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Hypothermia in Preterm Neonates in Oman: A Retrospective Study

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ABSTRACT

Objectives: To determine the prevalence of hypothermia among preterm infants born before 32 weeks of gestation and whether their temperature at admission is associated with neonatal and maternal risk factors and gestational age. Furthermore, the study evaluates the association between admission temperature, neonatal morbidity, and in-hospital mortality. ***Methods:*** This study involved an eight-year retrospective analysis of preterm neonates born < 32 weeks of gestation and admitted to the neonatal intensive care unit at a tertiary hospital in Oman, from 2010 to 2017. ***Results:*** The study included 587 preterm infants with a mean gestational age of 28.4 weeks, a mean birth weight of 1154.2 g, and a mean admission temperature of 35.5 °C. Hypothermia (axillary temperature < 36.5 °C) was present in 509 (86.7%) infants. In univariate analysis, only birth weight and neonatal resuscitation were associated with admission temperature (< 36.5 °C). In the multivariate analysis, only intraventricular hemorrhage demonstrated a significant association with the incidence of hypothermia. ***Conclusions:*** Most preterm newborns had hypothermia upon admission to the neonatal intensive care unit, which is associated with essential morbidities. More aggressive interventions are warranted to reduce the incidence of hypothermia in preterm infants.

Newborn hypothermia is a significant concern in neonatal care and is associated with an increased risk of morbidities such as intraventricular hemorrhage (IVH), respiratory distress, and even mortality.[1–3] The prevalence of this condition has been reported to be higher in low- and middle-income countries. However, comparing data is often difficult because studies have adopted different temperature thresholds (35–36.5 °C) for hypothermia.[4] One potential solution is to follow the universally acceptable definition of the World Health Organization (WHO). According to the WHO, neonatal hypothermia occurs when the axillary temperature falls below 36.5 °C.[5,6] The current study has adopted this global standard.

In very preterm neonates (< 32 weeks of gestation), the prevalence of hypothermia is much higher, mainly due to a larger surface area-to-body mass ratio and poor thermoregulation.[7] Interventions to minimize hypothermia in preterm newborns at birth are recommended in the Neonatal Resuscitation Program (NRP) guidelines, including the use of plastic bags, thermal mattresses, and radiant warmers, which are now part of the standard of care in neonatal intensive care units (NICUs).

Improvements in the thermal care of newborns in developed countries and increased awareness of the importance of maintaining body temperature at birth have significantly reduced morbidity and mortality rates among premature newborns. However, despite these measures, many preterm infants develop hypothermia at admission, especially in developing countries.[8,9]

The objective of our investigation was to ascertain the prevalence of hypothermia in very preterm newborns admitted to the NICU at Sultan Qaboos University Hospital (SQUH), Oman. The present study sought to evaluate the correlation between neonatal and maternal risk factors and the occurrence of hypothermia in babies born at very preterm gestational ages. Additionally, we investigated the correlation between admission temperature, newborn morbidity, and in-hospital death.

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METHODS

This is a retrospective, analytical, and descriptive study of all premature births with gestational ages > 23 weeks ($23^{0/6}$) and < 32 weeks ($31^{0/6}$)at SQUH and admitted to the NICU over an eight year period from January 2010 to December 2017. The study was approved by the Ethics Committee of SQUH (Ref. 2014/1519/-31/3).

Our institution's clinical practices remained consistent during the eight-year study period, with no significant changes that could have affected the rates of neonatal morbidity and mortality. Several methods have been used at the hospital to maintain stable neonatal temperatures. Based on the neonate's condition and gestational age, these included plastic bags and radiant warmers. The NICU was approximately 200 m from the delivery rooms. Infants were transported to the NICU in a fully equipped transport incubator to maintain the temperature.

All preterm infants with congenital anomalies and those born before 23 weeks of gestation were excluded from the study. We included infants with an admission time of ≥ 2 hours after birth; those admitted later than that were excluded. The axillary temperature of each infant admitted to the NICU was measured using a digital clinical thermometer. We followed the WHO classification and a temperature < 36.5 °C was recorded as hypothermic. Hypothermia was further classified into mild (36.0–36.4 °C), moderate (32.0–35.9 °C), and severe (< 32.0 °C).[5,10] The required demographic, clinical, and outcome details and evidence of possible risk factors for hypothermia were identified from previously published studies.

