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Factors associated with neonatal mortality in a tertiary hospital in Phnom Penh, Cambodia

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ABSTRACT

This study aimed to identify hospital neonatal mortality rate (NMR) and the causes of neonatal deaths, and to understand risk factors associated with neonatal mortality in a national tertiary hospital in Cambodia. The study included all newborn infants, aged 0–28 days old, hospitalized in the Pediatrics department of Khmer-Soviet Friendship Hospital between January 2016 and December 2017. In total, 925 infants were included in the study. The mean gestational age was 35.9 weeks (range, 24–42 weeks). Preterm infants and low birth weight accounted for 47.5% and 56.7%, respectively. With respect to payment methods, the government (53.5%) and non-governmental organizations (NGO) (13.7%) paid the fees as the families were not in a financial position to do so. The hospital NMR at the Pediatrics department was 9.3%. Respiratory distress syndrome (37.2%) was the main cause of deaths followed by hypoxic-ischemic encephalopathy (31.4%) and neonatal infection (21.0%). Factors associated with neonatal mortality were Apgar score at 5th minute <7 (adjusted odds ratio (AOR) = 3.57), payment by the government or NGO (AOR = 11.32), admission due to respiratory distress (AOR = 11.94), and hypothermia on admission (AOR = 9.41). The hospital NMR in the Pediatrics department was 9.3% (95% confidence interval 7.50–11.35) at Khmer-Soviet Friendship Hospital; prematurity and respiratory distress syndrome were the major causes of neonatal mortality. Introducing continuous positive airway pressure machine for respiratory distress syndrome and creating neonatal resuscitation guidelines and preventing hypothermia in delivery rooms are required to reduce the high NMR.

Keywords: Cambodia, neonatal infection, neonatal mortality, prematurity, respiratory distress syndrome

Abbreviations:
ANC: antenatal care
AOR: adjusted odds ratio
CPAP: continuous positive airway pressure
INC: Immediate Newborn Care
KSF Hospital: Khmer-Soviet Friendship Hospital
LBW: low birth weight
NGO: non-governmental organizations
NMR: neonatal mortality rate
RDS: respiratory distress syndrome

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INTRODUCTION

The first 28 days is the most vulnerable time for newborn infants to survive due to potential complications after birth or a weak immune system.[1,2] In 2017, the neonatal mortality rate (NMR) was 18 deaths per 1,000 live births globally and neonatal deaths accounted for 47% of all deaths in children under five years old.[3] Neonatal death is a global burden, especially in developing countries. In 2014, the Cambodia Demographic and Health Survey showed that the NMR in Cambodia was 18 deaths per 1,000 live births, which represented 63% of under-five mortality rate.[4] The Cambodian government set a target NMR of 14 deaths per 1,000 live births by 2020 in the Health Strategic Plan 2016–2020.[5] The NMR has been gradually decreasing to 14.9 deaths per 1,000 live births in 2017,[6] but has not yet reached the national target.

Khmer-Soviet Friendship (KSF) Hospital is one of the central hospitals in Phnom Penh, Cambodia, and has 600 beds and 26 departments. Most patients are low- or middle-income families from all over the country. KSF Hospital provides health services to patients at very low fees, namely 3–5 USD for consultation with medication at the Outpatient department and five USD for one-day hospitalization with medication. Low-income families who have "IDPoor," which is an identification card of poor household, are eligible for free healthcare service at public health facilities, including KSF Hospital, with the government support. Non-governmental organizations (NGO) also provide financial support for poor families who live near the organizations. Furthermore, when patients cannot afford treatment and do not have the IDPoor or qualify for NGO support, the treatment fees can be waived based on the hospital's decision. The Pediatrics department has 20 beds, including 11 beds for neonates, but there is no neonatal intensive care unit. At the end of 2017, the medical equipment for neonatal care included one incubator, two cots, two phototherapy devices, eight oxygen cylinders, six infant radiant warmers, two portable suctioning machines, one weighing machine, two sets of infant laryngoscopes and two pulse oximeters. Unfortunately, the department had no ultrasound, neonatal cardio-respiratory monitor, continuous positive airway pressure (CPAP) machine or neonatal mechanical ventilator. Although newborns in serious conditions need to be referred to a hospital that has a higher level of neonatal intensive care unit, this is sometimes impossible as the family refuses due to the financial burden.

There has been no report on hospital NMRs in Cambodia to date. The aims of this study were to identify the hospital NMR and causes of neonatal deaths and to understand risk factors associated with neonatal mortality in KSF Hospital. The results of this study can be used to develop the neonatal section and to improve the management of neonatal diseases.

METHODS

Study design and participants

This retrospective cohort study was carried out in the Pediatrics department of KSF Hospital in Phnom Penh, Cambodia. The study included all newborn infants who were 0–28 days old and hospitalized in the Pediatrics department between January 2016 and December 2017. However, newborn infants who were admitted but transferred to other hospitals before completion of their treatment or who were discharged against doctor's medical advice were excluded.

