

1 Neonatal Deaths in Cambodia: Findings from a Community-Based Mortality 2 Review

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17 18 Abstract

19
20 **Objectives:** The aim of this study was to describe potential factors contributing to neonatal mortality in
21 Takeo, Cambodia through assessment of verbal autopsies collected following newborn deaths in the
22 community. The mortality review was nested within a trial of a behavioral intervention to improve
23 newborn survival, and was conducted after the close of the trial, within the study setting. The World
24 Health Organization standardized definition of neonatal mortality was employed, and two pediatricians
25 independently reviewed data collected from each event to assign a cause of death. **Results:** Thirteen
26 newborn deaths of infants born in health facilities participating in a community based, behavioral
27 intervention were reported during February 2015 - November 2016. Ten deaths (76.92%) were early
28 neonatal deaths, two (15.38%) were late neonatal deaths, and one was a stillbirth. Five out of 13 deaths
29 (38.46%) occurred within the first day of life. The largest single contributor to mortality was neonatal
30 sepsis; six of 13 deaths (46.15%) were attributed to some form of sepsis. Twenty-three percent of deaths
31 were attributed to asphyxia. The study highlights the continuing need to improve quality of care and
32 infection prevention and control, and to fully address causes of sepsis, in order to effectively reduce
33 mortality in the newborn period.

34
35 **Keywords:** Infant, newborn; Cambodia; child mortality; perinatal mortality; health services

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37

38 **Introduction**

39 The first 28 days of life are critical for a child's survival, when infants face the highest risk of mortality.
40 In 2016, 46% of under-five deaths occurred during the neonatal period.[1] The vast majority of newborn
41 deaths occur in low-income countries where access to health care is restricted. In Cambodia, neonatal
42 mortality rates have dropped considerably in recent years, from 24 neonatal deaths per 1,000 live births in
43 2009 to 18 per 1,000 live births in 2014; however, regionally, the newborn mortality rate varies
44 significantly, from a high of 36 neonatal deaths per 1,000 live births in the Mondul Kiri and Ratank Kiri
45 provinces, to a low of 12 per 1,000 live births in Battambang and Pailin provinces.[2] The national rate is
46 still nearly three times higher than the World Health Organization Western Pacific regional average of
47 6.5, and a child born in Cambodia is still significantly more likely to die than one born in a high-income
48 country.[1] Formative research in the local setting found gaps in essential newborn care practices [3] and
49 barriers to infection prevention and control.[4] The data from that formative research guided an
50 intervention design for a clustered randomized trial, the Newborn Infection Control and Care Initiative
51 (NICCI) trial [5]. Study objectives included improving infection control and referral systems in selected
52 health centers, increasing knowledge and recognition of danger signs for sick newborns by mothers and
53 families of newborn infants, and diagnosing the causes of sepsis among infants with possible sepsis at
54 Takeo Province Hospital.

55 Following the end of the intervention, which took place over the course of 22 months, data on 13 neonatal
56 deaths that had occurred within the study site had been collected. Researchers conducted verbal autopsy
57 (VA) interviews using a standardized questionnaire with family members of newborns to ascertain cause
58 of death, as local medical records on these were not available for review by study personnel. Per the
59 World Health Organization (WHO), "Verbal autopsy is a method used to ascertain the cause of a death
60 based on an interview with next of kin or other caregivers. This is done using a standardized questionnaire
61 that elicits information on signs, symptoms, medical history and circumstances preceding death. The

62 cause of death, or the sequence of causes that led to death, are assigned based on the data collected by a
63 questionnaire and any other available information.” These interviews are used where the majority of
64 deaths occur at home or where there is little chance that deaths will be recorded and causes of death
65 determined.[6]

66 The current study aimed to describe the factors potentially contributing to the 13 deaths in the study
67 setting. Specifically, the study sought to analyze the verbal autopsies of perinatal deaths in both
68 intervention and control groups, describe the timing and causes of these deaths, describe the basic
69 demographics of newborns and mothers, and to understand factors surrounding these deaths.