In our logistic regression study, we classified temperature as a categorical variable, with normothermia as the reference group of 36.5–37.5 °C .[10,11]

Low birth weight was defined as a birth weight < 2500 g, while preterm birth was defined as a gestational age of < 37 weeks.[12]

We looked at newborn and maternal risk factors, as well as other neonatal morbidities and mortality rates. The neonatal risk factor data included sex, weight, gestational age, resuscitation at birth (yes or no), and surfactant administration (yes or no). Maternal risk factors included administration of steroids (yes or no), multiple births (single or multiple), mode of delivery (vaginal or cesarean section), and prolonged rupture of membranes (PROM).

Neonatal morbidities noted included respiratory distress syndrome (RDS),[13] necrotizing enterocolitis (NEC) grades II and III,[14,15] and IVH grades I to IV.[16] Bronchopulmonary dysplasia was defined as receiving supplemental oxygen for more than four weeks.[13,17]

Ruptured membranes were defined as membranes that spontaneously ruptured > 24 hours before birth. There were two types of resuscitation: basic (stimulation and airway management) and advanced (positive pressure ventilation, chest compressions, and medications). The American Academy of Pediatrics guidelines, which include clinical and radiographic criteria, were used to diagnose RDS.

Trained individuals abstracted this study data using a standardized data abstraction form. Data was collected on predesigned and approved data collection forms from admission and discharge registers in the NICU. The principal investigator oversaw the data abstraction process, and a manual of definitions was provided to ensure consistent data interpretation across different abstractors.

Data was analyzed using Stata 17 (StataCorp LLC, College Station, TX, USA). Descriptive analysis was used to determine means and SD for continuous variables, and frequencies for nominal and ordinal variables. The results were expressed as mean±SD, and categorical variables were expressed as numbers and percentages. Continuous variables were analyzed using the Mann-Whitney U test and Pearson correlation coefficient. Multivariate regression analysis was performed to determine the relationship between the variables.

RESULTS

The study included 587 preterm infants born between > 23 and < 32 weeks of gestation and admitted to the NICU. The vast majority (509; 86.7%) had hypothermia (< 36.5 °C) on admission. The mean admission temperature was 35.5 °C (range = 30.5–37.9 °C). The median gestational age was 29.0 weeks (mean = 28.4±2.2 weeks; range = 23–31), and the median birth weight was 1140.0 g (mean = 1154.2±350.9; range = 400–2100 g) [Table 1].

The premature infants in the study were classified based on their admission temperatures into the following categories: 385 (65.6%) cases of moderate hypothermia (32.0–35.9 °C), 121 (20.6%) cases of mild hypothermia (36.0–36.4 °C), and three (0.5%) cases of severe hypothermia (< 32.0 °C). The

Table 1: Demographic and other data of premature infants admitted to the NICU, classified by axial temperatures at admission (N = 587).

Variables	Hypothermic < 36.5 °C (n = 509) n (%)	Non-hypothermic 36.5–37.5 °C (n = 78) n (%)
Newborn risk factors		
Male	275 (54.0)	28 (35.9)
Female	234 (46.0)	50 (64.1)
≥ 29 weeks	283 (55.6)	46 (59.0)
< 29 weeks	226 (44.4)	32 (41.0)
≥ 1500 g	427 (83.9)	62 (79.5)
< 1500 g	82 (16.1)	18 (23.1)
Resuscitation	145 (28.5)	31 (39.7)
No resuscitation	364 (71.5)	47 (60.3)
Surfactant	179 (35.2)	36 (46.2)
No surfactant	330 (64.8)	42 (53.8)
Maternal risk factors		
Steroids used in mother	297 (58.3)	45 (57.7)
No steroids	212 (41.7)	33 (42.3)
Multiple births	159 (31.2)	28 (35.9)
Singleton	350 (68.8)	35 (44.9)
Vaginal delivery	190 (37.3)	36 (46.2)
Cesarean section	319 (62.7)	42 (53.8)
PROM	126 (24.8)	27 (34.6)
No PROM	383 (75.2)	51 (65.4)
Morbidities in neonate		
RDS	494 (97.1)	76 (97.4)
No RDS	15 (2.9)	2 (2.6)
NEC	30 (5.9)	5 (6.4)
No NEC	479 (94.1)	73 (93.6)
BPD	186 (36.5)	25 (32.1)
No BPD	23 (4.5)	53 (67.9)
IVH	56 (11.0)	17 (21.8)
No IVH	453 (89.0)	61 (78.2)
Died in NICU	60 (11.8)	5 (6.4)
Discharged alive	449 (88.2)	73 (93.6)

NICU: neonatal intensive care unit; PROM: prolonged rupture of membranes; RDS: respiratory distress syndrome; NEC: necrotizing enterocolitis; BPD: bronchopulmonary dysplasia; IVH: intraventricular hemorrhage.

