ELSEVIER

Seminars in Perinatology

Neonatal Hypothermia in Low-Resource Settings

Luke C. Mullany, PhD, MHS

Hypothermia among newborns is considered an important contributor to neonatal morbidity and mortality in low-resource settings. However, in these settings only limited progress has been made towards understanding the risk of mortality after hypothermia, describing how this relationship is dependent on both the degree or severity of exposure and the gestational age and weight status of the baby, and implementing interventions to mitigate both exposure and the associated risk of poor outcomes. Given the centrality of averting neonatal mortality to achieving global milestones towards reductions in child mortality by 2015, recent years have seen substantial resources and efforts implemented to improve understanding of global epidemiology of neonatal health. In this article, a summary of the burden, consequences, and risk factors of neonatal hypothermia in low-resources settings is presented, with a particular focus on community-based data. Context-appropriate interventions for reducing hypothermia exposure and the role of these interventions in reducing global neonatal mortality burden are explored.
Semin Perinatol 34:426-433

KEYWORDS **hypothermia, neonatal, mortality, morbidity, developing countries**

Each year an estimated 3.6 million neonatal deaths occur,[1] primarily attributable to infection, complications of preterm birth, and intrapartum-related hypoxic events.[2] Infections are estimated to account for approximately one-third of the global burden of neonatal death, with estimates rising to more than one-half in high-mortality settings.[2] One of the best-recognized signs of infection is fever, or an increase in body temperature of the newborn. However, the importance of abnormally low body temperature (hypothermia) in newborns remains less well understood in its contribution to neonatal mortality and morbidity, especially in low resource settings. The study of hypothermia, its incidence, risk factors, and consequences is not new. For at least 200 years, the need to maintain an optimal body temperature for infants, especially those born prematurely, has been recognized and is reflected by the development and improvement of early models of incubators during the 19th century.[3] These efforts were led by Parisian obstetrician, Dr Pierre Budin (1846-1907), who was among the first to demonstrate a potential relationship between temperature and mortality risk among newborns[3,4] and who included "warmth" and "keeping the baby with the mother" as 2 of the key components of appropriate management of the newborn infant. Reports of sclerema neonatorum and its possible association with neonatal cold injury also date to the 19th century.[5,6] More concentrated efforts to understand neonatal thermal regulation, the optimal thermal environment, and factors related to maintaining this environment were conducted via a series of studies in the mid 20th century, establishing our basic knowledge of the physiology of temperature control in newborns.[7-10]

Neonatal hypothermia as a factor contributing to morbidity and mortality risk of newborns has been recognized by the World Health Organization (WHO).[11] Hypothermia has been defined by WHO as body temperature below the normal range (36.5-37.5°C) and has been subclassified into 3 grades: mild (36.0-36.5°C), moderate (32.0-35.9°C), and severe (<32.0°C) hypothermia.[11] For each of these classifications, there are guidelines in place for responding to or managing hypothermia.[12] Furthermore, the WHO has published guidelines on thermal care and has included thermal care of newborns as one of the elements of essential newborn care that should be provided to all newborns regardless of setting.[13]

Despite this recognition within global guidelines and recommendations for neonatal care, there are major gaps in our understanding of the burden, risk factors, and consequences of neonatal hypothermia in the very settings where exposure is greatest.[14] In addition, there has been limited progress in identifying the optimal approaches to preventing hypother-

Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD.
This work was supported by a grant from the National Institute of Child Health and Development (HD0553466).
Address reprint requests to Luke C. Mullany, PhD, MHS, Department of International Health, 615 North Wolfe Street, Suite W5009, Baltimore, MD 21205. E-mail: lmullany@jhsph.edu

 0146-0005/10/$-see front matter
doi:10.1053/j.semperi.2010.09.007

mia or mitigating its consequences through rapid and appropriate management in low-resource settings.[15] This is especially true in locations in which a large proportion of births occur at home; in these settings there are very few data available even on the epidemiology of neonatal hypothermia, much less sufficient evidence on the role that thermal care practices may have in either hypothermia prevention or management, and thus, their potential role in improving neonatal survival.

In this article, the pathophysiology of neonatal hypothermia is briefly discussed, and the epidemiology of neonatal hypothermia in low-resource settings is reviewed. Studies that have estimated the incidence/prevalence of hypothermia in both hospital and community settings are summarized. The association between hypothermia and mortality is examined; particular attention is placed on estimation of how this relationship changes across temperatures in the hypothermic range and is followed by a discussion on how variability in this relationship can inform choice of cutoffs for defining severity grades for hypothermia. Risk factors for developing hypothermia in low-resource settings are reviewed and intervention approaches and the potential of these approaches for both reducing burden and impacting upon neonatal deaths is discussed.

