

# Unveiling Prevalence, Risk Factors and Morbidities Associated with Hypothermia in Preterm Neonates Less Than 32 Weeks: An 8-Year Retrospective Study

Mohamed Abdellatif<sup>1\*</sup>, Fatma Musallam Al Ghafri<sup>2</sup>, Murtadha Al Kahbori<sup>3</sup>,  
Ashfaq Ahmad Khan<sup>4</sup>, Nihal Al Riyami<sup>5</sup> and Moataz Hassan<sup>6</sup>

<sup>1</sup>Child Health Department, Sultan Qaboos University Hospital, Muscat, Oman

<sup>2</sup>Sultan Qaboos University, Muscat, Oman

<sup>3</sup>Hematology Department, Sultan Qaboos University Hospital, Muscat, Oman

<sup>4</sup>Neonatal Intensive Care Unit, Child Health Department, Sultan Qaboos University Hospital, Muscat, Oman

<sup>5</sup>Department Of Obstetrics and Gynecology, Sultan Qaboos University Hospital, Muscat, Oman

<sup>6</sup>Sultan Qaboos University Hospital, Muscat, Oman

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\*Corresponding author: mabdelmonem2015@gmail.com

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## ***Abstract***

**Objective:** This study aimed to determine the prevalence of hypothermia among preterm infants and whether admission temperature is associated with neonatal and maternal risk factors in extreme and very preterm infants stratified by postnatal age. We also assessed the association between admission temperature, neonatal morbidity, and in-hospital mortality.

**Methods:** This was an eight-year retrospective study of all inborn preterm neonates who were less than 32 (23<sup>0/7</sup> to 31<sup>6/7</sup>) gestational weeks admitted to the neonatal intensive care unit (NICU) at Sultan Qaboos University Hospital (SQUH) between January 2010 and December 2017.

**Results:** Five hundred eighty-seven preterm infants were included in the study; the mean admission temperature was 35.5°C. The prevalence of hypothermia (axillary temperature <36.5°C) was 86.7% (n = 509). The mean gestational age and birth weights were 28.42 weeks and 1154.20 gm respectively. In univariate analysis only birth weight and neonatal resuscitation were associated with admission temperature (<36.5°C). In the multivariate analysis, only intraventricular hemorrhage (IVH) demonstrated a statistically significant association with the incidence of hypothermia.

**Conclusion:** Many preterm newborns had hypothermia upon admission to the NICU at SQUH, which is associated with essential morbidities. Based on the results of this study, more aggressive interventions are warranted to reduce the incidence of hypothermia in preterm infants. Data access statement: All relevant data are within the paper and its Supporting Information files. Additional data related to this study is available from the authors upon reasonable request.

**Keywords:** Temperature; Hypothermia; Premature birth; Low birth weight; Sepsis.

## Introduction

Newborn hypothermia is a significant concern in neonatal care. It is linked to increased morbidity and mortality, particularly in low- and middle-income nations. Even though the thresholds for designating hypothermia may vary between studies,<sup>1</sup> its prevalence remains an essential indicator of the quality of neonatal care. Different prevalence rates of neonatal hypothermia have been described in the past. It is important to note that these rates may have been affected by the various cutoffs used in these studies. The consistent reporting of neonatal hypothermia, despite these variations, highlights its significance as a global health concern.

Neonatal hypothermia is a global issue, but it is more common in developing countries with insufficient financial resources; and a high incidence has been reported in Africa and South Asia. Supervising the thermal needs of preterm newborns at birth through admission to the neonatal unit remains a challenge for all health experts involved in caring for newborns. Hypothermia is defined by the World Health Organization (WHO) as "axillary temperature below 36.5°C".<sup>2,3</sup> It has been described differently by various investigators using different cutoffs and measuring body temperature at multiple sites, which might also account for the inconsistency in reporting separate incidences in other areas.<sup>3</sup>

In addition to comprehending its prevalence, it is essential to investigate the connection between admission temperature and various obstetric and neonatal risk factors. Such an investigation not only reveals potential causes and correlations, but also facilitates the development of targeted interventions.

