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Neonatal hypothermia in low-resource settings

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Abstract

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 subsequent to 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 to improve understanding of global epidemiology of neonatal health. In this seminar, 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.

Introduction

Each year an estimated 3.6 million neonatal deaths occur¹, primarily due to infection, complications of preterm birth, and intrapartum-related hypoxic events². Infections are estimated to account for approximately one-third of the global burden of neonatal death, with estimates rising to more than half in high mortality settings². 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 terms of 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 two hundred years, the need to maintain an optimal body temperature for babies, especially those born prematurely, has been recognized, and is reflected by the development and improvement of early models of incubators during the 19th century³. 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 two 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

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factors related to maintaining this environment were carried out via a series of studies in the mid 20th century, establishing our basic knowledge of the physiology of temperature control in newborns⁷⁻¹⁰.

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°C – 37.5°C) and has been sub-classified into three grades: mild (36.0°C – 36.5°C), moderate (32.0°C – 35.9°C), and severe (<32.0°C) hypothermia¹¹. For each of these classifications, there are guidelines in place for responding to or managing hypothermia¹². 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 (ENC) that should be provided to all newborns regardless of setting¹³. 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 greatest¹⁴. Additionally, there has been limited progress in identifying the optimal approaches to preventing hypothermia or mitigating its consequences through rapid and appropriate management in low-resource settings¹⁵. This is especially true in locations where 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 seminar, 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 the range of 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 (i.e. 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 four 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}.

In order to avoid substantial heat loss due to these mechanisms, the core body temperature in children and adults is maintained through regulatory processes that include vasoconstriction, and shivering and non-shivering thermogenesis. However, the extent to which newborn babies can control thermoregulation to maintain an optimal core body temperature is limited, relative to children and adults. While 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 shivering³. 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 babies have limited vasoconstriction capability compared to term infants¹⁶, greater surface-to-mass ratios, and preterm and/or low birth weight babies have lower brown fat deposits¹⁷ which are essential for non-shivering thermogenesis.

Heat loss through evaporation of the amniotic fluid from the baby's skin is the most important mechanism¹¹. 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 loss¹¹. 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 rise, which may depend on birth weight, ambient temperature, and proximity to the mother¹⁸⁻²⁰. The initial loss of heat can be quite large; for example in the first 10-20 minutes after birth it is not uncommon for a baby to lose 2-4°C, with further subsequent losses possible in the presence of the above practices¹⁵.

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 babies born in facilities and in the community.

Hospital-based studies—There have been numerous studies that have attempted to quantify the burden of neonatal hypothermia in low resource settings, but the majority 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, but also demonstrate the wide range of estimates of the proportion of babies that are observed as hypothermic. For example, near universal observation of temperatures in the hypothermia range has been reported among babies from Senegal²¹, Uganda²², Nepal²³, and Turkey²⁴ (Table 1). However, when the cutoff for defining hypothermia is reduced well below the WHO cutoff for any (i.e. mild, moderate, or severe) hypothermia (<36.5°C), the observed proportion of babies deemed hypothermic is lower. For example studies with cutoffs at 35.0°C or 34.5°C in Table 1 (see Shimla, India²⁵ and Bissau, Guinea-Bissau²⁶) report much lower proportion of hypothermia babies. 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 (i.e. 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 (i.e. axillary vs rectal)²⁷, frequency of measurement, and

the cutoff used to classify babies as hypothermic^{26,28}. Furthermore some of the estimates shown in Table 1 are among out-born sick babies 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 draw conclusions 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 above, and are not population-based. Given that a large proportion of babies 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 currently available from sub Saharan Africa. Three small cohort studies conducted in India have been published²⁹⁻³¹. Among 189 home-born infants in villages of Haryana, the axillary temperature was less than 36.5°C among 21 babies (11.1%). In this study, temperature was recorded once within 24 hours after birth²⁹. More frequent observation of babies occurred in another study, conducted as part of the SEARCH project in Gadchiroli³⁰. 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 Pradesh³¹ where 1732 babies had axillary temperature measures recorded within 36 hours (median age 16.0 hours), almost half (45%) of the infants were observed with temperatures <36.5°C. In all three of these studies there was some evidence of seasonality; the proportion of hypothermic babies 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 babies in winter compared with 3.1% in summer, and in Uttar Pradesh, 70.0% of babies 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 southern Nepal. Between 2002 and 2006, more than 23,000 babies from the northern third of the district (population ~280,000) were enrolled in a community-based cluster randomized trial of chlorhexidine antiseptic interventions of the skin³³ and umbilical cord³⁴. All live born babies during the period of the study were included in the cohort, regardless of the place of birth; approximately 92% of babies 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 mid-way 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 (a total of 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 babies (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 24-72 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 babies 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 above have also examined case-fatality rates 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°C – 35.9°C) hypothermia on admission was an independent risk factor for neonatal death (adjusted OR=3.49 [95%CI: 3.18 – 3.81])³⁵. In Iran, mortality was higher among babies with rectal temperatures less than 36.5°C 20 minutes after birth (8.8%) compared to normothermic babies (2.6%), but these were not adjusted for important factors such as weight and gestational age³⁶.

Relative to normothermic babies, unadjusted case-fatality was also more than two-fold higher among the 62.0% of babies who were hypothermic upon admission in Nigeria (CFR=2.26 [95%CI: 1.14 – 4.48])³⁷.