Thermal Regulation of the Newborn

Unlike poikilotherms whose body temperature can vary substantially with the external environment, humans are homeotherms and must generate heat to maintain a body temperature that varies only within a relatively small range (ie, normal variance of only 0.3%).[7] During development, the core body temperature of the fetus is closely correlated with the mother, and as such, the core temperature of the fetus will normally remain a consistent and approximate 1°C above that of the mother. After birth, however, the baby is exposed to an environment that is often substantially cooler and is subject to the 4 basic mechanisms through which all humans will start to lose heat. These processes are evaporative heat loss, which is a function of humidity, conduction (direct transfer of heat from baby to contact surface), convection (loss of heat to cooler surrounding air), and radiation (indirect transfer of heat to nearby lower temperature objects).[7,11]

To avoid substantial heat loss as the result of these mechanisms, the core body temperature in children and adults is maintained through regulatory processes that include vasoconstriction and shivering and nonshivering thermogenesis. However, the extent to which newborn infants can control thermoregulation to maintain an optimal core body temperature is limited, relative to children and adults. Although shivering thermogenesis is quantitatively the most important mechanism in adults, for newborns the primary mechanism is through chemical thermogenesis, in the absence of muscular contraction and shivering.[3] Beyond the fact that physiological and behavioral responses are relatively immature in the term newborn, the limited ability of newborns to maintain core body temperature is particularly compromised among babies born prematurely or those with low birth weight. These infants have limited vasoconstriction capability compared with term infants,[16] greater surface-to-mass ratios, and preterm and/or low birth weight babies have lower brown fat deposits[17] which are essential for nonshivering thermogenesis.

Heat loss through evaporation of the amniotic fluid from the baby's skin is the most important mechanism.[11] In addition, specific newborn care practices can contribute substantially to the loss of heat, especially in the first hours of life; these practices are more common in home births in developing countries, but unfortunately also occur among facility births. For example, birthing in an insufficiently warmed room, placing the baby uncovered on the ground, floor, or other surface while awaiting delivery of the placenta, insufficient or delayed drying or wrapping of the baby after birth, immediate bathing of the baby with cool or cold water and delayed drying, and delayed breastfeeding are all practices that might increase the risk of heat loss.[11] The heat loss occurs immediately after birth; continuous recording of body temperature in a variety of settings has demonstrated the initial drop is normally followed by a subsequent increase, which may depend on birth weight, ambient temperature, and proximity to the mother.[18-20] The initial loss of heat can be quite large; for example in the first 10 to 20 minutes after birth it is not uncommon for a baby to lose 2 to 4°C, with further subsequent losses possible in the presence of the above practices.[15]

Incidence of Neonatal Hypothermia in Low-Resource Settings

As a consequence of both the factors surrounding the immediate care of newborns and the risk these pose for heat loss, and the innate features of the neonate, it is of little surprise that hypothermia is a common phenomenon in low resources settings, including among infants born in facilities and in the community.

Hospital-Based Studies

There have been numerous studies in which the authors have attempted to quantify the burden of neonatal hypothermia in low-resource settings, but most of these has been conducted in hospital settings and thus do not necessarily provide a representation of the population-based burden. A sample of these hospital-based studies is described in Table 1; those selected represent both middle- and low-resource settings, are geographically variable and from a variety of institutions. Overall, these hospital-based studies indicate that exposure to hypothermia as defined by the WHO is substantial and demonstrate that estimates of the proportion of infants observed as hypothermic varies widely. For example, near-universal observation of temperatures in the hypothermia range has been reported among babies from Senegal,[21] Uganda,[22] Nepal,[23] and Turkey[24] (Table 1). However, when the cut-off for defining hypothermia is reduced well below the WHO

Table 1 Selected Facility-Based Estimates of the Burden of Hypothermia in Newborns of Low-Resource Settings

Author, Year	Location	n	Definition, °C	Outcome Measure	Estimate, %
Briend, 1981[21]	Dakar, Senegal	78	<36.0	Point Prevalence	94.9
Byaruhanga, 2005[22]	Nsambya, Uganda	300	<36.5	Prevalence at 60 minutes after birth*	83.0
da Mota Silveira, 2003[35]	Recife, Brazil	320	<36.5	Prevalence at Admission	31.6
Zayeri, 2007[49]	Tehran, Iran	900	<36.5	Prevalence at 20 minutes after birth	53.3
Ogunlesi, 2008[37]	Sagamu, Nigeria	150	<36.5	Prevalence at admission	62.0
Sodemann, 2008[26]	Bissau, Guinea-Bissau	2926	<34.5	Prevalence within 12 hours of birth	8.1
Johanson, 1992[23]	Kathmandu, Nepal	495	<36.0	Prevalence within 2 hours of birth†	85.0
Kambarami, 2003[50]	Harare, Zimbabwe	313	<36.0	Prevalence at admission to neo unit	85.0
Cheah, 2000[51]	Kuala Lumpur, Malaysia	227	<36.5	Prevalence immediately after birth	25.6
Sarman, 1989[24]	Istanbul, Turkey	60	<36.0	Prevalence at admission	88.3
Manji, 2003[52]	Dar-es-Salaam, Tanzania	1632	<36.0	Prevalence at admission	22.4
Kaushik, 1999[25]	Shimla, India	2063	<35.0	Prevalence within 24 hours	2.9