Hypothermia on admission to the neonatal unit is a common finding associated with increased mortality in newborn babies<sup>4,5</sup> and predisposes newborns to an increased risk of intraventricular hemorrhage, worsening respiratory distress, and Other morbidities.<sup>6</sup> The immediate drop in body temperature in very preterm newborns (<32 weeks of gestation) may be more pronounced, mainly due to a larger surface area-to-body mass ratio and poor thermoregulation.<sup>7</sup>

Interventions to decrease hypothermia in preterm newborns at birth are recommended in the Neonatal Resuscitation Program (NRP), including plastic bags, thermal mattresses, and radiant warmers, which are now the standard of care in the Neonatal Intensive Care Unit (NICU). 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, mainly in developing countries.<sup>8,9</sup> Many developing countries still have little understanding of the significance of neonatal hypothermia, resulting in increased hypothermia-associated morbidity and mortality. Efforts to increase awareness of hypothermia among premature newborns in these regions would help direct future recommendations and policies to decrease the incidence of hypothermia. The objective of our investigation was to ascertain the frequency of hypothermia in preterm newborns, specifically inside the neonatal intensive care unit (NICU) at Sultan Qaboos University Hospital (SQUH). The present study aimed to evaluate the correlation between neonatal and maternal risk factors and the occurrence of hypothermia in babies born at a very preterm gestational age. Additionally, we investigated the correlation between admission temperature, newborn morbidity, and in-hospital death. The results of our study emphasize the need to implement proactive measures to decrease hypothermia in premature newborns. Additionally, our findings bring attention to the necessity of improving educational programs, preventive strategies, and therapeutic approaches in this domain.

## Methods

This study is a retrospective, analytical, and descriptive study of all inborn births less than 32 (23<sup>0/6</sup> to 31<sup>0/6</sup>) weeks gestation born at Sultan Qaboos University Hospital (SQUH) and admitted to the neonatal intensive care unit (NICU) over eight years period (January 2010 – December 31, 2017). The study was approved by the Ethics Committee of SQUH.

Our institution's clinical practice remained consistent during the eight-year study period, with no significant changes that could have affected neonatal morbidity and mortality. Several methods have been used at our institution to maintain stable neonatal temperatures. Based on the neonate's condition and gestational age, these include 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.

The prevalence of hypothermia at the time of NICU admission was the primary outcome of this study. Secondary outcomes included neonatal morbidity and mortality and hypothermia-related factors, such as resuscitation type, duration of ruptured membranes, and RDS.

All infants with congenital anomalies and those born before 23 weeks of gestation were excluded from the study. The axillary temperature for all admissions was measured using a digital thermometer, measuring 32°C to 42.9°C. We followed the WHO classification; a temperature less than 36.5°C was recorded as hypothermic. Hypothermia was further classified into mild (36°C -36.4°C), moderate (32–35.9°C), and severe (<32°C).<sup>2,10</sup> The required demographic, clinical, and outcome details and evidence of possible risk factors for hypothermia were identified from previously published studies.

We included infants with an admission time of  $\geq 2$  h after birth. In our logistic regression study, we classified temperature as a categorical variable, with normothermia as the reference group of 36.5 - 37.5 degrees centigrade.<sup>10,11</sup>

Low birth weight is defined as a birth weight of less than 2500 g, while preterm birth is defined as a gestational age of less than 37 weeks.<sup>12</sup>

Obstetric services function as tertiary referral centers and accept high-risk deliveries from other health institutes in the country. Data were collected on predesigned and approved data collection forms from admission and discharge registers in the NICU.

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 delivery or cesarean section), and prolonged rupture of membranes (PROM). Neonatal morbidities include respiratory distress syndrome (RDS),<sup>13</sup> necrotizing enterocolitis (NEC) grades II and III,<sup>14,15</sup> and intraventricular hemorrhage (IVH) grades I, II, III, and IV.<sup>16</sup> Bronchopulmonary dysplasia (BPD) is defined as receiving supplemental oxygen for more than four weeks.<sup>13,17</sup>

Ruptured membranes were defined as membranes that spontaneously ruptured more than 24 h 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 (AAP) guidelines, which include clinical and radiographic criteria, were used to diagnose respiratory distress syndrome (RDS), including clinical and radiographic findings.