70 **Main text**

71 The study examining neonatal deaths was conducted through a retrospective review of 13 verbal autopsy
72 reports. The standardized definition from the WHO for neonatal mortality was used as the inclusion
73 criteria for this study. Local medical records on the deaths were not available for review. Two
74 pediatricians reviewed verbal autopsy data and assigned a presumed cause of death, per WHO verbal
75 autopsy guidelines.[6] Neonatal death was defined as death of a live-born child occurring within 28 days
76 of life. Early neonatal death referred to death occurring within seven days of life while death occurring on
77 or after seven days but before 28 days was referred to as late neonatal death.[7] Additionally, the WHO
78 definition of intrapartum and very early neonatal mortality—occurring within the first 24 hours of life and
79 excluding newborns under 2,500 grams—was used to identify births that occurred due to intrapartum
80 events.[8]

81 **Setting**

82 Takeo province is located in southern Cambodia, bordering Vietnam. The population, as of 2013, was
83 923,373.[9] There are eight national hospitals and in Takeo, there are 73 health centers, three primary
84 referral hospitals, and one secondary referral hospital.[10]

85

86

87 **Data collection and analysis**

88 Verbal autopsy questionnaires were administered in Khmer language by trained members of the larger
89 intervention study, during the process of monitoring newborn deaths in the study area, and who had post
90 secondary education in midwifery. The questionnaire had both open and closed-ended questions and
91 included portions that provided for respondent's verbatim account of the circumstances leading to the
92 death of the child. Immediate caregivers (most often mothers) were the primary target respondents. The
93 interviews were conducted on average of 2 months after death had occurred. Interviews lasted between 30
94 minutes and one hour and informed consent was obtained from all participants.

95 **Ethics approval and consent to participate**

96 Written informed consent was obtained from all participants. The study was approved by the National
97 Ethics Committee on Health Research of the Cambodia Ministry of Health and by the Institutional
98 Review Board of Tulane University. Informed consent to participate was obtained in writing from
99 all participants and no identifying information is presented in this manuscript requiring additional
100 consent

101 The parent study was registered with ClinicalTrials.gov, number NCT02271737. Descriptive data were
102 extracted from 13 verbal autopsy forms reporting on deaths between February 2015 and November 2016.
103 Analysis included summary statistics of causes and timing of deaths, as well as a qualitative description
104 of circumstances surrounding the birth and death.

105 **Results**

106 Thirteen newborn deaths occurred. Eight of those deaths (61.54%) occurred within the control group.
107 Ten out of all 13 deaths (76.92%) were early neonatal deaths, two (15.38%) were late neonatal deaths,
108 and one was a stillbirth. The largest single contributor to neonatal death in the sample, per cause of death
109 assigned by consulting pediatricians, was neonatal sepsis. Six out of 13 deaths (46.15%) were attributed

110 to some form of sepsis. Twenty-three percent of the deaths were attributed to asphyxia. Other causes of
111 death included stillbirth and prematurity.

112 The majority of the newborns (76.92%) were male, and their mothers' ages ranged from 19 to 35, whom
113 were married between the ages of 17 and 27. The mothers had an average of 6.7 years of schooling and
114 their average household size was 6.4 people per home.

115 The number of mothers' antenatal care visits ranged from two to nine, with an average of five. At those
116 visits, only six women were informed of any danger signs to be aware of during pregnancy or where to go
117 if she was experiencing any of those signs.

118 All 13 newborns were born in a health facility, and five (38.46%) died at the same facility in which they
119 were born. Of the eight babies who went home after birth, four (50%) were referred to a hospital upon
120 discharge of the facility where they were born; all four died in the hospital after referral. Of those
121 mother/baby pairs who went home after birth, none of them reported being visited by a community health
122 worker at home.

123 Twelve out of 13 (92.31%) deliveries were vaginal, with the exception being the stillbirth, where cesarean
124 section was used to deliver the baby. Of the 12 vaginal deliveries, three (25%) were with forceps. Four of
125 the 13 babies (23.08%) were ever breastfed, and seven of 13 (53.85%) were fed either a pre-mixed
126 formula or powdered formula mixed with a liquid. Three out of 13 mothers (23.08%) received
127 counselling upon discharge of the birth facility that did *not* include referral to a hospital; two of those
128 three were in the intervention group.

129
130 Ten out of the 13 recorded deaths (76.92%) were within the first week of life, five of which (38.46%)
131 occurred between zero and one day. Four out of the 10 early neonatal deaths (40%) were within the
132 intervention group. The largest contributors to early neonatal death in our sample were neonatal sepsis
133 and asphyxia. Three of the 10 early neonatal deaths (30%) were due to neonatal sepsis and three more of

134 the 10 (30%) were due to asphyxia. Other causes of early neonatal death recorded were other/unspecified,
135 pneumonia, and prematurity. Two of the 13 recorded deaths (15.38%) occurred between the 7th and 28th
136 day of life—one from the control group and one from the intervention group. Neonatal sepsis was the
137 cause of death in both cases.

138 We report on the causes of deaths of 13 neonates following verbal autopsy interviews with family
139 members of the deceased. Five of the deaths reported (38.46%) were linked to intrapartum events,
140 including four of the five deaths that occurred within the intervention group. Severe infection was the
141 most common cause of death, followed by asphyxia.