Data collection

Data were collected from patient records, including neonatal characteristics (age at admission, gestational age at birth, sex, birth weight, causes of admission, and Apgar score), obstetrical and maternal data (residence of mother, mode of delivery, level of delivery facilities and payment methods), and neonatal outcomes (duration of hospitalization, mode of discharge and causes of deaths). The causes of neonatal admission and death were decided by pediatric specialists (Dr. Ponloeu Leak and Dr. Pisey Noy) with reviewing medical records. The payment methods were categorized into four groups: (1) out-of-pocket (full payment by patients), (2) out-of-pocket + hospital (partial payment by patients as per the hospital's decision), (3) government (free of charge due to IDPoor or the hospital decision), and (4) NGO (free of charge due to the support of NGO).

Definition of medical terms

'Prematurity' of newborn infant was defined by a gestational age less than 37 weeks. Subcategories of preterm birth were based on gestational weeks as follows; 'extremely preterm' (<28 weeks), 'very preterm' (28–31 weeks), and 'moderate to late preterm' (32–36 weeks).[7] The low birth weight (LBW) was defined as less than 2,500 g.[8] 'Respiratory distress' was used for patients who had clinical signs, such as tachypnea, nasal flaring, chest retraction, and grunting.[2] Diagnosis of 'respiratory distress syndrome (RDS)' was made based on chest radiographic findings and clinical signs of respiratory distress. Based on the National Clinical Practice Guidelines, 'neonatal infection' was diagnosed in the following cases: (1) when patients had either of three infectious risk factors from their mothers, namely a prolonged period from membrane rupture to delivery (>18 hours), maternal fever during delivery (≥38.5ºC), and foul-smelling or purulent amniotic fluid; (2) when patients showed either of clinical signs that could not be explained by other causes, namely fever, hypothermia, pallor, jaundice, refusal to feed, vomiting, abdominal distension, hypotonia altered consciousness, convulsions, and coma; (3) when patients had either of the following biological criteria: white blood cells >30,000/mm^3, white blood cells <6,000/mm^3, and C-reactive proteins >10mg/L.[9] Bacterial cultures were unavailable in the hospital. 'Hypoxic-ischemic encephalopathy' was clinically diagnosed based on perinatal asphyxia with neurologic signs, namely decreasing muscle tone and reflexes, absence of crying, hypersensitive, subnormal level of consciousness, coma with or without convulsions, and difficulty with respiration.[10] Neuroimaging techniques, such as magnetic resonance imaging (MRI), and the pH analysis of arterial umbilical cord blood were unavailable to confirm the diagnosis in the hospital. 'Meconium aspiration syndrome' was defined as respiratory distress occurring after birth from a meconium stained milieu with compatible radiological findings which could not be otherwise explained.[11] Hypothermia was defined as body temperature below 36.5ºC.[12]

Statistical analysis

Kaplan-Meier curve was made to estimate survival time. A logistic regression model was used to determine 95% confidence intervals and odds ratio. A p-value <0.05 was deemed to be statistically significant. Data were analyzed by Statistical Package for the Social Sciences version 25.0 (IBM SPSS Inc., New York, USA).

Ethical considerations

Written informed consent was waived due to the retrospective study. This study was approved by the National Ethic Committee for Health Research, Ministry of Health (issue number: 219NECHR).

RESULTS

A total 925 newborn babies met the criteria of the study. The percentage of males was 51.7% and 87.4% of patients were hospitalized in the first 24 hours after birth (Table 1). The mean gestational age was 35.9 weeks (range, 24–42 weeks) and preterm infants accounted for 47.5%. The mean of birth weight was 2,480 g (range, 800–5,200 g) and 56.7% of patients were classified as LBW. Neonates who were born by Caesarean section accounted for 29.0% of the patients. The level of delivery facility was national hospital in 910 cases (98.5%), all of whom were born at KSF Hospital. There were 909 cases transferred after delivery, including 900 cases

Table 1 Characteristics of newborn infants

Characteristics	Male (N=478)		Female (N=447)		Total (N=925)	
	n	%	n	%	n	%
Age at admission						
0–24 hours	409	85.5	399	89.3	808	87.4
1–7 days	50	10.5	41	9.2	91	9.8
8–28 days	19	4.0	7	1.5	26	2.8
Gestational age (weeks)						
< 28	5	1.1	7	1.5	12	1.3
28–31	74	15.5	58	13.0	132	14.3
32–36	135	28.2	160	35.8	295	31.9
≥ 37	264	55.2	222	49.7	486	52.5
Birth weight (g)						
<1,000	3	0.6	3	0.7	6	0.7
1,000 – < 1,500	29	6.1	28	6.3	57	6.2
1,500 – < 2,500	210	43.9	251	56.1	461	49.8
≥ 2,500	236	49.4	165	36.9	401	43.3
Mode of delivery						
Vaginal delivery	343	71.8	314	70.2	657	71.0
Caesarean section	135	28.2	133	29.8	268	29.0
Level of facilities of delivery						
National hospital	466	97.5	444	99.3	910	98.5
Others[a]	12	2.5	3	0.7	15	1.5
Apgar score at 5th minute						
< 7	261	54.6	239	53.5	500	54.1
≥ 7	217	45.4	208	46.5	425	45.9
Duration of hospitalization						
0–24 hours	16	3.4	12	2.7	28	3.0
1–7 days	320	66.9	313	70.0	633	68.4
≥ 8 days	142	29.7	122	27.3	264	28.6
Payment methods						
Out-of-pocket	47	9.8	50	11.2	97	10.5
Out-of-pocket + hospital	104	21.8	102	22.8	206	22.3
Government	251	52.5	244	54.6	495	53.5
NGO	76	15.9	51	11.4	127	13.7
Residence of mothers						
Phnom Penh	240	50.2	243	54.3	483	52.2
Provinces	238	49.8	204	45.7	442	47.8