*Temperature was also assessed at 10, 30, and 90 minutes after delivery; proportion was 29%, 82%, and 79%, respectively.
†Temperature was also assessed at 24 hours after birth; the proportion was 48.9%.

cutoff for any (ie, mild, moderate, or severe) hypothermia (<36.5°C), the observed proportion of infants deemed hypothermic is lower. For example, studies with cutoffs at 35.0 or 34.5°C in Table 1 (see Shimla, India,[25] and Bissau, Guinea-Bissau[26]) report a much lower proportion of hypothermic infants. The frequent use of different cutoffs for defining hypothermia poses some difficulty for comparison across sites.

In addition to the underlying true variability in incidence of hypothermia, there are many study-specific factors that contribute to the wide range of estimates seen in these hospital-based studies. The most important of such factors is seasonality (ie, when during the year was the study conducted), the age of the infants at first measurement, and the weight and gestational age distribution of the infants included. Other important elements to consider are method of measuring temperature (ie, axillary vs rectal),[27] frequency of measurement, and the cut-off used to classify babies as hypothermic.[26,28] Furthermore, some of the estimates shown in Table 1 are among out-born sick infants presenting to a hospital, some included only hospital births that are admitted for special care to a neonatal nursery or intensive care unit, while others include a combination of in/out born as well as sick and well babies.

It is difficult to conclude about either the overall incidence of hypothermia or the mortality risk associated with hypothermia from these studies. In addition to the lack of adjustment for important variables of seasonality, age at measurement, weight, and gestational age, these studies have other substantial sources of heterogeneity discussed previously, and are not population based. Given that a large proportion of infants are born at home and do not access the formal health system during the early neonatal period, and that these births contribute disproportionately to the global burden of neonatal death, it is critical to examine data available from community settings on both the incidence and association with mortality.

Community-Based Studies

There have been relatively few population-based studies that provide an estimate of the burden in specific settings; none are available from sub Saharan Africa. Three small cohort studies conducted in India have been published.[29-31] Among 189 home-born infants in villages of Haryana, the axillary temperature was less than 36.5°C among 21 infants (11.1%). In this study, temperature was recorded once within 24 hours after birth.[29] More frequent observation of infants occurred in another study, conducted as part of the SEARCH project in Gadchiroli.[30] Among 763 infants (95% of which were born at home), 130 (17.0%) were observed with temperatures less than 35.0°C over multiple visits through the first month of life (days 1, 2, 3, 5, 7, 15, 21, and 28). A larger and more recent study conducted by Darmstadt et al in Uttar Pradesh,[31] where 1732 infants had axillary temperature measures recorded within 36 hours (median age 16.0 h), almost one-half (45%) of the infants were observed with temperatures less than 36.5°C. In all 3 of these studies there was some evidence of seasonality; the proportion of hypothermic infants increased in the winter season but still remained high in the warm period. For example, in the Haryana study, hypothermia was observed within 24 hours among 19.3% of infants in winter compared with 3.1% in summer, and in Uttar Pradesh, 70.0% of infants were hypothermic in the coldest quarter of the year, compared with 32.1% in the warmest quarter.

More recently, our group has published a series of articles[14,28,32] on hypothermia among a large, population-based, universal cohort of newborns born in Sarlahi District in

Table 2 Incidence of Hypothermia in Community-Based Studies from South Asia

Author, Year	Location	n	Measurement(s) and Definition(s)		Key Findings
Kumar, 1998[29]	Haryana, India	189	Axillary temperatures within 24 hours of life	<35.6°C	11.1% hypothermic 19.3% winter vs. 3.1% in summer
Bang, 2005[30]	Gadchiroli, India	763	Axillary temperatures on days 1, 2, 3, 5, 7, 15, 21, 28	<35.0°C	17.0% hypothermic 21.5% winter vs. 13.8% in summer
Darmstadt, 2006[31]	Uttar Pradesh, India	1732	Axillary temperatures as soon as possible after birth (range 3-36 h)	<36.5°C	45% overall 70% in coldest quarter vs 20% in warmest quarter
Mullany, 2010[14]	Sarlahi, Nepal	23,240	Axillary temperatures on days 1-4, 6, 8, 10, 14, 21, 28	<36.5°C	92.3% overall RR of hypothermia 4.03 times higher in coldest quintile vs warmest quintile of ambient temperature
				<36.0°C	48.6% overall
				<32.0	

southern Nepal. Between 2002 and 2006, more than 23,000 infants from the northern third of the district (population ~280,000) were enrolled in a community-based cluster randomized trial of chlorhexidine antisepsis interventions of the skin[33] and umbilical cord.[34] All live-born babies during the period of the study were included in the cohort, regardless of the place of birth; approximately 92% of infants were born at home. The infants were visited at home repeatedly by project workers: daily through the first 4 days after birth, then every other day until midway through the neonatal period, and then on days 21 and 28 (maximum 11 visits). At each of these visits, project workers recorded axillary temperature using a digital thermometer (213,616 axillary temperature measures were collected). Ambient temperature and age of measurements in hours was available for each one of these measurements.

