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ORIGINAL ARTICLE

Risk factors and morbimortality associated with hypothermia upon admission to the neonatal intensive care unit

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Abstract

Objective: To determine the incidence of hypothermia, risk factors, and outcomes associated with low body temperature upon admission to the neonatal intensive care unit in very low birth weight infants. **Methods:** Longitudinal, observational, prospective study. Very low birth weight newborns admitted to a neonatal intensive care unit between October/2017 and September/2018 were included. The dependent variable was axillary temperature upon admission. We calculated the incidence of hypothermia and compared average temperatures with the risk factors and evaluated. Statistical tests: measures of central tendency, relative/absolute frequencies, Kolmogorov-Smirnov, Levene and Student's t test, considering $p < 0.05$ as significant. **Results:** 128 very low birth weight newborns were included, with mean weight and gestational age, respectively, 1079.2g and 29 weeks. Of these, 110 (85.9%) had moderate hypothermia, 13 (10.2%) had mild hypothermia and only 5 (3.9%) were normothermic upon admission. The average temperature found was 34.7ºC. The following risk factors remained associated with low temperature upon admission: weight and gestational age, Apgar score and neonatal resuscitation. The associated outcomes were respiratory distress syndrome, use of mechanical ventilation and vasoactive drugs, pulmonary hemorrhage, use of oxygen at 28 days of life, late-onset sepsis, and death. **Conclusions:** The incidence of hypothermia found was high and the lowest temperature at admission was associated with higher morbidity and mortality. It is necessary to pay attention to care practices to maintain the temperature of very low birth weight newborns, especially those with lower weights and gestational ages and who need neonatal resuscitation.

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INTRODUCTION

The World Health Organization (WHO) defines the core body temperature in newborns (NB) between 36.5°C and 37.5°C[1] as normothermia; neonatal hypothermia when below 36.5°C - graded as mild, moderate and severe. Mild hypothermia is when the temperature is between 36.0 and 36.4°C; moderate when the temperature is between 32.0 and 35.9°C; and considered severe when it is lower than 32.0°C[1].

Newborns tend to lose body heat more easily and quickly, when compared to older children, and have greater difficulty generating heat to keep warm due to some factors: reduced thermal insulation capacity, greater contact surface in relation to body weight, increased net losses from skin evaporation, central nervous system (CNS) immaturity and limited energy reserves[1,2,3]. In preterm infants, especially those with very low birth weight (VLW) and extremely low birth weight (ELW), these factors are even more present; and therefore, these NB are even more susceptible to hypothermia.

Hypothermia is related to some negative outcomes within a neonatal intensive care unit (NICU), such as: late neonatal sepsis, peri-intraventricular hemorrhage (PIVH), bronchopulmonary dysplasia (BPD), respiratory distress syndrome (RDS), pulmonary hemorrhage and death[1,2,3,4,5,6]. The decrease in the temperature of these NB is related to the increase in the metabolism rate of these babies, leading to hypoglycemia, in addition to the increase in oxygen consumption, causing or worsening respiratory discomfort. This increase in oxygen consumption also causes relative tissue hypoxia, causing cerebral vasodilation and favoring the emergence of intraventricular hemorrhage.

Hypothermia is a strong predictor of morbidity and mortality at all gestational ages[1,2,7], being considered an indicator of the quality of care in the delivery room and care performance in the neonatal unit[7].

The maintenance and control of a normothermic environment is the responsibility of the entire healthcare team. This care must occur from the care with the mother and newborn temperature in the delivery room, during transport and continuing in the neonatal unit.

At birth, as the newborn makes the transition to extrauterine life, the core temperature decreases, falling by about 0.3°C per minute, and there may be a decrease of 1°C to 3°C before leaving the delivery room[1].

Despite the adoption of neonatal resuscitation guidelines, updated in 2016, which reinforce hypothermia prevention strategies (temperature control in the delivery room, radiant heat crib, use of plastic/cotton caps, use of plastic bags without drying the body, thermal mattress, transport in a heated incubator)[1,2,3,8], the prevalence of hypothermic newborns admitted to the NICU is still very expressive.

Therefore, this study aimed to determine the incidence of hypothermia upon admission to the neonatal unit, the risk factors and outcomes associated with lower axillary temperature in very low birth weight newborns admitted to the maternity ward of a tertiary university reference institution in pregnancy and high-risk delivery in the state of Rio Grande do Norte. Knowledge of these data will provide subsidies to further improve the planning and care of these babies in the delivery room, in their transport and in moving within the NICU, reducing morbidity and mortality and improving the prognosis of these patients.