[a] Provincial hospital in one case, referral hospitals in six cases, health center in one case, private clinics in three cases, home in two cases, and on the way to hospital in two cases.
NGO: non-governmental organization.

from the Maternity department of KSF Hospital and nine cases from other facilities or home. Sixteen cases visited outpatient department from their home and were hospitalized at 4–27 days old. The mean of Apgar score was 5.7 at 1st minute and 6.5 at 5th minute. The proportion of cases whose Apgar score was <7 at the 1st and 5th minute was 65.9% and 54.1%, respectively. Only 10.5% cases paid by their families; the government and NGO paid in 53.5% and 13.7% of cases, respectively. The mean duration of hospitalization was 5.9 days (range, 0–52 days), and 68.4% of patients stayed in the hospital for 1–7 days. In terms of the mother's residence, 47.8% of cases came from provinces, mostly from provinces close to Phnom Penh, such as Kandal, Prey Veng, Kampong Cham, Kampong Chhnang and Svay Rieng Provinces. However, some patients came from Ratanakiri, Bantheay Meanchey and Palin Provinces which are 351–636 km from Phnom Penh. There were no statistically differences in all characteristics between male and female patients.

The major causes of admission were complications by prematurity, which accounted for 47.5% of patients (Table 2). Of 439 preterm babies, 404 cases had complications such as hypothermia, respiratory distress, perinatal asphyxia, and neonatal infection. Among non-preterm babies, the major admission cause was perinatal asphyxia in 173 cases, including 47 cases with respiratory distress, two cases with altered consciousness and two cases with meconium aspiration syndrome. The second cause among non-preterm babies was neonatal infection in 156 cases (16.8%). There were 207 preterm babies and 27 full-term babies who were admitted due to hypothermia; however, 76.5% of all newborns (708 cases) had hypothermia on admission regardless of causes of admission.

In 2016–2017, 86 neonates died and the hospital NMR in the Pediatrics department was 9.3% (95% confidence interval 7.50–11.35). The NMR in all deliveries at KSF Hospital was 1.4%,

Table 2 Causes of neonatal admission

Diagnosis	Male (N=478)		Female (N=447)		Total (N=925)	
	n	%	n	%	n	%
< 37 weeks of gestational age						
Prematurity	214	44.7	225	50.4	439	47.5
Without complication	13	2.7	22	4.9	35	3.8
Hypothermia	88	18.4	119	26.6	207	22.4
Respiratory distress	56	11.7	39	8.7	95	10.3
Perinatal asphyxia	44	9.2	39	8.8	83	8.9
Infection	13	2.7	6	1.4	19	2.1
≥ 37 weeks of gestational age						
Perinatal asphyxia	102	21.3	71	15.8	173	18.7
Without severe signs	68	14.2	54	12.1	122	13.2
Respiratory distress	32	6.7	15	3.3	47	5.1
Altered consciousness	1	0.2	1	0.2	2	0.2
MAS	1	0.2	1	0.2	2	0.2
Neonatal infection[a]	83	17.4	73	16.3	156	16.8
Low birth weight	28	5.9	48	10.7	76	8.2
Hypothermia[a]	18	3.8	9	2.0	27	2.9
Macrosomia	11	2.2	10	2.2	21	2.3
Neonatal RDS[a]	8	1.7	6	1.3	14	1.5
Neonatal jaundice[a]	7	1.5	3	0.8	10	1.1
Other	7	1.5	2	0.5	9	1.0

[a] Excluding cases related to prematurity and perinatal asphyxia
MAS: meconium aspiration syndrome
RDS: respiratory distress syndrome.