In this study, 21,459 of 23,240 infants (92.3%) had one or more axillary temperature measures <36.5°, half of babies were moderately to severely hypothermic, and risk peaked in the first 24 to 72 hours of life. The risk of moderate-to-severe hypothermia increased by 41.3% for each 5°C decrease in ambient temperature. Even in the hottest season of the year, almost one-fifth of infants were hypothermic. The key results of the smaller community studies and the data from this large population-based cohort are presented in Table 2.

Consequences of Neonatal Hypothermia in Low-Resource Settings

A number of the hospital- and community-based studies described previously have also examined case-fatality rates (CFRs) between those babies with and without hypothermia, and concluded that the risk of mortality is higher among those exposed (Table 3). An analysis of 320 babies arriving at a tertiary care facility in Recife, Brazil indicated that moderate (32.0-35.9°C) hypothermia on admission was an independent risk factor for neonatal death (adjusted odds ratio = 3.49; 95% confidence interval = 3.18-3.81)].[35] In Islamic Republic of Iran, mortality was greater among babies with rectal temperatures less than 36.5°C 20 minutes after birth (8.8%) compared with normothermic babies (2.6%), but these were not adjusted for important factors, such as weight and gestational age.[36] Relative to normothermic infants, unadjusted case-fatality was also more than 2-fold greater among the 62.0% of babies who were hypothermic upon admission in Nigeria [CFR = 2.26; 95% confidence interval = 1.14-4.48)].[37]

Efforts to link population-based estimates of hypothermia exposure to subsequent mortality are even fewer. In the aforementioned Bang study,[30] the case-fatality among 130 infants with hypothermia was estimated at 15.4%. Unfortunately, the study size was small (763 infants with only 20 deaths), and only a single fixed axillary temperature cutoff (35.0°C) was used to classify infants. In one of the studies highlighted in Table 1 where temperature measurements were made in a hospital setting in Guinea-Bissau,[26] investigators were able to go back to the community and estimate overall neonatal and postneonatal mortality rates among infants with exposure to hypothermia. Strengths of this study include the early timing and near uniformity of the ambient temperature at the time of the measurement, and the high rates of community-based follow-up that was achieved. Because delivery rates in the hospital were very high, the near-complete follow up of vital status for each of the babies leads to a population-based estimate of mortality associated with temperature. Furthermore, the investigators had sufficient data to construct a limited temperature-specific mortality function, which was then used to select an appropriate cutoff for examining mortality. Those with temperatures less

Table 3 Selected Studies of the Association Between Hypothermia and Mortality Risk in Hospital and Communities of Low-Resource Settings

Author, Year	Location	n	Study Type	Key Mortality Findings
da Mota Silveira, 2003[35]	Recife, Brazil	320	Hospital	Adjusted odds of death among babies with hypothermia was odds ratio = 3.49 [95% CI = 3.18-3.81])
Zayeri, 2007[49]	Tehran, Iran	900	Hospital	Unadjusted fatality was 8.8% among hypothermic infants compared with 2.6 among normothermic
Ogunlesi, 2008[37]	Sagamu, Nigeria	150	Hospital	Unadjusted fatality rate among hypothermic infants was 2.26 [95% CI = 1.14-4.48] greater than normothermic infants
Bang, 2005[30]	Gadchiroli, India	763	Community	Case-fatality of hypothermia was 15.4%, and was significantly greater than those without hypothermia
Sodemann 2008[26]	Bissau, Guinea-Bissau	2926	Hospital to Community	Adjusted for weight, temperatures <34.5°C were associated with mortality 4.81 [95% CI: 2.90-8.00] times greater in the first 7 days of life Hypothermia-associated mortality risk was elevated through 2 months of life
Mullany, 2010[14]	Sarlahi, Nepal	23,240	Community	Adjusted mortality risk increased 80% for every 1°C decrease in first observed axillary temperature Adjusted mortality risk was 6.11 [95% CI = 3.98-9.38] times higher among infants <35.0°C Preterm babies at higher risk of hypothermia-associated mortality

Abbreviation: CI = confidence interval.

than 34.5°C were at almost 5 times greater risk of mortality in the first week of life, and risk remained elevated through 2 months of age.[26]