Table 2: Prevalence of hypothermia among premature infants (N = 587).

Hypothermia category	n (%)
Severe (< 32.0 °C)	3 (0.5)
Moderate (32.0–35.9 °C)	385 (65.5)
Mild (36.0–36.4 °C)	121 (20.6)
Normal temperature (36.5–37.5 °C)	78 (13.3)
Total	587 (100)

Table 3: The potential risk factors associated with hypothermia among premature infants as per univariate analysis (N = 587).

Risk factors	Unadjusted odds ratio	*p*-value	95% CI
Neonatal risk factors			
Sex	0.66	0.090	0.40–1.08
Gestational age	1.06	0.330	0.95–1.18
Birth weight	1.00	0.040*	1.00–1.01
Resuscitation	0.80	0.040*	0.64–0.99
Surfactant	0.63	0.060	0 .39–1.02
Maternal risk factors			
Steroids	0.97	0.910	0 .60–1.58
Multiple pregnancies	0.92	0.670	0.63–1.35
Mode of delivery	0.87	0.100	0.74–1.03
PROM	1.61	0.070	0.97–2.67
Morbidities			
RDS	1.15	0.850	0.26–5.15
NEC	1.09	0.860	0.41–2.91
BPD	0.82	0.440	0.49–1.36
IVH	1.29	0.090	0.96–1.74
Mortality	0.51	0.170	0.19–1.32

**Significance. PROM: prolonged rupture of membranes; RDS: respiratory distress syndrome; NEC: necrotizing enterocolitis; BPD: bronchopulmonary dysplasia; IVH: intraventricular hemorrhage.*

remaining infants (78; 13.3%) had normal temperature (36.5–37.5 °C) on admission [Table 2].

In univariate analysis, only birth weight and neonatal resuscitation were significantly associated with admission hypothermia [Table 3], and in multivariate regression, only IVH was significant [Table 4].

DISCUSSION

In this large cohort of 587 very preterm newborns, 86.7% were hypothermic (< 36.5 °C) on admission to the NICU. In univariate analysis, birth weight and neonatal resuscitation were significantly associated with hypothermia. In multivariate analysis, only IVH demonstrated a significant association with hypothermia. Our findings are supported by many studies worldwide that have reported a high prevalence of hypothermia (< 36.5 °C) among preterm infants at their admission to the NICU, despite advancements in technology and care protocols for this extremely vulnerable population.

Previous research has attributed preterm neonates' susceptibility to hypothermia to their immature thermoregulation system, exacerbated by their high surface area-to-body weight ratio, undeveloped epidermis, and thin subcutaneous fat layer.[5,10] The

Table 4: Potential risk factors associated with hypothermia among premature infants as per multivariate analysis (N = 587).

Risk factors	Adjusted odds ratio	*p*-value	95% CI
Neonatal			
Gestational age	0.92	0.440	0.75–1.12
Birth weight	1.00	0.210	0.99–1.00
Surfactant	0.78	0.480	0 .38–1.56
Resuscitation	0.89	0.450	0.65–1.21
Maternal			
Steroids	0.87	0.610	0.52–1.45
Multiple pregnancies	1.03	0.900	0 .68–1.54
Mode of delivery	0.90	0.260	0 .75–1.08
PROM	1.55	0.110	0.89–2.66
RDS	1.37	0.700	0 .29–6.46
NEC	1.33	0.590	0.47–3.79
BPD	0.94	0.850	0.47–1.87
IVH	1.44	0.030*	1.03–2.02
Mortality	0.55	0.270	0.19–1.59

**Significance. PROM: prolonged rupture of membranes; RDS: respiratory distress syndrome; NEC: necrotizing enterocolitis; BPD: bronchopulmonary dysplasia; IVH: intraventricular hemorrhage.*

worldwide prevalence of neonatal hypothermia varies substantially (35–85%),[18] possibly due to the interplay of diverse variables including geoclimatic factors, availability of NICUs, delivery and newborn care protocols, and economic disparities.