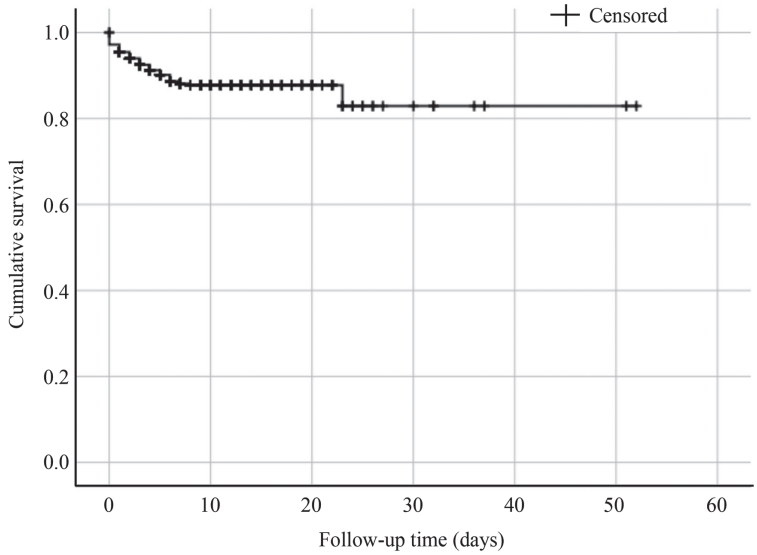

Fig. 1 Kaplan-Meier survival estimate of neonates hospitalized at Khmer-Soviet Friendship Hospital in 2016–2017

because there were 5,987 deliveries in 2016–2017 and 84 of the 86 dead patients were born at the hospital. Twenty-six neonates (30.2%) died within the first day of hospitalization and 58 neonates (67.4%) died within 2–7 days of hospitalization. The mortality significantly decreased after the newborns survived the first seven days of hospitalization (Fig. 1). The mortality rate in extremely preterm infants, very preterm, moderate to late preterm, and term was 100.0%, 25.8%, 6.1%, and 4.6%, respectively. In terms of birth weights, the mortality rate was 100.0% in six cases in weight <1,000 g and decreased to 47.4% in weight <1,500 g, 7.4% in weight <2,500 g and 5.2% in weight ≥2500 g. RDS was the main cause of deaths accounting for 37.2% followed by hypoxic-ischemic encephalopathy (31.4%) and neonatal infection (21.0%) (Table 3). Seven cases died due to congenital anomalies with the major anomaly being heart disease. The

Table 3 Causes of deaths in preterm and full-term infants

Diagnosis	Gestational age				Total (N=86)	
	< 37 weeks (N= 64)		≥ 37 weeks (N=22)			
	n	%	n	%	n	%
Respiratory distress syndrome	32	50.0	0	0.0	32	37.2
Hypoxic-ischemic encephalopathy	13	20.2	14	63.7	27	31.4
Neonatal infection	16	25.0	2	9.0	18	21.0
Neonatal sepsis	10	15.6	1	4.5	11	12.8
Necrotizing enterocolitis	5	7.8	0	0.0	5	5.9
Pneumonia	1	1.6	1	4.5	2	2.3
Meconium aspiration syndrome	0	0.0	2	9.0	2	2.3
Congenital anomalies	3	4.8	4	18.3	7	8.1
Heart disease	0	0.0	4	18.3	4	4.5
Hydrocephalus	1	1.6	0	0.0	1	1.2
Achondrodisplasia	1	1.6	0	0.0	1	1.2
Multiple congenital anomaly	1	1.6	0	0.0	1	1.2

percentage of death cases caused by RDS and neonatal infections in preterm infants were 50.0% (32/64) and 25.0% (16/64).

Bivariate logistic regression analysis on neonatal mortality showed that babies of preterm delivery, LBW, age at admission <24 hours old, Apgar score at 5th minute <7, mother's residence in provinces, payment by the government or NGO, admission due to respiratory distress or infection, and hypothermia on admission had significantly higher mortality than the others (Table 4). To identify risk factors of neonatal mortality in the hospital, multiple logistic regression analysis was performed and adjusted for all factors. The results showed that Apgar score at 5th minute <7 (adjusted odds ratio (AOR) = 3.57), payment by the government or NGO (AOR = 11.32), admission due to respiratory distress syndrome (AOR = 11.94), and hypothermia on admission (AOR = 9.41) were significantly associated with neonatal mortality (Table 4).

Table 4 Bivariate and multivariate logistic regression for predictors of neonatal mortality among newborn babies hospitalized in pediatrics department