METHODS

This is an observational, longitudinal and prospective study involving preterm infants with VLW (birth weight less than 1500g) admitted to the neonatal intensive care unit of a tertiary university maternity hospital that is a reference for high-risk pregnancy and delivery in the state of Rio Grande do Norte, during the period from October 2017 to September 2018. This institution has about 300 monthly deliveries, 30% of which are premature. The study was approved by the Research Ethics Committee of the Hospital Universitário Onofre Lopes (HUOL), according to the Presentation Certificate for Ethical Assessment (CAAE) 11315419.6.0000.5292, with an Informed Consent Form (ICF) duly signed by the person responsible for each patient.

The newborns included had birth weight (BW) below 1,500g. The exclusion criteria used were not signing the informed consent form, presence of congenital infections (toxoplasmosis, rubella, cytomegalovirus, herpes simplex, syphilis and arbovirus), severe congenital malformations, inborn errors of metabolism, chromosomal disorders, multiple twinning (more than 2 fetuses) or those with no record of the admission temperature in the medical chart.

The diagnosis of hypothermia was made from the measurement of axillary temperature by the nursing team in the department, within the first 15 minutes of admission to the NICU. For statistical analysis, the sample was based on the average temperature upon admission, which the WHO considers normal when between 36.5ºC and 37.5ºC[1].

We assessed the following risk factors for lower axillary temperature at the time of admission to the NICU: birth weight (categorized into two groups: up to 999g and ≥ 1000g), gestational age (GA) at birth (estimated by means of first trimester ultrasound or by the date of the last menstrual period. Variable categorized into two groups: up to 28.6 weeks and ≥ 29 weeks), sex, type of delivery, need for resuscitation in the delivery room, Apgar score at the fifth minute of life, maternal hypertensive disease, antenatal corticosteroid use, weight adequacy for gestational age at birth by the Intergrowth project charts (being small for gestational age (SGA), those allocated below the 10th percentile, according to gestational age in weeks and days, and adequate for gestational age (AGA) being those classified between the 10th and 90th percentile)[9,10].

The outcomes analyzed in relation to lower temperature at admission to the NICU were: extrauterine growth restriction (EUGR) (assessed at the time of hospital discharge, by the presence of a Z score of weight < -2 by the curves of the Intergrowth project[11]), patent ductus arteriosus (PCA) after 72 hours of life (diagnosed with the GE Vivid I Echocardiogram device,

performed by pediatric cardiologists at the institution), peri-intraventricular hemorrhage (defined by the classification of Papile et al.1978, detected by transfontanellar ultrasound performed from the first week of life, with the Philips Affiniti 50 ultrasound equipment, with Linear transducer L12-4 (4 - 12 MHz)[12]), pulmonary hemorrhage (presence of blood in the orotracheal tube associated with the need to increase ventilatory parameters[13]) , respiratory distress syndrome requiring intratracheal surfactant, need for oxygen at 28 days of life[14], use of vasoactive drugs vas (VAD) in the first week of life, use of mechanical pulmonary ventilation (MPV), early and late sepsis (laboratory or clinical, defined when the manifestation occurs in the first 48 hours of life or after this period, respectively), according to criteria defined by the National Health Surveillance Agency (ANVISA)[15] and outcome (discharge, transfer or death).

With the statistical analysis we calculated the absolute and relative frequencies, in addition to measures of central tendency and dispersion. The normal distribution of quantitative variables was verified using the Kolmogorov-Smirnov test and homogeneity of variances using the Levene test. The comparison of temperature means in the risk factors and outcomes studied was performed using the Student's t-test. Results were considered significant when $p < 0.05$. The software used was the Statistical Package for Social Sciences (SPSS), version 22.

RESULTS

From October 2017 to September 2018, 141 preterm infants weighing less than 1500g were admitted to the NICU of the maternity unit studied. Of these, 13 met one or more exclusion criteria: severe congenital malformations (total of 2 newborns), parents' refusal to participate in the study (totaling 3), absence of admission temperature records (4 babies) and multiple twins due to the possibility of the children's birth order interfere with the outcomes (4 patients - quadruplets). Therefore, 128 babies were included in the study and their characteristics are described in table 1.

Table 1. Classification of very low birth weight newborns admitted to the Neonatal Intensive Care Unit of the tertiary-care maternity hospital in Natal/RN - Brazil, between October of 2017 and September of 2018 (n = 128).