More recently, the population-based data from Nepal was used to examine the relationship between axillary temperature over the entire range of hypothermia values and mortality after the first temperature observed.[28] We found that after adjusting for age and ambient temperature at measurement and other covariates (such as sex, weight, gestational age, ethnicity), mortality was increased by approximately 80% for every degree decrease in first observed axillary temperature. Mortality associated with hypothermia was substantially greater among preterm infants, and relative risk of death ranged from 2 to 30 times within the current WHO classification for moderate hypothermia, increasing with greater severity of hypothermia.[28]

Both our study and the work by Sodemann and colleagues[26] in Guinea-Bissau strongly suggest that the current WHO classification scheme for hypothermia might be adjusted to more appropriately reflect the overall mortality-hypothermia risk relationship. In particular, we have suggested that the current "moderate" category is too wide (32.0-35.9°C) and includes in a single classification exposures that have substantially different consequences. One solution we have proposed[28] is to expand the "severe" category to exposures <34.0°C (grade 4) and split the remainder of the "moderate" category into 2 separate categories (grade 3: 34.0-34.9°C and grade 2: 35.0-35.9°C). This new classification system better reflects the dependence of subsequent mortality risk across the range of observable temperatures, heightens the awareness of hypothermia by expanding the most severe category, and allows better flexibility in guidelines for appropriate actions which can be targeted by risk profile (ie, for low birth weight or premature infants; Table 4).

Risk Factors for Neonatal Hypothermia

To design effective strategies for reducing both the risk of hypothermia and the negative consequences, an improved understanding of factors that lead to hypothermia is required. Kumar et al[15] provide a detailed discussion of possible risk factors for neonatal hypothermia, classifying these factors into contextual (eg, seasonality), physiological (eg, low birth weight), behavioral (eg, early bathing), and socioeconomic factors (eg, poverty). Behavioral fac-

Table 4 Possible New Classification System for Neonatal Hypothermia

Grade	Definition	Proportion in Rural Nepal, %*	Adjusted Mortality Risk*	Possible Guideline: Preterm	Possible Guideline: Full Term
Normothermic	(36.5-37.5)	42.8	1.00		
Grade 1	(36.0-36.5)	25.6	1.51	Reinforcement of thermal care messages	Reinforcement of thermal care messages
Grade 2	(35.0-36.0)	21.1	1.75	Immediate in-home demonstration of improved thermal care plus follow up visits	Reinforcement of thermal care messages
Grade 3	(34.0-35.0)	6.9	5.03	Immediate skilled care and referral	Immediate in-home demonstration of improved thermal care plus follow up visits
Grade 4	<34.0	3.6	9.21	Immediate skilled care and referral	Immediate skilled care and referral

*Data from population-based study in rural Sarlahi District, Nepal.[28]

tors appear to play a central role in risk of hypothermia and are highlighted by the WHO's guidelines to optimize thermal care, described as a warm chain.[11] The warm-chain consists of 10 steps to minimize risk of exposure and includes the following: keeping the delivery room warm, drying immediately, skin-to-skin contact, breastfeeding, delayed bathing, appropriate clothing, warm transport (if necessary), keeping mother and baby together, warm resuscitation, and improved awareness and recognition of hypothermia risk. Importantly, there are very few data that explicitly link these factors, or other newborn care and behavioral practices to observations of neonatal hypothermia. Rather, the link has generally been ecological in nature; that is, in settings in which the incidence or prevalence of hypothermia is high, this observation has been explained by describing concurrent observations of behaviors or factors that are obstacles to achieving the WHO-recommended warm-chain. Although Kumar et al[15] provide some specific examples of settings in which behaviors, such as early bathing or delayed wrapping, are common, the authors also note that insufficient data are available on risk factors in community settings.

There are 2 factors that appear to be of paramount importance: seasonality and preterm/low birth weight; and substantially more information is available to quantify the role these factors play. Furthermore, the degree to which the above-discussed behavioral factors will increase risk of hypothermia depends significantly on the status of these 2 determining factors. Data in Table 2 provide an indication of the importance of ambient temperature. It is critical to note that risk of hypothermia remains high even in the hot season of tropical climates, and that the disparity between low birth weight and normal birth weight infants in hypothermia risk may be elevated during warmer periods. Community-based data from Nepal[32] indicate that hypothermia risk is correlated closely along the entire spectrum of body weight. For every 100-g decrement in weight less than 2000 g, hypothermia risk increased by 31.3%; risks were lower but still significant for weight decrements between 2000 and 2500 g (13.5% per 100 g) and between 2500 and 3000 g (7.4% per 100 g).