Trained individuals abstracted the data for this study using a standardized data abstraction form. The principal investigator oversaw the data abstraction process, and a manual of definitions was provided to ensure consistent interpretation of the data across different abstractors. All relevant data are presented in the paper and its Supporting Information files.

Data were analyzed using STATA 17 (StataCorp). Descriptive analysis was used to determine the means and standard deviations for continuous variables, and frequencies for nominal and ordinal variables. The results are expressed as the mean  $\pm$  standard deviation, and numbers and percentages are reported for categorical variables. 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. The study was approved by the SQU ethical board (2014/1519/-31/3).

## Result

Five hundred eighty-seven preterm infants aged < 32 weeks were admitted to the NICU during the study period. The prevalence of hypothermia (axillary temperature <36.5°C) was 86.7% (n = 509) in the study population. The mean admission temperature was 35.5°C, ranging from 30.5 – to 37.9°C. The median gestational age was 29 weeks; the mean was 28.41, ranging from 23–31 weeks, and st dev. of 2.23. The median birth weight was 1140 gm, and the mean was 1154.20 gm, ranging between 400 and 2100 g, and st dev. of 350 .98 gm. In univariate analysis only birth weight and neonatal resuscitation were associated with admission hypothermia, as shown in Table 3 and only IVH was significant on multivariate regression analysis, as depicted in Table 4.

**Table 1:** Demonstrates the prevalence of hypothermia.

TEMP	Freq.	Percent
Severe (<32°C)	3	0.51
Moderate (32–35.9°C)	385	65.59
Mild (36°C -36.4°C)	121	20.61
Normal (36.5–37.5°C)	78	13.29
Total	587	100.00

**Table 2:** Demographic data of newborn infants admitted to the NICU at SQUH for newborns between January 2010 and December 2017.

Newborn risk factors	36.5- 37.5 °C	< 36.5 °C
Male	28/78(45.90%)	275/509(54.03%)
Female	50/78(64.10%)	234/509 (45.97%)
≥ 29 weeks	46/78 (58.97%)	283/509(55.60%)
< 29 weeks	32/78(41.03%)	226/509(44.40%)
≥ 1500gm	62/78(79.49%)	427/509(83.89%)
< 1500g	18/78 (23.08%)	82/509 (16.11%)
Resuscitation	31/78(39.74%)	145/509 (28.48%)
No resuscitation	47/78(60.26%)	364/509 (71.51%)
Surfactant	36/78(46.15%)	179/509(35.17%)
No Surfactant	42/78(53.85%)	330/50(64.83%)
<b>Maternal risk factors</b>		
Steroids	45 /78(57.69%)	297/509 (58.35%)
No steroids	33/78 (42.31%)	212/509 (41.65%)
Multiple birth	28/78 (35.90%)	159/509 (31.24%)
Singleton	35/78 (44.87%)	350/509 (68.76%)
Vaginal delivery	36/78	190/509 (37.33%)
Cesarean section	42/78 (34.63%)	319/509 (62.67%)
PROM	27/78	126/509 (24.75%)
No PROM	51/78 (65.38%)	383/509 (74.25%)
<b>Morbidities</b>		
RDS	76/78 (97.44%)	494/509 (97.05%)
No RDS	2/78 (2.56%)	15/509 ((2.95%)
NEC	5/78	30/509 (5.89%)
No NEC	73/78	479/509 (94.11%)
BPD	25/78 (35.90%)	186/509 (36.54%)
No BPD	53/78 (67.95%)	23/509 (63.46%)
IVH	17/78 (21%)	56/509 (11%)
No IVH	61/78 (78.21%)	453/509 (88.90%)
Mortality	5/78 (6.41%)	60/509 (11.79%)
Alive	73/78(93.59%)	449/509 (88.21%)

