



Admission Temperature and Associated Mortality and Morbidity among Moderately and Extremely Preterm Infants

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Objective To evaluate the temperature distribution among moderately preterm (MPT, 29-33 weeks) and extremely preterm (EPT, <29 weeks) infants upon neonatal intensive care unit (NICU) admission in 2012-2013, the change in admission temperature distribution for EPT infants between 2002-2003 and 2012-2013, and associations between admission temperature and mortality and morbidity for both MPT and EPT infants.

Study design Prospectively collected data from 18 centers in the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Neonatal Research Network were used to examine NICU admission temperature of inborn MPT and EPT infants. Associations between admission temperature and mortality and morbidity were determined by multivariable logistic regression. EPT infants from 2002-2003 and 2012-2013 were compared.

Results MPT and EPT cohorts consisted of 5818 and 3213 infants, respectively. The distribution of admission temperatures differed between the MPT vs EPT ($P < .01$), including the percentage <36.5°C (38.6% vs 40.9%), 36.5°C-37.5°C (57.3% vs 52.9%), and >37.5°C (4.2% vs 6.2%). For EPT infants in 2012-2013 compared with 2002-2003, the percentage of temperatures between 36.5°C and 37.5°C more than doubled and the percentage of temperatures >37.5°C more than tripled. Admission temperature was inversely associated with in-hospital mortality.

Conclusions Low and high admission temperatures are more frequent among EPT than MPT infants. Compared with a decade earlier, fewer EPT infants experience low admission temperatures but more have elevated temperatures. In spite of a change in distribution of NICU admission temperature, an inverse association between temperature and mortality risk persists. (*J Pediatr* 2018;192:53-9).

The National Institute of Child Health and Human Development Neonatal Research Network (NRN) reported admission temperatures of inborn infants with birth weights 401-1499 g born in 2002 and 2003.¹ Low admission temperatures were common (46.9% were <36.0°C) and were inversely associated with the risks of mortality and late-onset sepsis. Multiple randomized trials, primarily in extremely preterm (EPT) neonates, have tested interventions to reduce the proportion of infants admitted to neonatal intensive care units (NICUs) with low temperatures. Interventions tested included polyethylene wraps,² exothermic mattresses,^{3,4} polyethylene caps,⁵ active warming during cesarean delivery,⁶ increased delivery room temperature,⁷ and humidified and heated air during stabilization.⁸ Evidence-based interventions to prevent low temperatures at birth are now part of neonatal resuscitation.⁹ Quality improvement initiatives demonstrated a reduced proportion of preterm infants with low temperatures upon NICU admission,¹⁰⁻¹² but elevated admission temperatures also have been reported among preterm infants who received interventions to prevent low temperatures.¹³⁻¹⁶

In view of the efforts to prevent hypothermia at birth, it is likely that the distribution of admission temperatures has changed compared with our earlier report.¹ A recent time-limited observational study of moderately preterm (MPT) infants

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Funded by the National Institutes of Health (M01 RR80), the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) (U10 HD21364, U10 HD21373, U10 HD21385, U10 HD27851, U10 HD27853, U10 HD27856, U10 HD27880, U10 HD27904, U10 HD34216, U10 HD36790, U10 HD40492, U10 HD40689, U10 HD53089, U10 HD53109, U10 HD68244, U10 HD68263, U10 HD68270, U10 HD68278, U10 HD68284), and the National Center for Advancing Translational Sciences (UL1 TR6, UL1 TR41, UL1 TR42, UL1 TR77, UL1 TR93, UL1 TR442, UL1 TR454, UL1 TR1117, UL1 TR1111). The National Institutes of Health, NICHD, and the National Center for Advancing Translational Sciences provided grant support for the Neonatal Research Network's (NRN) Generic Database and Moderate Preterm Registry through cooperative agreements. Participating NRN sites collected data and transmitted it to RTI International, the data coordinating center for the network, which stored, managed, and analyzed the data for this study. Although NICHD staff did have input into the study design, conduct, analysis, and manuscript drafting, the content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The authors declare no conflicts of interest.

EPT	Extremely preterm
ICH	Intracranial hemorrhage
MPT	Moderately preterm
NEC	Necrotizing enterocolitis
NICU	Neonatal intensive care unit
NRN	Neonatal Research Network

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<https://doi.org/10.1016/j.jpeds.2017.09.021>

(29⁰-33⁶ weeks of gestation) conducted by the NRN combined with a standing registry of mortality and morbidity for EPT infants, <29 weeks) facilitated examination of admission temperature over a broad gestational age range. The objectives of this report were to determine the frequency of low and high admission temperature among a recent cohort of MPT and EPT infants born in 2012 and 2013, the change in distribution of admission temperature among EPT infants compared with those born in 2002 and 2003, and associations between admission temperature and mortality and morbidity in both the MPT and EPT infant cohorts.