142 Verbal autopsy analyses conducted in other countries indicate that sepsis and asphyxia are often among
143 the top three causes of neonatal deaths. When conducting verbal autopsies in Morang, Nepal, Khanal et
144 al. found that infection (41%), birth asphyxia (37%), and prematurity or low birth weight (18.4%) were
145 the most common causes of neonatal death.[11] An analysis of verbal autopsies in Nigeria found that
146 sepsis (31.5%), birth injury/asphyxia (22.3%), and pneumonia (19.9%) were the largest contributors to
147 death.[12] A verbal and social autopsy (VASA) investigation conducted by the World Health
148 Organization and UNICEF to estimate the causes of neonatal and child deaths in several high priority
149 countries found that severe neonatal infection and asphyxia were the leading causes of neonatal death in
150 Niger in 2010.[13]

151 One study identified an important linkage to mother's age--more than half of recorded stillbirths in that
152 study were to women under 21 years old, and babies born to mothers under 25 years old were less likely
153 to survive compared to older mothers.[14] Research in Bangladesh and Malawi found delays in care-
154 seeking to be an underlying cause of neonatal deaths.[15,16] In the current study, only one verbal
155 autopsy reported pre-term delivery and there was limited information on care-seeking, likely related to the
156 small sample size.

157 Prompt initiation and exclusive breastfeeding, which are known to protect against neonatal illness
158 including sepsis [17,18] were not widely practiced among study participants, with only five families
159 reporting breastfeeding of baby before death.

160 Additionally, the VA interviews highlight several important gaps regarding referral and postnatal care.
161 First, no respondent who left the facility where she gave birth reported being visited by a community
162 health worker at home, pointing to a lack of care coordination between health center staff and village
163 health volunteers. Second, while seven mothers received some form of counselling upon discharge, four
164 of those women were referred to a hospital, and of the three mothers who received counselling other than
165 a hospital referral, only two received information regarding danger signs of newborn illness.

166 **Limitations**

167 This study's limitations include the small number of cases identified, the inability to review local medical
168 records related to the newborn deaths, and the descriptive, retrospective nature of this study. Additionally,
169 four of the respondents interviewed were not the mothers of the deceased (but rather were close family
170 members who confirmed being present for pregnancy, delivery, and during the child's illness and death)
171 which may have impacted recall. Finally, some VA records contained very limited narrative detail,
172 indicating that participants in the interviews were not able to provide comprehensive responses. Limited
173 information such as this is common in community-based studies, and is to be expected given the sensitive
174 nature and length of verbal autopsy interviews, but nonetheless restricts comprehensive analysis.

175

176 Improving quality of neonatal care is critical to reaching the Sustainable Development Goals [19]. This
177 study sought to explore the continuing challenges related to perinatal survival in Takeo province, within
178 the context of an intervention that aimed to improve care practices, coordination, and the recognition of
179 danger signs of newborn illness.

180 All of the parents interviewed in our sample sought care for their newborns at local health centers, and the
181 majority of newborn deaths were early neonatal deaths. Improving quality of care and health center
182 protocols for managing birth complications at small health facilities must be a priority. For example,
183 being able to identify and assist a newborn suffering birth asphyxia can reduce mortality--asphyxia
184 accounted for 23% of the deaths in our sample.[20] In addition, nearly half of deaths in this study were
185 due to some form of neonatal sepsis, indicating infection prevention control at the level of the health
186 centers may have been inadequate. Sub-optimal infection prevention and control (IPC) practices have
187 been identified in other settings as important contributors to mortality and morbidity.[21] In addition, ore
188 than half of the babies in our sample were never breastfed, and upon discharge only three women received
189 any type of counselling, which includes advice on practices such as breastfeeding.

190 A systematic approach to understanding, identifying, and managing barriers to improving quality of care
191 for neonatal illness is critical to ensuring that Cambodia's trends of lower neonatal mortality rates
192 continues.

193

194 **Declarations**

195 **Ethics approval**

196 The study was approved by the National Ethics Committee Health Research of the Cambodia Ministry of
197 Health #397NECHR, and by the Institutional Review Board of Tulane University #15-812593I.

198 **Consent to publish**

199 Not applicable.

200 **Availability of data and materials**

201 The data used for this study is maintained by the National Institute of Public Health, Phnom
202 Penh, Cambodia and all requests to access the data should be directed there.

203 **Competing interests**

204 The authors declare that they have no competing interests to report.

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210 **Authors contributions**

211 A.N.B., C.V., D.W., R.D., R.A.O. contributed equally to the conception, design, validation, investigation,
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221 **Abbreviations**

Newborn Infection Control and Care Initiative trial	NICCI
Verbal and social autopsy	VASA
Verbal autopsy	VA
World Health Organization	WHO

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