Qualitative Variables		n (%)
Gestational age upon birth	Up to 28.6 weeks	58 (45.3)
	≥ 29 weeks	70 (54.7)
Birth weight	Up to 999g	47 (36.7)
	≥ 1000g	81 (63.3)
Sex	Males	71 (55.5)
	Females	57 (44.5)
Delivery mode	Vaginal	43 (33.6)
	C-Section	85 (66.4)
Need for resuscitation	No	48 (37.5)
	Yes	80 (62.5)
Temperature upon admission	< 32ºC	0 (0)
	32-35.9ºC	110 (85.9)
	36-36.4ºC	13 (10.2)
	36.5-37.5ºC	5 (3.9)
5th minute Apgar	< 7	23 (18.1)
	≥ 7	104 (81.9)
Gestational hypertension	Yes	63 (49.2)
	No	65 (50.8)
Prenatal steroid use	No	38 (29.9)
	Yes	89 (70.1)
Weight/Gestational age classification	SGA	32 (25)
	AGA	96 (75)
Intrauterine growth restriction	Yes	39 (41.1)
	No	56 (58.9)
Late sepsis	Yes	74 (58.3)
	No	53 (41.7)
Early sepsis	Yes	64 (50)
	No	64 (50)
Peri-intraventricular hemorrhage	Yes	37 (33.3)
	No	74 (66.7)
Surfactant use	Yes	78 (60.9)
	No	50 (39.1)
Ductus arteriosus persistent	Yes	37 (33.6)
	No	73 (66.4)
Outcome	Discharge	95 (74.2)
	Death	33 (25.8)
Mechanical ventilation use	Yes	98 (76.6)
	No	30 (23.4)
Oxygen at 28 days of life	Yes	38 (38.4)
	No	61 (61.6)
Pulmonary hemorrhage	Yes	36 (28.1)
	No	92 (71.9)
Use of vasoactive drugs in the first week of life	Yes	60 (48)
	No	65 (52)

Of the newborns included in the study, the mean birth weight and gestational age at birth were 1079.2g (SD ±270.8) and 29 weeks (SD ±2.6), respectively. The lower the GA and NW, the lower the mean temperature at admission, as shown in table 2.

The overall frequency of hypothermia in newborns admitted to the study was 123, which represents 96% of the sample. Of these, 110 (85.9%) had moderate hypothermia, that is, body temperature between 32ºC and 35.9ºC and only 5 (3.9%) of them were admitted with normothermia, as shown in table 1. The mean temperature of the babies was 34.7ºC (SD ± 1.14). No child had hyperthermia.

Risk factors and outcomes associated with lower axillary temperature at the time of admission to the NICU were evaluated using a bivariate analysis (Student's t-test, all variables had normal distribution). Table 3 shows the following risk factors as relevant: birth weight, gestational age at birth, Apgar score at the fifth minute of life and need for neonatal resuscitation in the delivery room.

In the analysis, we found that all babies born with less than 1 kg were admitted with a temperature lower than 36ºC ($p<0.05$). And in relation to gestational age, those who were born with less than 29 weeks, 93.1% of them were admitted with a temperature lower than 36ºC ($p<0.05$).

Table 4 lists the outcomes that were found to be associated, such as RDS with need for surfactant, use of mechanical lung ventilation, pulmonary hemorrhage, need for oxygen at 28 days of life, use of vasoactive drugs, late-onset sepsis and death.

Table 2. Mean temperature upon admission to the Neonatal Intensive Care Unit, according to gestational age and birth at weight, in newborns of very low weight in Natal/RN, between October 2017 and September 2018. (n = 128).

Variables		Mean temperature (ºC) ± Standard deviation
Gestational age at birth, in weeks	< 28	34.0 ± 1.14
	28 to 31.6	34.9 ± 0.98
	32 to 33.6	35.2 ± 1.04
	34 to 36.6	35.8 ± 0.31
Weight at birth, in grams	500 to 749	33.5 ± 0.91
	750 to 999	34.3 ± 0.88
	1000 to 1249	35.1 ± 0.92
	1250 to 1499	35.2 ± 1.01

Table 3. Analysis of risk factors for the lowest temperature upon admission of very low weight newborns in the Neonatal Intensive Care Unit of a Tertiary Level Maternity in Natal/RN, between October of 2017 to September of 2018 (n = 128).

