were analyzed using Stata version 10 (StataCorp, College Station, TX, USA). At analysis, characteristics of the neonates who died and survivors (near-miss cases) were compared. For continuous variables, means and standard deviations are reported. For categorical variables, frequencies and percentages are presented. The incidence of early neonatal death was estimated as the proportion of newborns who died within 7 days of birth. To assess risk factors for early neonatal death, characteristics of the neonates and their mothers were compared with those of survivors and their mothers. For continuous/numerical variables and categorical variables, t tests and χ^2 tests, respectively, were used at the 5% confidence level. To assess independent contribution of these risk factors for mortality, hierarchical multivariate analysis was performed, in which all independent variables with a P value of less than 0.2 were included.

3. Results

During the study period, 635 neonates were admitted to the NICU. A total of 341 met the inclusion criteria. Reasons for non-inclusion were very low birth weight (67 newborns weighed <800 g, 49 of whom died within the first 72 hours after birth), gestational age of less than 28 weeks (53 newborns, 28 of whom died within the first 72 hours after birth), admission to the NICU later than 24 hours after birth (78 newborns), admission for observation with no overt morbidity (22 newborns), mother or caretaker unavailable to give informed consent (45 newborns, five of whom died within the first 72 hours after birth), and severe congenital anomalies (three with hydrocephalus, two with anencephaly, and two with omphalocele).

A total of 79 (12.4%) of the 635 neonates admitted to the NICU died within 7 days (early neonatal deaths). Of the 341 neonates included in the present study, 37 (10.9%) died within 7 days, giving an early neonatal mortality incidence in the study population of 109 deaths per 1000

live births (or 3 deaths per 100 person-days). Seventeen (45.9%) of the 37 early neonatal deaths in the study population occurred on the first day of life, 7 (18.9%) on the second day, 4 (10.8%) on the third day, and 9 (24.3%) between the fourth and seventh days. After discharge, no neonatal deaths occurred, although four newborns who were not discharged and remained in the NICU died between 8 and 28 days.

During the study period, there were 4551 live births at Mulago Hospital. The 79 early neonatal deaths in the NICU constitute an early neonatal mortality rate of 17.4 per 1000 live births, while the 37 early neonatal deaths in the study population constitute an early neonatal mortality rate of 8.1 per 1000 live births.

Table 1 shows the sociodemographic characteristics of the mothers of the 341 neonates in the study population. Most mothers were aged 20–29 years (68.7%), had given birth once or twice previously (58.9%), and had attained at least a secondary level of education (97.9%). A total of 310 (90.9%) had attended prenatal care and booked for delivery in a health facility. A total of 174 (51.0%) were emergency referrals to Mulago Hospital from peripheral health units.

Of the 341 newborns, the average gestational age at delivery was 36.0 ± 1.3 weeks. A total of 209 (61.3%) were male, 334 (97.9%) required neonatal resuscitation, and 162 (47.5%) showed clinical evidence of respiratory distress at admission to the NICU. Fifteen (4.4%) had birth injuries: 5 (1.5%) had fractures, 2 (0.6%) cephalohematomas, and 8 (2.3%) large caput succedaneums. The average time from delivery to initial assessment in the NICU was 4.6 ± 0.2 hours, and all initial assessments occurred within 8 hours of birth.

Table 2 shows a stratified analysis of the risk of early neonatal mortality by specific clinical characteristics and mothers' demographic characteristics. A blue skin color (cyanosis of extremities and mucus membranes) was associated with approximately a five-fold increase in risk of death ($P < 0.001$), while respiratory distress increased the risk of death by more than 3.5 times ($P = 0.003$) (Table 2). Mortality of newborns of mothers who had formal or informal employment was significantly lower than when mothers were unemployed or housewives ($P = 0.042$) (Table 2). Neonates whose mothers had attended prenatal care at least four times and were booked to deliver at a health facility actually had a higher incidence risk of mortality compared with those whose mothers had attended prenatal care three times or fewer,

Table 1
Baseline sociodemographic characteristics of mothers of neonates included in the study population (n = 341).

Characteristic	No. (%)
Marital status	
Married	269 (78.9)
Unmarried	72 (21.1)
Level of education	
Primary	7 (2.1)
Secondary	101 (29.6)
Tertiary	233 (68.3)
Mothers' occupation	
Not employed	18 (5.3)
Salary earner[a]	54 (15.8)
Businesswoman[b]	91 (26.7)
Housewife	178 (52.2)
Mother's age, y	
15–19	48 (14.0)
20–24	134 (39.3)
25–29	100 (29.3)
30–34	39 (11.4)
>35	20 (5.9)
Parity	
1–2	201 (58.9)
3–4	92 (27.0)
>5	48 (14.1)

[a] Women in formal employment.
[b] Women in informal employment.