Variable	Death		Survival		Crude OR (95% CI)	Adjusted OR (95% CI)
	n	(%)	n	(%)		
Sex						
Female	33	(38.4)	414	(49.3)	1	1
Male	53	(61.6)	425	(50.6)	1.56 (0.99–2.46)	1.44 (0.83–2.51)
Gestational age						
Term	22	(25.6)	464	(55.2)	1	1
Preterm	64	(74.4)	375	(44.8)	6.67 (1.61–27.49)**	1.95 (0.65–5.91)
Birth weight (g)						
≥ 2,500	19	(22.1)	382	(45.5)	1	1
< 2,500	67	(77.9)	457	(54.5)	2.94 (1.74–4.99)***	1.61 (0.49–5.31)
Age at admission						
≥ 24 hours	2	(2.3)	115	(13.7)	1	1
< 24 hours	84	(97.7)	724	(86.3)	6.67 (1.61–27.49)**	1.20 (0.23–6.21)
Apgar at 5th minute						
≥ 7	16	(18.6)	409	(48.7)	1	1
< 7	70	(81.4)	430	(51.3)	4.16 (2.37–7.28)***	3.57 (1.84–6.96)***
Residence of mothers						
Phnom Penh	36	(41.9)	447	(53.3)	1	1
Provinces	50	(58.1)	392	(46.7)	1.58 (1.01–2.48)*	1.26 (0.73–2.18)
Methods of Payment						
Out-of-pocket[a]	6	(7.0)	297	(35.4)	1	1
Government/NGO	80	(93.0)	542	(64.6)	7.30 (3.15–16.95)***	11.32 (4.58–28.00)***
Admission due to respiratory distress						
No	32	(37.2)	737	(87.8)	1	1
Yes	54	(62.8)	102	(12.2)	12.19 (7.51–19.78)***	11.94 (6.71–21.27)***
Admission due to infection						
No	84	(97.7)	665	(79.3)	1	1
Yes	2	(2.3)	174	(20.7)	0.09 (0.02–0.37)**	1.22 (0.25–6.01)
Hypothermia on admission						
No	1	(1.2)	216	(25.7)	1	1
Yes	85	(98.8)	623	(74.3)	29.47 (4.09–212.92)**	9.41 (1.25–71.08)*

[a] Out-of-pocket includes patients who paid all by out-of-pocket and patients who paid by out-of-pocket with some supports by the hospital.
* $P < 0.05$; ** $P < 0.01$;*** $P < 0.001$
NGO: non-governmental organization
OR: odds ratio
CI: confidence interval

DISCUSSION

First, this study showed that the hospital NMR in the Pediatrics department of KSF Hospital in 2016–2017 was 9.3%, which was lower than those reported in other developing countries; 15.7% at the sub-urban hospital in Cameroon, and 10.0–22.9% at the referral hospitals in Cameroon, Iraq and Southern Ethiopia.[13-16] This is probably because some of the severely ill newborns at KSF Hospital were transferred to other hospitals with more appropriate neonatal intensive care units. In this study, the proportion of admission due to prematurity was 47.5% and the mortality of preterm babies accounted for 74.4% (64/86) of all neonatal deaths. The association between high mortality rate and prematurity was consistent with the results of previous studies that were conducted in other developing countries.[13,14,17,18] These findings suggest that prematurity is the most challenging problem for neonatology in developing countries. Therefore, prevention of preterm delivery and management of preterm infants should be priority of maternal and neonatal development program in order to reduce the NMR in developing countries including Cambodia.

Second, the major cause of deaths was RDS, which represented 37.2% of all causes. In KSF Hospital, two doses of intravenous dexamethasone with a 24-hour interval (12 mg per dose) are administered to pregnant patients who are less than 34 weeks of gestation 48 hours prior to delivery to prevent RDS. The treatment for RDS was only oxygen through a nasal cannula because surfactant therapy, CPAP machine, or neonatal mechanical ventilator were unavailable. Surfactant administration is a standard care for preterm infants with RDS globally,[19] but very expansive. The safety and efficacy of CPAP in developing countries were reported as the introduction of CPAP greatly decreased the hospital mortality of preterm infants.[20] CPAP machine may be a feasible solution to control RDS in preterm babies in KSF Hospital.

In this study, neonatal infection was the third cause of deaths. Most death cases by infections were diagnosed with neonatal sepsis, and all 11 infants who died due to neonatal sepsis were born with LBW (1,000–1,900 g). LBW has been reported as a risk factor of neonatal sepsis.[21-23] Due to the limited number of healthcare workers, family members have to look after their babies who are hospitalized in KSF Hospital such as bottle or gavage feeding, oral administration, changing diapers, and bathing. However, it seemed that the family members did not sufficiently follow the instructions of doctors and nurses, and this may have caused more neonatal deaths. Family integrated care in neonatal intensive care unit was reported to lead better neonatal outcomes compared to the standard care by medical staff.[24] These results suggest that care by family members might not be appropriate for babies in KSF Hospital and could lead to catastrophic outcomes as no educational training programs were provided to family members. Therefore, the neonatal infection control guidelines and programs of training for medical professionals and family members should be developed, especially with respect to hygiene.[25]

Thirdly, factors associated with neonatal mortality were Apgar score at 5th minute <7, payment by the government or NGO, admission due to respiratory distress, and hypothermia on admission. Previous studies reported that a low Apgar score at 5th minute had a strong association with neonatal death,[26-28] although the Apgar score can be affected by many factors including gestational age.[29] Hypothermia has been reported as one of risk factors of neonatal mortality and as common complication in developing countries.[30] The percentage of newborns with a Apgar score at 5th minute <7 and hypothermia on admission were higher in this study than those of previous studies in developing countries.[26,31,32] These results suggest that newborn care and neonatal resuscitation in delivery rooms by midwives and doctors in the Maternity department may be inappropriate. Another reason may be that, due to the limited number of healthcare professionals, pediatric teams could not attend all deliveries that needed neonatal resuscitation in delivery rooms.