In 2016, the Effective Perinatal Intensive Care in Europe population-based cohort study by Wilson et al,[19] across 11 European countries investigated hypothermia among 5697 very premature infants (< 32 weeks) admitted to NICUs. The study found a strong association between the rates of hypothermia on admission and morbidity and mortality rates. A review of the Effective Perinatal Intensive Care in Europe study emphasized the importance of preventing hypothermia in premature infants to increase positive health outcomes.[20]

In Brazil, De Almeida et al,[21] found that low NICU admission temperature was critically associated with neonatal mortality. A 2015 study from Canada on premature infants (< 33 weeks) emphasized the need for maintaining optimum admission temperature to prevent severe morbidity and mortality.[22] In Iran, Zayeri et al,[23] studied thermal management in a more heterogeneous group of newborns, and reported a significantly high prevalence of hypothermia among premature neonates. The consistent findings across studies from various countries, conducted on ethnically diverse neonatal populations, give ample evidence for the need for optimal thermal management of premature neonates.

Newborns in low-income countries are even more vulnerable to hypothermic risk, as shown by studies in East Africa.[24–26] A 2020 systematic review and meta-analysis of North African studies found that preterm birth and low birth weight were the main factors associated with newborn hypothermia.[24] In these infants, hypothermia was significantly associated with failure to provide basic thermal protection, such as not using warm blankets and loss of temperature due to prolonged skin-to-skin contact immediately after birth.[24] In Southwest Ethiopia, Ukke et al,[25] discovered a strong relationship between newborn hypothermia at NICU admission and low gestational age, delayed breastfeeding initiation, and insufficient maternal education on neonatal care. Likewise, Alebachew Bayih et al,[26] in Eastern Ethiopia identified several inadequate infant warming practices leading to hypothermia within the first six hours after delivery. These included not using warm clothing or blankets immediately after birth, prolonged skin-to-skin contact, and conducting delivery at home.

These investigations brought out additional newborn hypothermia risks in East African populations.[24–26] In areas lacking hospital delivery options, women and birth attendants need to be educated on taking precautions against newborn hypothermia, such as prewarming the swaddling blankets and avoiding prolonged skin-to-skin contact immediately after delivery. Comprehensive education regarding preserving newborn warmth and identifying hypothermia symptoms must be given to mothers, midwives, and healthcare workers. It is also crucial to conduct community outreach programs to improve access to healthcare institutions to reduce home deliveries.[25,26]

Further risks associated with hypothermia include morbidities such as hypoxia, increased energy use, metabolic acidosis, and hypoglycemia, which significantly raise the mortality risk of premature infants and those with low birth weight.[27,28] This adds to the immense importance of preventing newborn hypothermia at all costs.

In the univariate analysis of our data, a significant connection was observed between the occurrence of hypothermia and the administration of newborn resuscitation after delivery. This finding is consistent

with previous research showing an increased risk of hypothermia in premature infants undergoing resuscitation during birth. These studies propose that neonates requiring resuscitation have difficulty maintaining their central body temperature due to their smaller size and more severe condition.[28] Also, premature infants already have low surfactant levels, reduced further by hypothermia.[29]

In our multivariate analysis, a significant association was revealed between hypothermia and IVH. This is consistent with previous studies showing a substantial association between hypothermia and IVH.[16] A consistent U-shaped association has been established between the admission temperature and the degree of neurological impairment.[16] The association between hypothermia and IVH is known to be multifaceted. Central to this relationship are the coagulation defects induced by lowered body temperatures. These defects cause disruptions in the coagulation cascade, platelet dysfunction, and vascular compromise, and have been extensively demonstrated in human and animal studies. Notably, the temperature-dependent nature of enzymatic reactions in the coagulation cascade and the impaired platelet function under hypothermic conditions underscore the increased risk of IVH. This intricate interplay emphasizes the critical importance of meticulous temperature management in clinical settings to mitigate the risk of hemorrhagic complications.[30,31]