Methods

This study analyzed prospectively collected maternal and infant data abstracted from the medical record by trained research nurses at 18 centers of the Eunice Kennedy Shriver National Institute of Child Health and Human Development's NRN. Data were entered into a computerized database approved by the institutional review board at each participating site. Inclusion criteria were infants who were born at an NRN center and admitted directly to the NICU from a delivery or operating room with a gestational age between 22⁰ and 33⁶ weeks. Data were collected from March 1, 2012 through October 31, 2013 for MPT infants with gestational ages of 29⁰ through 33⁶ weeks (MPT) and throughout 2012 and 2013 for EPT infants with gestational ages of 22⁰ through 28⁶ weeks (EPT). Exclusion criteria included congenital brain malformations, malformations resulting in an open lesion (eg, myelomeningocele, abdominal wall defects), noninitiation of medical therapy for infants who died within 12 hours, a prenatal diagnosis with a decision to withdraw or limit intensive care, missing admission temperature measurements, and first temperature recorded at >2 hours of age.

The first temperature after NICU admission from Labor and Delivery was recorded as the admission temperature. For centers that admit infants to a holding area or delivery room stabilization area, the first temperature recorded in this area was recorded as the admission temperature. The date and time of the admission temperature and the site of temperature measurement (axilla, rectal, or skin) were recorded. Temperatures recorded in the delivery room or during transport to the NICU were not recorded. Use of a thermal wrap (NeoWrap [Fisher-Paykel Healthcare, Auckland, New Zealand], or thin plastic food wrap) was collected if this information was available. The database does not contain information on any other intervention to maintain temperature at birth (eg, exothermic mattress, hat, etc).

Data for 2012-2013 included (1) maternal variables including maternal hypertension, multiple births, antenatal steroids, antibiotics; (2) intrapartum variables including chorioamnionitis (clinical and histologic), duration of rupture of membranes, and delivery mode; (3) infant characteristics including birth weight, gestational age (obstetric estimate), sex, race, and ethnicity; (4) delivery room events including intubation, chest compressions, medications, and Apgar scores; and (5) Network center. Neonatal outcomes included death before

discharge, highest mode of respiratory support at day 28 (high-frequency or conventional ventilation, continuous positive airway pressure, nasal cannula/oxygen, or no support), grade III or IV (severe) intracranial hemorrhage (ICH), early or late-onset sepsis (positive blood culture before or after 72 hours, respectively), and necrotizing enterocolitis (NEC, modified Bell's stage II or above treated medically or surgically¹⁷). Neonatal outcomes were collected until hospital discharge, 120 days or death, whichever came first.

For comparison of 2012-2013 and 2002-2003, data were used only from centers participating in the NRN during both epochs. Infants with admission temperatures and born in 2002-2003 were included if they had gestational ages of 22⁰-28⁶ weeks.

A temperature of 36.5°C-37.5°C was considered normothermia as suggested by the World Health Organization.¹⁸ Descriptive statistics characterized the distribution of admission temperatures among MPT and EPT infants. Statistical significance was calculated using χ^2 tests and logistic regressions. Associations between admission temperature and neonatal outcomes were initially explored with bivariate analyses. Variables significant at the 0.10 level were entered into logistic regression models to adjust for covariates using admission temperature as a continuous variable. Variables included in the models were antenatal steroid exposure, sex, race, birth weight, intubation, Apgar at 5 minutes, center, prematurity level (MPT or EPT), and the interaction between admission temperature and type of infant (MPT/EPT) if present. Results were expressed using ORs and 95% CIs. The results prompted 2 post-hoc analyses. Short-term outcomes of EPT infants with admission temperatures >37.5°C were explored with adjusted logistic regression for differences with infants whose admission temperature was 36.5°C-37.5°C or <36.5°C. The sample size was determined by the number of infants available in the database registries. With the available MPT and EPT infants in 2012-2013, the power was greater than 90% among both cohorts to detect a 10% reduction in the frequency of admission temperature less than 36.0°C based on 2002-2003 data.

In a sensitivity analysis, associations were evaluated between missing temperatures and mortality. Two logistic regression models adjusting for the above listed covariates were run: the first comparing mortality among MPT and EPT infants between those missing vs those not missing admission temperatures and a second model comparing mortality between the 4 categories of admission temperature (<36.5°C, 36.5°C-37.5°C, >37.5°C, and missing).

Results

During 2012-2013, a total of 10 965 infants were entered into the Moderate Preterm Database (7051 MPT) and Generic Database (3914 EPT) with gestational ages from 22⁰ to 33⁶ weeks. The final cohort included 9031 infants (5818 MPT and 3213 EPT) after excluding 705 (6.4%) outborn infants (637 MPT and 68 EPT), 405 (3.7%) infants with anomalies or limited care, and 824 (7.5%) infants with missing or late admission temperature recordings. Exclusions because of missing temperature or time of temperature recordings were similar for MPT

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