Newborns with poor families had higher mortality compared to those who could afford

treatment. The odds ratio for the government/NGO payment might be overestimated, because babies with poor families had to stay at KSF Hospital even if they needed to be transferred to higher level hospitals. According to the Cambodia Demographic and Health Survey in 2014, low income status was associated with many factors of pregnant women, such as coverage of antenatal care (ANC), skilled birth attendance (SBA), institute delivery rate, lower level of education, malnutrition and a lower percentage of women taking iron supplements during pregnancy.[4] Public health facilities in Cambodia provide free iron and folic acid for pregnant women. In this study, most mothers had SBA and institutional deliveries and were assumed to have had more ANC visits than the general pregnant population in Cambodia. However, poorer mothers might have less ANC visits than those in a more financially secure position. Previous studies in low- and middle-income countries concluded that ANC visits and poor income status were significantly associated with neonatal deaths.[33-35] Moreover, it has been reported that multiple-micronutrients supplement containing iron and folic acid during pregnancy reduced neonatal mortality and significantly decreased preterm deliveries and LBW.[36-38] These results suggest that financial support for poor pregnant women should be increased, such as incentives for ANC visits, free transportation services to visit health facilites, and free food service for patients and family members during hospitalization for childbirth.[39]

To reduce infant mortality, the Ministry of Health established 'Five-Year Action Plan For New-born Care, 2016–2020' in 2015.[40] In the plan, early essential newborn care was introduced as a comprehensive intervention delivered to mothers and newborns. Early essential newborn care consists of Intrapartum and Immediate Newborn Care (INC) and Expanded INC. INC includes (1) immediate and throughout drying, immediate skin-to-skin contact, appropriate timed cord crumping, and early exclusive breastfeeding, and (2) using bag and mask ventilation for newborns who are not breathing despite throughout drying. Expanded INC includes (1) preventing unnecessary inductions and Caesarean sections, antibiotics for premature pre-labor rupture of membranes, antenatal steroids and the Kangaroo Mother's Care approach, and (2) identification of babies at high risk (birth asphyxia, neonatal sepsis, and complications of delivery) and management of sepsis and other common problems. In 2012, INC coaching sessions for referral hospital staff began and all participants were coached until they completed at least 90.0% of all clinical tasks correctly. Implementation of INC by all health professionals is needed to improve the NMR in Cambodia.[41]

This study has some limitations. There was no maternal information such as age, number of ANC visits, education level, number of parity, and disease complications during pregnancy. These factors are also important because it was reported that the maternal factors were significantly associated with neonatal mortality.[34,42,43] Second, diagnosis of hypoxic-ischemic encephalopathy, neonatal sepsis, and congenital heart diseases were diagnosed with only clinical symptoms, although the diagnosis should be made using neuroimaging technique, pH analysis, blood cultures, and heart ultrasound. The causes of admission or deaths in this study might not be correct, but this is due to the limited medical equipment in KSF Hospital. Third, 16 newborn infants were discharged against medical advice and they might have died at their home. Another 16 newborns were transferred to other hospitals for further treatment, and their outcomes were unavailable. Consequently, the neonatal mortality rate in this study might be underestimated. Therefore, further studies will be needed to investigate more clearly about risk factors associated with neonatal mortality.

In conclusion, the hospital NMR at the Pediatrics department was 9.3% and prematurity was the major cause of admission to KSF Hospital. RDS was the main cause of deaths followed by hypoxic-ischemic encephalopathy and neonatal infection. Apgar score at 5th minute <7, payment by the government or NGO, admission due to respiratory distress and hypothermia on admission

were associated with neonatal mortality. This study suggests that prevention of preterm delivery, using CPAP machine for RDS, and creating guidelines and providing training programs of neonatal resuscitation and prevention of neonatal hypothermia in delivery rooms may be suitable solutions in this setting.

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CONFLICT OF INTEREST

The authors have nothing to disclose.

REFERENCES

1 Lawn JE, Davidge R, Paul VK, et al. Born too soon: care for the preterm baby. *Reprod Health.* 2013;10 (Suppl 1):S5. doi:10.1186/1742-4755-10-S1-S5.

2 Kliegman RM, Stanton BF, III JWSG, Schor NF, Behrman RE. *Nelson Textbook of Pediatrics*. 19th ed. Philadelphia: Elsevier; 2011.

3 United Nations Inter-agency Group for Child Mortality Estimation. *Levels & Trends in Child Mortality: Report 2018, Estimates developed by the United Nations Inter-agency Group for Child Mortality Estimation*. New York: UNICEF; 2018.

4 National Institute of Statistics, Directorate General for Health, ICF Macro. *Cambodia Demographic and Health Survey 2014.* Phnom Penh, Cambodia, and Rockville, Maryland, USA: National Institute of Statistics, Directorate General for Health, and ICF International; 2015.

5 Department of Planning & Health Information. *Health strategic plan 2016–2020.* Phnom Penh, Cambodia: Ministry of Health; 2016: 67.