**Table 3:** The potential risk factor associated with hypothermia in univariate analysis.

	<b>Unadjusted odds</b>	<b>p-value</b>	<b>CI</b>
<b>Neonatal</b>			
Sex	0.66	0.09	0.40-1.08
Gestational age	1.06	0.33	0.95-1.18
Birth weight	1.00	0.04	1.00-1.01
Resuscitation	0.80	0.04	0.64-0.99
Surfactant	0.63	0.06	0.39-1.02
<b>Maternal risk factors</b>			
Steroids	0.97	0.91	0.60-1.58
Multiple pregnancies	0.92	0.67	0.63-1.35
Mode of delivery	0.87	0.10	0.74-1.03
PROM	1.61	0.07	0.97-2.67
<b>Morbidities</b>			
RDS	1.15	0.85	0.26-5.15
NEC	1.09	0.86	0.41-2.91
BPD	0.82	0.44	0.49-1.36
IVH	1.29	0.09	0.96-1.74
Mortality	0.51	0.17	0.19-1.32

**Table 4:** Potential risk factors associated with hypothermia in multivariate analysis.

<b>Risk factors</b>	<b>Adjusted odds ratio</b>	<b>p-value</b>	<b>95% CI</b>
<b>Neonatal</b>			
Gestational age	0.92	0.44	0.75-1.12
Birth weight	1.00	0.21	0.99-1.00
Surfactant	0.78	0.48	0.38-1.56
Resuscitation	0.89	0.45	0.65-1.21
<b>Maternal</b>			
Steroids	0.87	0.61	0.52-1.45
Multiple pregnancy	1.03	0.90	0.68-1.54
Mode of delivery	0.90	0.262	0.75-1.08
PROM	1.55	0.11	0.89-2.66
RDS	1.37	0.70	0.29-6.46
NEC	1.33	0.59	0.47-3.79
BPD	0.94	0.85	0.47-1.87
IVH	1.44	0.03	1.03-2.02
Mortality	0.55	0.27	0.19-1.59

## Discussion

In this large cohort of very preterm newborns, we found that more than eighty-five percent of newborns under 32 weeks had a body temperature of less than 36.5 °C at admission to neonatal intensive care. Hypothermia was prevalent in 86.7% of the 587 preterm infants admitted to the NICU during the study period (axillary temperature, 36.5°C). The temperature at admission ranged from 30.5 to 37.9°C, an average of 35.5°C. The average gestational age was 28.41 weeks, and the average birth weight was 1154.20 gm. In univariate analysis, only birth weight and neonatal resuscitation were associated with admission temperature (<36.5°C). In the multivariate analysis, only intraventricular hemorrhage (IVH) demonstrated a statistically significant association with the incidence of hypothermia. This study confirms the frequent occurrence of hypothermia (temperature 36.5C) upon admission in numerous tertiary facilities across developing countries despite advancements in the neonatal intensive care of preterm infants.

Similar hypothermia results in more than 50% of admissions have been reported from other countries: 53% in European cohorts,<sup>18-20</sup> and 51% in a Brazilian study from 2014<sup>21</sup> compared with only 36% in a survey published in

Canada.<sup>21,22</sup> Research from Iran shows the incidence of hypothermia to be 33.8%.<sup>23</sup> According to a meta-analysis conducted on the global burden of neonatal hypothermia, the prevalence of hypothermia fluctuated between 35% and 85%.<sup>1</sup>

Most newborns affected with hypothermia are infants weighing less than 2.5 kg and those with a gestational age of less than 34 weeks; several studies found a significant association between low birth weight and hypothermia.<sup>24-26</sup>

The risk factors for preterm newborns to develop hypothermia, such as poor thermoregulation, large surface area-to-body weight ratio, immature skin, and a thin subcutaneous fat layer, are well recognized.<sup>5,10</sup>

Several reports have demonstrated higher mortality among preterm newborns with reduced temperature than those maintaining average body temperature.<sup>8</sup> Most deaths related to hypothermia occurred in low-birth-weight infants and lower gestational ages, like other studies that investigated the association of hypothermia on admission with mortality in preterm babies. Previous studies<sup>14,17,19,23</sup> reported that admission temperatures <36.0C were related to higher mortality in preterm babies aged < 34 weeks than in older babies. The increased mortality associated with hypothermia is described by the fact that hypothermia leads to hypoxia, increased energy consumption, and accelerates the risk of metabolic acidosis, hypoxia, and hypoglycemia; however, the biological processes associated with hypothermia and mortality have not been identified.<sup>26-28</sup>