Variables		Mean temperature ± SD	p value
Gender	Males	34.6ºC ± 1.26	0.363
	Females	34.8ºC ± 0.97	
Mode of delivery	Vaginal	34.5°C ± 1.36	0.353
	C-section	34.7°C ± 1.01	
Neonatal resuscitation	No	35.1ºC ± 0.94	0.001
	Yes	34.4ºC ± 1.19	
5th minute Apgar	<7	34.1ºC ± 1.32	0.012
	≥7	34.8ºC ± 1.07	
Gestational hypertension	Yes	34.6ºC ± 1.11	0.434
	No	34.8ºC ± 1.17	
Antenatal steroid	No	34.5ºC ± 1.17	0.303
	Yes	34.7ºC ± 1.13	
Gestational age/weight classification	SGA	34.8ºC ± 1.21	0.669
Weight at birth	AGA	34.7ºC ± 1.12	
	Up to 999g	33.9ºC ± 0.96	< 0.001
Gestational age	≥1000g	35.2ºC ± 0.95	
	Up to 28.6 weeks	34.1ºC ± 1.17	< 0.001
	≥ 29 weeks	35.1ºC ± 0.89	

SD: standard deviation; SGA: small for the gestational age; AGA: adequate for the gestational age.
Statistical test used: Student-t test.

Table 4. analysis of the outcomes associated with the lowest temperature upon admission of very low birth weight newborn at the Neonatal Intensive Care Unit of a Tertiary Level Maternity in Natal/RN, between October 2017 and September of 2018 (n = 128).

Variables		Mean temperature ± SD	P value
RDS	Yes	34.3ºC ± 1.13	< 0.001
	No	35.2ºC ± 0.97	
EUGR	Yes	34.9ºC ± 0.88	0.257
	No	35.1ºC ± 1.06	
Early sepsis	Yes	34.6ºC ± 1.19	0.287
	No	34.8ºC ± 1.09	
Late sepsis	Yes	34.5ºC ± 1.08	0.020
	No	35.0ºC ± 1.17	
PIVH	Yes	34.6ºC ± 1.05	0.065
	No	35.0ºC ± 1.00	
PDA	Yes	34.6ºC ± 1.12	0.065
	No	35.0ºC ± 0.97	
BPD	Yes	34.5ºC ± 1.02	0.001
	No	35.2ºC ± 0.90	
MPV	Yes	34.5ºC ± 1.14	0.001
	No	35.3ºC ± 0.93	
Pulmonary hemorrhage	Yes	34.2ºC ± 1.02	0.002
	No	34.9ºC ± 1.13	
VAD	Yes	34.3ºC ± 1.13	< 0.001
	No	35.1ºC ± 1.00	
Outcome-death	Discharge	35.0ºC ± 0.99	< 0.001
	Death	33.7ºC ± 1.04	

SD: standard-deviation; RDS: respiratory distress syndrome; EUGR: extrauterine growth restriction; PIVH: peri-intraventricular hemorrhage; PDA: persistent ductus arteriosus; BPD: broncho-pulmonary dysplasia; MPV: mechanical pulmonary ventilation; VAD: vasoactive drug. Statistical test-used: Student T-test.

DISCUSSION

Due to the disproportion between the contact surface and body weight and the reduced capacity for thermoregulation of these babies[1,2,3], especially premature babies, hypothermia is a very common event in this population, as also found in this study - where the incidence of hypothermia was 96%, with a mean temperature of 34.7ºC (±1.14).

These numbers are higher than others reported in the literature. An Indian study carried out in 2016 showed that the occurrence of hypothermia was 70%[16]. A Korean cohort study found that the incidence of this event in newborns with less than 33 weeks of GA admitted with a temperature below 36.5°C was 74.1%, with a mean of 36.1°C (±0.6°C); and those admitted with normothermia were 25.2%, in contrast to what was found in our study of only 3.9%[17].

In a population-based study that worked with samples from 11 European countries, the prevalence of hypothermia was 53.4% in newborns admitted with less than 32 weeks of gestational age. Of these, 12.9% had temperatures below 35.5˚C[3,18,19]. In a Canadian retrospective observational study that worked with NBs below 33 weeks of gestational age admitted to the NICU between January 2010 and December 2012, the incidence of hypothermia was 35.8%[4].

The incidence of hypothermia upon admission in 4356 VLW infants distributed in 20 intensive care units in Brazil was 53.7% (in this study, hypothermia was considered when axillary temperature was below 36°C up to one hour after admission). This frequency ranged from 19.8% to 93.3% in the centers studied. When considering the number of children with a temperature lower than 36.5°C upon admission, these numbers increase, with hypothermia being seen in 100% of babies in one of the units where the study was carried out[19].

These discrepancies in incidence can be attributed to differences in the methodologies applied in each service, such as, for example, different time intervals considered for measuring the temperature after admission to the NICU.

Although the delivery room team of the institution where the study was carried out follows the rules of the Neonatal Resuscitation Program, the high incidence of hypothermia found reveals the need to identify flaws in the care process, such as room temperature, maternal temperature, need to use thermal mattress for younger NBs (not yet available in the service), care in the use of plastic/cotton caps and plastic bags, not forgetting handling during transport in an incubator with inadequate temperature.