6 UNICEF. Child mortality estimates: country-specific neonatal mortality rate. 2018. Available at https://data.unicef.org/wp-content/uploads/2017/10/IMR_deaths_2018.xls. Accessed April 20, 2019.

7 March of Dimes, Partnership for maternal newborn and child health, Save the Children, WHO. *Born too soon: the global action report on preterm birth*. CP Howson MK, JE Lawn, editors. Geneva: WHO; 2012. Available at https://www.who.int/maternal_child_adolescent/documents/born_too_soon/en/. Accessed January 24, 2019.

8 United Nations Children's Fund and World Health Organization. *Low birthweight: country, regional and global estimates.* New York: UNICEF; 2004. Available at https://apps.who.int/iris/bitstream/handle/10665/43184/9280638327.pdf?sequence=1&isAllowed=y. Accessed January 24, 2019.

9 Spong CY. Defining "term" pregnancy: recommendations from the Defining "Term" Pregnancy Workgroup. *JAMA.* 2013;309(23):2445-2446. doi:10.1001/jama.2013.6235.

10 D'Alton ME, Hankins GDV, Berkowitz RL, et al. Executive summary: neonatal encephalopathy and neurologic outcome, second edition. Report of the American College of Obstetricians and Gynecologists' Task Force on Neonatal Encephalopathy. *Obstet Gynecol.* 2014;123(4):896–901. doi:10.1097/01.AOG.0000445580.65983.d2.

11 Raju U, Sondhi V, Patnaik S. Meconium aspiration syndrome: an insight. *Med J Armed Forces India.* 2010;66(2):152–157. doi: 10.1016/s0377-1237(10)80131-5.

12 World Health Organization, Maternal Health and Safe Motherhood Programme & Meeting of Technical Working Group. *Thermal control of the newborn: a practical guide.* Geneva: World Health Organization; 1993. Available at https://apps.who.int/iris/bitstream/handle/10665/60042/WHO_FHE_MSM_93.2.pdf?sequence=1&isAllowed=y. Accessed Jan 24, 2019.

13 Ndombo PK, Ekei QM, Tochie JN, et al. A cohort analysis of neonatal hospital mortality rate and predictors of neonatal mortality in a sub-urban hospital of Cameroon. *Ital J Pediatr.* 2017;43(1):52. doi: 10.1186/s13052-017-0369-5.