The compromised ability of low birth weight and preterm babies to thermoregulate (discussed above) leads to both higher incidence of hypothermia among these babies and more severe consequences; this observation too is not new. Case-fatality in hospital settings was noted to vary substantially by weight and prematurity of the baby; more than 100 years ago Pierre Budin published case-fatality estimates by weight of the newborn.[4] Among 318 infants whose temperature upon admission was <33.5°C, case-fatality was uniformly high but was greatest among those <1500 g (171/175%, 97.7%) compared with babies 1500-1999 g (109/122%, 89.3%) or those >=2000 g (15/21%, 71.4%).[4] The community-based hypothermia-mortality risk relationship among rural babies from Nepal was modified substantially by preterm status (Fig. 1).[28]

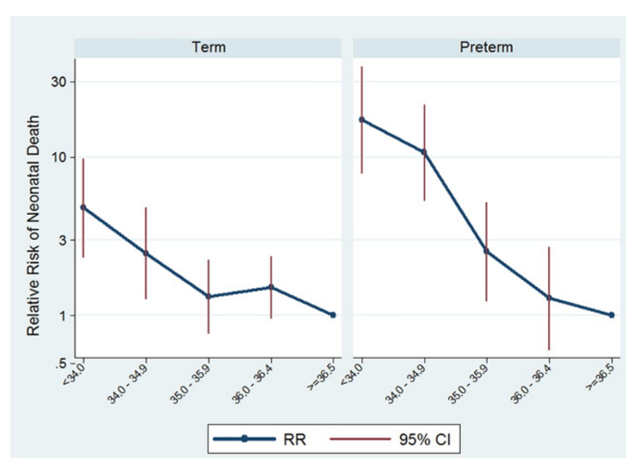

Figure 1 Relative risk of neonatal death after hypothermia, by preterm status. (Adapted from Mullany, 2010.[28]) (Color version of figure is available online.)

Interventions to Prevent Neonatal Hypothermia

Given the high incidence and serious consequences of hypothermia in low-resource settings and the limitations that these settings present in implementing standard warming techniques (including incubators) of greater-resource settings, the focus in low-resource facilities and communities is on behavioral practices. The WHO has provided guidelines for thermal care in low-resource settings and the 10-step warm chain described previously highlights specific practices that need to be promoted for both home and facility births. A specific recommendation is to delay bathing for at least 6 hours after birth; a randomized trial in an Ugandan hospital showed that bathing of newborns increased hypothermia even in the presence of skin-to-skin contact and the use of warm water.[38] Another recommendation for reducing risk of hypothermia or for rewarming infants that are already exposed is skin-to-skin contact. The transfer of heat from mother (or other caretaker) to the newborn facilitated by direct skin contact has been demonstrated to be at least as effective as incubator care for rewarming[39] and for preventing hypothermia in preterm low birth weight babies.[40]

A number of summaries of skin-to-skin care and its benefits for reducing hypothermia risk have been published,[15,31] including a metaanalysis indicating improved survival among preterm babies <2000 g in hospitals.[41] Early initiation of breastfeeding (ie, within 24 h) can reduce the risk of hypothermia,[32] and exclusive breastfeeding was associated with lower hypothermia among infants in a Zambian hospital.[42] Early breastfeeding reduces hypothermia risk through close contact with the mother and provides the fat supply essential for active heat production in newborns;[20,43] this mechanism may be partially responsible for the observed lower mortality among newborns breastfed within 24 hours.[44,45]

In recent years, several studies have demonstrated that packages of neonatal care practices delivered at the community level can substantially reduce mortality.[46,47] Many of these integrated packages include messages targeted towards improved thermal care, and it is possible that the thermal care component played a critical role in the overall mortality reductions observed. An excellent example is provided by an integrated package of behavioral interventions promoted by outreach workers in rural Shivgarh, India.[48] Here, behavioral change communications focused on early breastfeeding initiation, skin-to-skin contact, delayed bathing, and immediate wrapping and drying, as well as hygiene (clean delivery and cord care) and resulted in a 54% reduction in neonatal mortality. Identifying the impact of individual components within studies that evaluate integrated packages is challenging, and further work is needed to refine estimates of the potential reductions in all-cause and cause-specific neonatal mortality that are achievable through improved thermal care practices.

Conclusions

Newborn hypothermia remains one of the most important contributors to neonatal mortality and morbidity in both facilities and communities of low-resource settings. Recent data from the community in Nepal and India have expanded our understanding of the population-based burden in South Asia, and the hypothermia-mortality risk relationship is becoming increasingly clear. While no community-based data are available from sub-Saharan Africa, several current and future studies of interventions to improve neonatal survival will likely provide clarity on the burden and consequences of hypothermia in these settings. Neonatal health promotion programs for home births need to focus on the behavioral changes necessary to optimize thermal care of newborns, especially in the hours immediately after birth. Research to further elucidate both the impact of specific thermal care interventions on hypothermia risk and the overall contribution of these practices in improving survival is required.