Another relevant data found in this study was that the main risk factors associated with lower temperature upon admission to the NICU are weight and gestational age at birth, since 100% of NB with BW up to 1Kg and 93.1% of NB with up to 28 weeks and 6 days of GA were admitted with a temperature lower than 36˚C. A Canadian study reinforces this finding, showing that birth weight was associated with admission temperature, as temperature increased 0.025˚C for each 100g increase in birth weight[4].

In addition, similar to what is found in the scientific literature, the mean temperature at admission increased as the range of birth weight and gestational age increased.

Other variables associated with lower temperature at admission were Apgar score at the fifth minute of life and neonatal resuscitation. In data published in the literature, admission temperature increased the risk of an Apgar score less than 7 in the fifth minute of life by 1.5 and 2.1 times for infants admitted with a temperature between 36-36.4˚C and <35.9ºC, respectively[17].

This positive association can perhaps be explained by the fact that babies who need resuscitation are usually sicker NBs and thermal control during resuscitation is more difficult and neglected compared to other active and immediate measures needed at the moment. In addition, heating and humidification of the inhaled gas for respiratory support during neonatal resuscitation is not routinely performed in the maternity unit studied, which may contribute to the occurrence of hypothermia in these NBs.

As for morbidities associated with hypothermia, some studies show that the admission temperature is inversely proportional to the mortality rate and late neonatal sepsis, showing that the drop in each 1˚C in the temperature of these NB is related to a 28% increase in the rate of death and an 11% increase in late-onset sepsis[1,2,4,8]. These studies corroborate the data found in this study, in which newborns who presented late-onset sepsis and died had lower temperature upon admission to the NICU. Although the reason for this association is not yet fully understood, low temperature seems to alter the adaptive immune function, causing damage to the activation and functioning of immune cells, influencing the response to infections[20].

Still showing similar data, in a cohort study the incidence of deaths increased by 1.38 (95%CI 1.04-1.83), 1.44 (95%CI 1.05-1.97) and 1.86 (95%CI 1.22-2.82) for infants with hypothermia upon admission of 36-36.4°C, 35-35.9°C and <35°C, respectively[17]. Another study states that the mortality rate of NBs admitted with hypothermia was 65.6%, compared to those admitted with normal temperature (6.1%)[21].

Other outcomes found in association with hypothermia were: RDS requiring the use of surfactant, bronchopulmonary dysplasia, use of MPV, pulmonary hemorrhage and use of vasoactive drugs. In all these cases, the NBs who evolved during the hospital stay with these outcomes were admitted with a lower mean temperature when compared to babies who did not present such complications.

The scientific literature also reports that hypothermia upon admission to the NICU is related to a 1.64-fold increase in early neonatal death. In addition to showing that VLW NBs with moderate hypothermia after birth had more moderate to severe bronchopulmonary dysplasia. On the other hand, the reduction in hypothermia upon admission was associated with a decrease in the incidence of pulmonary hemorrhage from 10.9% to 1.6% (p=0.017)[3]. Along these same lines, Na Hyun Lee et al. reported an increase in the odds of developing LBW by 1.26 (95%CI 1.01–1.57) and 1.81 (95%CI 1.20-2.86), for infants admitted with temperatures between 35-35.9°C and <35°C, respectively[17].

Considering that the advance in perinatal intensive care and the improvement of care provided through protocols and with the adoption of preventive measures has been a gain in medicine, hypothermia continues to be a challenge, making clear the need to identify failures in the care of newborns, correct them and further improve neonatal care.

This study has the limitation of having been carried out in only one center, with a small sample size. However, the data were collected prospectively, increasing the reliability of the information acquired, in addition to bringing important results regarding hypothermia upon admission to the neonatal ICU, risk factors and outcomes associated with lower temperature at that time, and demonstrating the importance of monitoring care practices, so that flaws in the process can be corrected.

Our study showed a very high incidence of hypothermia and the association of higher morbidity and mortality with lower body temperature upon admission to the NICU in very low-birth-weight newborns. It comes as a way of knowing and understanding the limitations during the provision of care to these newborns and trying to plan a safer and more effective way of assisting these babies (especially those with lower gestational ages and birth weights and who need resuscitation maneuvers after birth), according to the guidelines recommended by the Neonatal Resuscitation Program of the Brazilian Society of Pediatrics. We also demonstrate it is essential to show the entire health team the importance and weight of this condition in relation to the prognosis of premature NBs, alerting to the damage resulting from hypothermia, trying to minimize the risks and acting early and actively when already installed, in order to improve neonatal care and clinical practice.

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