14 Orsido TT, Asseffa NA, Berheto TM. Predictors of neonatal mortality in neonatal intensive care unit at referral Hospital in Southern Ethiopia: a retrospective cohort study. *BMC Pregnancy Childbirth.* 2019;19(1):83. doi: 10.1186/s12884-019-2227-5.
15 Mah-Mungyeh E, Chiabi A, Tchokoteu FL, et al. Neonatal mortality in a referral hospital in Cameroon over a seven year period: trends, associated factors and causes. *Afr Health Sci.* 2014;14(4):985–992. doi: 10.4314/ahs.v14i4.30.
16 Umran RM, Al-Jammali A. Neonatal outcomes in a level II regional neonatal intensive care unit. *Pediatr Int.* 2017;59(5):557–563. doi: 10.1111/ped.13200.
17 Schmidt S, Bounnack S, Hoehn T. Neonatal mortality and morbidity in the post-implementation period of a neonatal teaching program in provincial hospitals in Laos. *Public Health.* 2018;154:123-129. doi: 10.1016/j.puhe.2017.10.021.
18 Beck S, Wojdyla D, Say L, et al. The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. *Bull World Health Organ.* 2010;88(1):31–38. doi: 10.2471/blt.08.062554.
19 Sardesai S, Biniwale M, Wertheimer F, Garingo A, Ramanathan R. Evolution of surfactant therapy for respiratory distress syndrome: past, present, and future. *Pediatr Res.* 2017;81(1-2):240–248. doi: 10.1038/pr.2016.203.
20 Thukral A, Sankar MJ, Chandrasekaran A, Agarwal R, Paul VK. Efficacy and safety of CPAP in low- and middle-income countries. *J Perinatol.* 2016;36(Suppl 1):S21-S28. doi:10.1038/jp.2016.29.
21 Turhan EE, Gürsoy T, Ovalı F. Factors which affect mortality in neonatal sepsis. *Turk Pediatri Ars.* 2015;50(3):170–175. doi:10.5152/TurkPediatriArs.2015.2627.
22 Jiang JH, Chiu NC, Huang FY, et al. Neonatal sepsis in the neonatal intensive care unit: characteristics of early versus late onset. *J Microbiol Immunol Infect.* 2004;37(5):301–306.
23 Rodríguez Cervilla J, Fraga JM, García Riestra C, Fernández Lorenzo JR, Martínez Soto I. Neonatal sepsis: epidemiologic indicators and relation to birth weight and length of hospitalization time [in Spanish]. *An Esp Pediatr.* 1998;48(4):401–408.
24 O'Brien K, Bracht M, Robson K, et al. Evaluation of the Family Integrated Care model of neonatal intensive care: a cluster randomized controlled trial in Canada and Australia. *BMC Pediatr.* 2015;15:210. doi: 10.1186/s12887-015-0527-0.
25 Sansam S, Yamamoto E, Srun S, et al. Assessment of hand hygiene compliance after hand hygiene education among health care workers in Cambodia. *Nagoya J Med Sci.* 2016;78(2):151–162.
26 Abdellatif M, Ahmed M, Bataclan MF, Khan AA, Al Battashi A, Al Maniri A. The patterns and causes of neonatal mortality at a tertiary hospital in Oman. *Oman Med J.* 2013;28(6):422–426. doi: 10.5001/omj.2013.119.
27 Iliodromiti S, Mackay DF, Smith GC, Pell JP, Nelson SM. Apgar score and the risk of cause-specific infant mortality: a population-based cohort study. *Lancet.* 2014;384(9956):1749–1755. doi:10.1016/s0140-6736(14)61135-1.
28 Migoto MT, Oliveira RP, Silva AMR, Freire MHS. Early neonatal mortality and risk factors: a case-control study in Parana State. *Rev Bras Enferm.* 2018;71(5):2527–2534. doi:10.1590/0034-7167-2016-0586.
29 American Academy of Pediatrics Committee on Fetus Newborn, American College of Obstetricians Gynecologists Committee on Obstetric Practice. The Apgar Score. *Pediatrics.* 2015;136(4):819–822. doi:10.1542/peds.2015-2651.
30 Lunze K, Bloom DE, Jamison DT, Hamer DH. The global burden of neonatal hypothermia: systematic review of a major challenge for newborn survival. *BMC Med.* 2013;11:24. doi:10.1186/1741-7015-11-24.
31 Ogunlesi TA, Ogunfowora OB, Adekanmbi FA, Fetuga BM, Olanrewaju DM. Point-of-admission hypothermia among high-risk Nigerian newborns. *BMC Pediatr.* 2008;8:40. doi:10.1186/1471-2431-8-40.
32 Christensson K, Bhat GJ, Eriksson B, Shilalukey-Ngoma MP, Sterky G. The effect of routine hospital care on the health of hypothermic newborn infants in Zambia. *J Trop Pediatr.* 1995;41(4):210–214. doi: 10.1093/tropej/41.4.210.
33 Roy S, Haque MA. Effect of antenatal care and social well-being on early neonatal mortality in Bangladesh. *BMC Pregnancy Childbirth.* 2018;18(1):485. doi: 10.1186/s12884-018-2129-y.
34 Doku DT, Neupane S. Survival analysis of the association between antenatal care attendance and neonatal mortality in 57 low- and middle-income countries. *Int J Epidemiol.* 2017;46(5):1668–1677. doi:10.1093/ije/dyx125.
35 Frozanfar MK, Yoshida Y, Yamamoto E, et al. Acute malnutrition among under-five children in Faryab, Afghanistan: prevalence and causes. *Nagoya J Med Sci.* 2016;78(1):41–53.
36 Haider BA, Bhutta ZA. Multiple – micronutrient supplementation for women during pregnancy. *Cochrane Database Syst Rev.* 2017;4(4):CD004905. doi:10.1002/14651858.CD004905.pub5.

37 Smith ER, Shankar AH, Wu LSF, et al. Modifiers of the effect of maternal multiple micronutrient supplementation on stillbirth, birth outcomes, and infant mortality: a meta-analysis of individual patient data from 17 randomised trials in low-income and middle-income countries. *Lancet Glob Health.* 2017;5(11):e1090-e1100. doi: 10.1016/S2214-109X(17)30371-6.

38 Azimi MW, Yamamoto E, Saw YM, et al. Factors associated with antenatal care visits in Afghanistan: secondary analysis of Afghanistan Demographic and Health Survey 2015. *Nagoya J Med Sci.* 2019;81(1):121–131. doi:10.18999/nagjms.81.1.121.

39 Chankham T, Yamamoto E, Reyer JA, et al. Knowledge of free delivery policy among women who delivered at health facilities in Oudomxay Province, Lao PDR. *Nagoya J Med Sci.* 2017;79(2):135–145. doi:10.18999/nagjms.79.2.135.

40 Ministry of Health. *Five year action plan for newborn care*. Phnom Penh, Cambodia: Ministry of Health; 2015.

41 Surenjav E, Sovd T, Yoshida Y, Yamamoto E, Reyer JA, Hamajima N. Trends in amenable mortality rate in the Mongolian population, 2007-2014. *Nagoya J Med Sci.* 2016;78(1):55–68.

42 Kidus F, Woldemichael K, Hiko D. Predictors of neonatal mortality in Assosa zone, Western Ethiopia: a matched case control study. *BMC Pregnancy Childbirth.* 2019;19(1):108. doi: 10.1186/s12884-019-2243-5.

43 Bashir AO, Ibrahim GH, Bashier IA, Adam I. Neonatal mortality in Sudan: analysis of the Sudan household survey, 2010. *BMC Public Health.* 2013;13:287. doi: 10.1186/1471-2458-13-287.