Efforts to link population-based estimates of hypothermia exposure to subsequent mortality are even fewer. In the Bang study above³⁰, 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 Bissau²⁶, investigators were able to go back to the community and estimate overall neonatal and post-neonatal 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. Since 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 utilized to select an appropriate cut-off for examining mortality. Those with temperatures <34.5°C were at almost 5 times higher mortality risk in the first week of life, and risk remained elevated through 2 months of age²⁶.

More recently, the population-based data from Nepal was utilized to examine the relationship between axillary temperature over the entire range of hypothermia values and mortality subsequent to the first temperature observed²⁸. We found that after adjusting for age and ambient temperature at measurement and other covariates (such as sex, weight, gestational age, ethnicity, etc), mortality was increased by approximately 80% for every degree decrease in first observed axillary temperature. Mortality associated with hypothermia was substantially higher among preterm babies, and relative risk of death ranged from 2 to 30 times within the current WHO classification for moderate hypothermia, increasing with greater severity of hypothermia²⁸.

Both our study and the work by Sodemann and colleagues 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°C to 35.9°C) and includes in a single classification exposures that have substantially different consequences. One solution we have proposed²⁸ is to expand the “severe” category to exposures <34.0°C (Grade 4) and split the remainder of the “moderate” category into two separate categories (Grade 3: 34.0°C – 34.9°C and Grade 2: 35.0°C – 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 (i.e. for low birth weight or premature babies) (Table 4).

Risk factors for neonatal hypothermia

In order 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 provide a detailed discussion of possible risk factors for neonatal hypothermia, classifying these factors into contextual (e.g. seasonality), physiological (e.g. low birth weight), behavioral (e.g. early bathing), and socio-economic factors (e.g. poverty)¹⁵. Behavioral factors 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 chain¹¹. 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 where hypothermia incidence or prevalence 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. While Kumar et al¹⁵ provide some specific examples of settings where 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 two 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 two 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 terms of hypothermia risk may be elevated during warmer periods. Community-based data from Nepal³² indicate that hypothermia risk is correlated closely along the entire spectrum of body weight. For every 100 gram decrement in weight below 2000 grams, hypothermia risk increased by 31.3%; risks were lower but still significant for weight decrements between 2000 and 2500 grams (13.5% per 100 grams) and between 2500 and 3000 grams (7.4% per 100 grams).

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 newborn⁴. Among 318 infants whose temperature upon admission was less than 33.5°C, case-fatality was uniformly high, but was highest among those <1500 grams (171/175, 97.7%) compared to babies 1500-1999 grams (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 pre-term status (Figure 1)²⁸.

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 higher-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 above highlights specific practices that need to be promoted for both home and facility births. A specific recommendation is to delay bathing for at least six hours after birth; a randomized trial in a Ugandan hospital showed that bathing of newborns increased hypothermia even in the presence of skin-to-skin contact and the use of warm water³⁸. Another recommendation for reducing risk of hypothermia or for re-warming babies 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 rewarming³⁹ and for preventing hypothermia in preterm low birth weight babies⁴⁰. A number of summaries of skin to skin care and its benefits for reducing hypothermia risk have been published^{15,31}, including a meta analysis indicating improved survival among preterm babies <2000 grams in hospitals⁴¹. Early initiation of breastfeeding (i.e. within 24 hours) can reduce the risk of hypothermia³², and exclusive breastfeeding was associated with lower hypothermia among babies in a Zambian hospital⁴². 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, a number of 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, India⁴⁸. 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. Teasing out individual components of studies like these that test 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.

Conclusion

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, a number of 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.

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Figure 1.
Relative risk of neonatal death subsequent to hypothermia, by preterm status. (Adapted from Mullany, 2010²⁸)

Table 1

Selected facility-based estimates of the burden of hypothermia in newborns of low-resource settings

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

^aTemperature was also assessed at 10, 30, and 90 minutes post delivery; proportion was 29, 82, and 79%, respectively

^bTemperature was also assessed at 24 hours after birth; the proportion was 48.9%

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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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)	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 92.3% overall • RR of hypothermia 4.03 times higher in coldest quintile vs warmest quintile of ambient temperature
				<ul style="list-style-type: none"> • 48.6% overall

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 OR=3.49 [95%CI: 3.18 – 3.81])
Zayeri, 2007 ⁴⁹	Tehran, Iran	900	Hospital	• Unadjusted fatality was 8.8% among hypothermic babies compared to 2.6 among normothermic
Ogunlesi, 2008 ³⁷	Sagamu, Nigeria	150	Hospital	• Unadjusted fatality rate among hypothermic babies was 2.26 [95%CI: 1.14 – 4.48] higher than normothermic babies
Bang, 2005 ³⁰	Gadchiroli, India	763	Hospital to Community	• Case-fatality of hypothermia was 15.4%, and was significantly higher than those without hypothermia
Sodemann 2008 ²⁶	Bissau, Guinea-Bissau	2926	Community	• Adjusted for weight, temperatures <34.5°C were associated with mortality 4.81 [95%CI: 2.90 – 8.00] times higher 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 babies <35.0°C • Preterm babies at higher risk of hypothermia-associated mortality

Table 4

Possible new classification system for neonatal hypothermia

Grade	Definition	Proportion in rural Nepal ^a	Adjusted Mortality Risk ^a	Possible Guideline	
				Preterm	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

^aData from population-based study in rural Sarlahi District, Nepal²⁸