Our univariate analysis found no association between admission temperature and significant neonatal morbidities, including RDS and necrotizing enterocolitis. This was consistent with the findings of Laptook et al.[28] Also, it did not reveal any significant association between hypothermia and bronchopulmonary dysplasia. A limited number of studies have reported an association between the two, but the underlying reasons for this remains unexplained.[7]

In contrast to previous studies, we did not find a significant correlation between hypothermia and RDS. The available evidence suggests that hypothermia can potentially exacerbate respiratory distress, resulting in elevated oxygen use and reduced surfactant synthesis. These difficulties often need the help of enhanced respiratory support and treatments. Efforts implemented in industrialized countries to reduce the occurrence of hypothermia cases upon admission to newborn units have consistently shown improved respiratory outcomes.[29]

Maternal factors such as cesarean delivery, PROM antenatal steroid administration, and multiple birth administrations were not associated with hypothermia in this study; similar results were reported earlier in the literature.[14] Interestingly, antenatal steroids and chorioamnionitis have been reported to decrease the odds of hypothermia.[32] Antenatal steroids may stimulate the maturation of the epidermal skin layer, which may increase temperature regulation. Newborns who received steroids antenatally had lower skin-air temperature gradients and a reduced need for thermal support than infants who did not receive steroids.[33] Chorioamnionitis frequently occurs in mothers of infants with PROM. The possibility exists that intrauterine infections can cause maternal chorioamnionitis and subsequent inflammatory reactions in the fetus. These reactions may increase cytokine and chemokine production, which may increase newborns' body temperature. The higher incidence of normothermia observed in neonates exposed to chorioamnionitis may be explained by this mechanism.[34]

In response to the current study findings, we initiated a strict program to reduce the incidence of hypothermia in our unit. This included thorough training sessions for midwives, neonatal nurses, and resident doctors, focusing on the dangers of neonatal hypothermia and the necessity of preserving thermal stability, especially in infants with very low birth weights. We ensured that thermal mattresses were consistently available for receiving and enclosing newborns in response to equipment deficiencies discovered in labor rooms. According to recent research, thermal mattresses are crucial to prevent neonatal hypothermia and to properly regulate body temperatures, providing preterm infants with a stable, thermally favorable environment.[32] Their consistent use can significantly lower the risk of hypothermia, underscoring their significance in neonatal care. We also follow the NRP recommendation to wrap newborns under 32 weeks of gestation in plastic wrap. This approach is integrated into our protocol with radiant warmers, tailored to the neonate's condition and gestational age.

Some improvements required logistic support from the maintenance team, such as consistent maintenance of the labor room temperature at 25–26 °C. We also sought better temperature control during the transition from the delivery ward to the

NICU by mandating the use of transport incubators for all preterm infants. The necessity of keeping all incubators' batteries charged was emphasized. We are monitoring and auditing these implementations to assess their effectiveness. Preliminary findings are encouraging. We plan to discuss our experiences in a subsequent paper.

The strength of this study is the large sample size, which boosts the reliability of the results. In addition, this study accounts for a wide range of neonatal and maternal factors that may contribute to neonatal hypothermia. Extensive data collection on maternal and neonatal variables and morbidity outcomes supports these findings.

The limitations of this study are its retrospective design, the data collection bias, and the use of existing medical records. Moreover, not all possible confounding factors were accounted for in the analysis. Without more information, we might assume that the study's limited generalizability is due, at least in part, to the fact that it was conducted at a single center. We recognized the challenges in accurately subclassifying and analyzing hypothermia. This difficulty was caused by the insufficient statistical power available for a thorough examination within each hypothermia category. Future studies could fill this knowledge gap to improve clinical understanding and management of hypothermia in preterm infants.

CONCLUSION

We discovered a high prevalence of hypothermia among inborn preterm infants born at < 32 weeks gestation at our hospital. There was a strong link between hypothermia, RDS, and low birth weight. In response to these alarming findings, we initiated a strict program to reduce the incidence of hypothermia. The program, which included the use of thermal mattresses and strict adherence to the NRP guidelines, has yielded positive results.

Rigorous temperature management is vital to mitigate neonatal hypothermia in very premature newborns. High-risk infants should be promptly identified and managed strictly as per NRP protocols. The consistent implementation of these protocols should be monitored and audited periodically.

Disclosure

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