References

1. Black RE, Cousens S, Johnson HL, et al: Global, regional, and national causes of child mortality in 2008: as systematic analysis. Lancet 375: 1969-1987, 2010
2. Lawn JE, Wilczynska-Ketende K, Cousens SN: Estimating the causes of 4 million neonatal deaths in the year 2000. Int J Epidemiol 35:706-718, 2006
3. Stern L: Thermoregulation in the newborn infant: historical, physiological and clinical considerations, in Smith GF, Vidyasagar D (eds): Historical Review and Recent Advances in Neonatal and Perinatal Medicine. Evansville, IN, Mead Johnson Nutritional Division, 1980
4. Budin P, Carr WL: The nursling, in The Feeding and Hygiene of Premature and Full-Term Infants: New York London, Imperial Publ, Co, Caxton Publ, Co, 1906
5. Ballantyne JW: Remarks on sclerema and œdema neonatorum. BMJ 1:403-406, 1890
6. Zeb A, Darmstadt GL: Sclerema neonatorum: a review of nomenclature, clinical presentation, histological features, differential diagnoses and management. J Perinatol 28:453-460, 2008
7. Polin RA, Fox WW, Abman SH: Fetal and Neonatal Physiology (ed 3). Philadelphia, W. B. Saunders, 2004
8. Day RL, Caliguiri L, Kamenski C, et al: Body temperature and survival of premature infants. Pediatrics 34:171-181, 1964
9. Silverman WA, Fertig JW, Berger AP: The influence of the thermal environment upon the survival of newly born premature infants. Pediatrics 22:876-886, 1958
10. Brueck K: Temperature regulation in the newborn infant. Biol. J Neonatol 3:65-119, 1961
11. World Health Organization: Thermal Protection of the Newborn: A Practical Guide. Report No.: WHO/RHT/MSM/97.2. Geneva, World Health Organization, 1997
12. World Health Organization: Pregnancy, Childbirth, Postpartum, and Neonatal Care: A Guide for Essential Practice. Geneva, World Health Organization, 2007
13. World Health Organization: Essential Newborn Care. Report Number WHO/FRH/MSM/96.13. Geneva, World Health Organization, 1996
14. Mullany LC, Katz J, Khatry SK, et al: Incidence and seasonality of hypothermia among newborns in southern Nepal. Arch Pediatr Adolesc Med 164:71-77, 2010
15. Kumar V, Shearer JC, Kumar A, et al: Neonatal hypothermia in low resource settings: a review. J Perinatol 29:401-412, 2009
16. Knobel RB, Holditch-Davis D, Schwartz TA, et al: Extremely low birthweight preterm infants lack vasomotor response in relationship to cold body temperatures at birth. J Perinatol 29:814-821, 2009