This study's univariate analysis found no association between admission temperature and significant neonatal morbidities, including RDS and NEC. This result was consistent with the findings of Laptok et al.<sup>28</sup> In the conducted multivariate analysis, a significant association was shown between hypothermia and (IVH). This discovery is consistent with previous studies showing a substantial association between hypothermia and intraventricular hemorrhage (IVH). It is worth noting that a constant U-shaped link has been established between the admission temperature and the degree of neurological impairment.<sup>16</sup> The association between hypothermia and intraventricular hemorrhage (IVH) is multifaceted. Central to this relationship are the coagulation defects induced by lowered body temperatures. These defects, which encompass disruptions in the coagulation cascade, platelet dysfunction, and vascular compromise, 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.<sup>29,30</sup>

Despite our univariate analysis not revealing a significant link between hypothermia and BPD, it's worth noting that only a handful of studies have reported an association between the two, and the underlying reasons for this connection remain largely unexplained.<sup>7</sup>

In the univariate analysis, a statistically significant connection was seen between the occurrence of hypothermia and the administration of newborn resuscitation after delivery. This discovery 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.<sup>28</sup> Also, premature infants already have low surfactant levels, reduced further by hypothermia.<sup>31</sup>

In contrast to previous research findings, our study did not identify any significant correlation between hypothermia and respiratory distress syndrome (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.<sup>31</sup>

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.<sup>14</sup> Interestingly, antenatal steroids and chorioamnionitis have been reported to decrease the odds of

hypothermia.<sup>32</sup> 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.<sup>33</sup> 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 lead to an increase in 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.<sup>34</sup>

In response to our findings, we initiated a strict program to reduce the incidence of hypothermia in our unit. This program 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, these thermal mattresses are crucial in the fight against neonatal hypothermia by providing preterm infants with a stable, thermally favorable environment in which they need to properly regulate their body temperatures.<sup>32</sup> Their consistent use can significantly lower the risk of hypothermia, underscoring their significance in neonatal care. We followed the Neonatal Resuscitation Program (NRP) recommendation to wrap newborns under 32 weeks of gestation in plastic wrap. We tried consistently maintaining the labor room temperature between 25 and 26 °C by working with the maintenance division. This optimizes temperature control during the transition from the delivery ward to the NICU and the mandatory use of transport incubators for all preterm infants. The necessity of constant-incubator battery charging was emphasized. We are currently re-auditing these implementations to assess their effectiveness. The initial findings showed improvement in the results. We wish to track this development and discuss our experiences in a subsequent publication. These reviews helped us identify practical barriers to maintaining charged batteries and to develop changes to overcome these barriers.

## Conclusion

We discovered a significant prevalence of hypothermia in this retrospective study of inborn preterm infants born at less than 32 weeks gestation at our hospital, with an alarming 86.7% of infants exhibiting admission temperatures of less than 36.5°C. Our study found a strong link between hypothermia, respiratory distress syndrome, and low birth weight. These findings highlight the urgent need for efficient interventions and strategies to maintain optimal thermal control and lower the associated morbidities in preterm infants. Preliminary results indicate improved outcomes and our subsequent use of thermal mattresses and adherence to the Neonatal Resuscitation Program guidelines aim to close this gap. To ensure that these measures work in practice and raise neonatal care standards at our institution, ongoing audits and evaluations are essential.

The strength of this study lies in its 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. 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. The potential shortcomings of this study stem from its retrospective design, such as data collection bias and the use of existing medical records. Moreover, not all possible confounding factors were accounted for in the analysis. We have recognized the challenge our study encountered in accurately subclassifying and analyzing hypothermia. This difficulty was mainly caused by the insufficient statistical power available for a thorough examination within each hypothermia category. Future study could fill this knowledge gap in order to improve clinical understanding and management of hypothermia in this vulnerable population.

Implications for clinical practice: Better perinatal care is needed, particularly for temperature management, because of the high incidence of neonatal hypothermia in premature infants. Targeted interventions for high-risk neonates can be determined by identifying low birth weight and RDS as significant risk factors for hypothermia. These results also highlight the significance of advanced care and constant temperature monitoring in infants with associated risk factors.

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