17. Aherne W, Hull D: Brown adipose tissue and heat production in the newborn infant. J Pathol Bacteriol 91:223-234, 1966
18. Ellis M, Manandhar N, Shakya U, et al: Postnatal hypothermia and cold stress among newborn infants in Nepal monitored by continuous ambulatory recording. Arch Dis Child Fetal Neonatal Ed 75:F42-F45, 1996
19. Robertson NJ, Nakakeeto M, Hagmann C, et al: Therapeutic hypothermia for birth asphyxia in low-resource settings: a pilot randomised controlled trial. Lancet 372:801-803, 2008
20. Christensson K, Ransjo-Arvidson AB, Kakoma C, et al: Midwifery care routines and prevention of heat loss in the newborn: a study in Zambia. J Trop Pediatr 34:208-212, 1988
21. Briend A, de Schampheleire I: Neonatal hypothermia in West Africa. Lancet 1:846-847, 1981
22. Byaruhanga R, Bergstrom A, Okong P: Neonatal hypothermia in Uganda: prevalence and risk factors. J Trop Pediatr 51:212-215, 2005
23. Johanson RB, Spencer SA, Rolfe P, et al: Effect of post-delivery care on neonatal body temperature. Acta Paediatr 81:859-863, 1992
24. Sarman I, Can G, Tunell R: Rewarming preterm infants on a heated, water-filled mattress. Arch Dis Child 64:687-692, 1989
25. Kaushik S, Grover N, Parmer VR, et al: Neonatal morbidity in a hospital at Shimla. Indian J Pediatr 66:15-19, 1999
26. Sodemann M, Nielsen J, Veirum J, et al: Hypothermia of newborns is associated with excess mortality in the first 2 months of life in Guinea-Bissau, West Africa. Trop Med Int Health 13:980-986, 2008
27. Craig JV, Lancaster GA, Williamson PR, et al: Temperature measured at the axilla compared with rectum in children and young people: systematic review. BMJ 320:1174-1178, 2000
28. Mullany LC, Katz J, Khatry SK, et al: Hypothermia during the neonatal period and associated risk of mortality in southern Nepal. Arch Pediatr Adolesc Med 164:650-656, 2010
29. Kumar R, Aggarwal AK: Body temperatures of home delivered newborns in north India. Trop Doct 28:134-136, 1998
30. Bang AT, Reddy HM, Baitule SB, et al: The incidence of morbidities in a cohort of neonates in rural Gadchiroli, India: seasonal and temporal variation and a hypothesis about prevention. J Perinatol 25:S18-S28, 2005 (suppl 1)
31. Darmstadt GL, Kumar V, Yadav R, et al: Introduction of community-based skin-to-skin care in rural Uttar Pradesh, India. J Perinatol 26: 597-604, 2006
32. Mullany LC, Katz J, Khatry SK, et al: Neonatal hypothermia and associated risk factors among newborns of southern Nepal. BMC Med 8:43, 2010
33. Tielsch JM, Darmstadt GL, Mullany LC, et al: Impact of newborn skin-cleansing with chlorhexidine on neonatal mortality in southern Nepal: a community-based, cluster-randomized trial. Pediatrics 119:e330-e340, 2007
34. Mullany LC, Darmstadt GL, Khatry SK, et al: Topical applications of chlorhexidine to the umbilical cord for prevention of omphalitis and neonatal mortality in southern Nepal: a community-based, cluster-randomised trial. Lancet 367:910-918, 2006
35. da Mota Silveira SM, Goncalves de Mello MJ, de Arruda VS, et al: Hypothermia on admission: a risk factor for death in newborns referred to the Pernambuco Institute of Mother and Child Health. J Trop Pediatr 49:115-120, 2003
36. Zayeri F, Kazemnejad A, Ganjali M, et al: Hypothermia in Iranian newborns. Incidence, risk factors and related complications. Saudi Med J 26:1367-1371, 2005
37. Ogunlesi TA, Ogunfowora OB, Adekanmbi FA, et al: Point-of-admission hypothermia among high-risk Nigerian newborns. BMC Pediatr 8:40, 2008
38. Bergstrom A, Byaruhanga R, Okong P: The impact of newborn bathing on the prevalence of neonatal hypothermia in Uganda: a randomized, controlled trial. Acta Paediatr 94:1462-1467, 2005
39. Christensson K, Bhat GJ, Amadi BC, et al: Randomised study of skin-to-skin versus incubator care for rewarming low-risk hypothermic neonates. Lancet 352:1115, 1998
40. Ibe OE, Austin T, Sullivan K, et al: A comparison of kangaroo mother care and conventional incubator care for thermal regulation of infants <2000 g in Nigeria using continuous ambulatory temperature monitoring. Ann Trop Paediatr 24:245-251, 2004
41. Lawn JE, Mwansa-Kambafwile J, Horta BL, et al: Kangaroo mother care‘ to prevent neonatal deaths due to preterm birth complications. Int J Epidemiol 39:i144-i154, 2010 (suppl 1)
42. Christensson K, Bhat GJ, Eriksson B, et al: The effect of routine hospital care on the health of hypothermic newborn infants in Zambia. J Trop Pediatr 41:210-214, 1995
43. Huffman SL, Zehner ER, Victora C: Can improvements in breast-feeding practices reduce neonatal mortality in developing countries? Midwifery 17:80-92, 2001
44. Mullany LC, Katz J, Li YM, et al: Breast-feeding patterns, time to initiation, and mortality risk among newborns in southern Nepal. J Nutr 138:599-603, 2008
45. Edmond KM, Zandoh C, Quigley MA, et al: Delayed breastfeeding initiation increases risk of neonatal mortality. Pediatrics 117:e380-e386, 2006
46. Friberg IK, Bhutta ZA, Darmstadt GL, et al: Comparing modeled predictions of neonatal mortality impacts using LiST with observed results of community-based intervention trials in South Asia. Int J Epidemiol 39:i11-i20, 2010 (suppl 1)
47. Schiffman J, Darmstadt GL, Agarwal S, et al. Community-based intervention packages for improving perinatal health in developing countries: a review of the evidence. Semin Perinatol 34:462-476, 2010
48. Kumar V, Mohanty S, Kumar A, et al: Effect of community-based behaviour change management on neonatal mortality in Shivgarh, Uttar Pradesh, India: a cluster-randomised controlled trial. Lancet 372:1151-1162, 2008
49. Zayeri F, Kazemnejad A, Ganjali M, et al: Incidence and risk factors of neonatal hypothermia at referral hospitals in Tehran, Islamic Republic of Iran. East Mediterr Health J 13:1308-1318, 2007
50. Kambarami R, Chidede O: Neonatal hypothermia levels and risk factors for mortality in a tropical country. Cent Afr J Med 49:103-106, 2003
51. Cheah FC, Boo NY: Risk factors associated with neonatal hypothermia during cleaning of newborn infants in labour rooms. J Trop Pediatr 46:46-50, 2000
52. Manji KP, Kisenge R: Neonatal hypothermia on admission to a special care unit in Dar-es-Salaam, Tanzania: a cause for concern. Cent Afr J Med 49:23-27, 2003