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Original Research

Hypothermia on admission and its association with neonatal mortality and morbidity in neonatal intensive care unit

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Abstract.
BACKGROUND: Neonatal hypothermia is a drop in the newborn's core temperature less than 36.5°C. It is crucial in neonatal morbidity and mortality, particularly in preterm infants. This research aimed to assess the incidence and risk factors of neonatal hypothermia and its effect on neonatal mortality and short-term morbidity during Neonatal Intensive Care Unit (NICU) admission.
METHODS: This observational study was conducted on all neonates admitted to the NICU at Benha University Hospital. The core temperature was measured on admission for all admitted neonates and were followed up to assess the impact of hypothermia on short-term outcomes and mortality.
RESULTS: A total of 323 neonates were admitted to the NICU throughout the research period. Thirty-five cases were excluded due to congenital anomalies or missing or late admission temperature recordings. The study included 288 neonates whose mean gestational age was 34.6 ± 3.4 weeks, and their mean birth weight was 2.35 ± 0.9 kg. Two-thirds (66%) of the neonates had core temperatures indicating hypothermia (axillary temperature of less than 36.5°C), one-third (33%) were normothermic, and only three (1%) were hyperthermic. Neonates with hypothermia had statistically lower gestational age, higher frequency of multiple births, prolonged need for respiratory support, higher rates of pulmonary hemorrhage, sepsis, intraventricular hemorrhage (IVH), and necrotizing enterocolitis, longer hospital stay, and mortality.
CONCLUSIONS: There is a high incidence of neonatal hypothermia at NICU admission. Lower gestational age, increased multiples, lower APGAR score, lower birth weight, and lack of antenatal steroids were significantly associated with hypothermia at NICU admission. Hypothermia was found to be a significant factor contributing to increased mortality and morbidity rates in affected neonates.

Keywords: Hypothermia, neonatal mortality and morbidity, neonatal intensive care unit

1. Introduction

The World Health Organization (WHO) defines mild hypothermia as a temperature of 36.0°C to 36.4°C, moderate hypothermia as 32.0°C to 35.9°C, and severe hypothermia as below 32.0°C, with a

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recommendation to maintain neonatal body temperature between 36.5°C and 37.5°C [1].

Worldwide, about 2.5 million newborns die annually during the first four weeks of life, accounting for 47% of all under-five years deaths [2]. In Egypt, Neonatal mortality is 10/1000 life birth, constituting more than 50% of the under-five years child mortality rate [3]. Most neonatal deaths are due to prematurity, birth asphyxia, infection, or birth defects [4]. While neonatal hypothermia is not a frequent direct cause of mortality, it is considered a comorbidity, especially in high-risk and low-birth-weight infants [5, 6].

Hypothermia in newborns is a global health issue, with higher rates reported in nations with limited resources [7]. The prevalence of neonatal hypothermia ranges from 32% to 85% in hospitals and from 11% to 92% in private residences [8]. Despite the knowledge and development of new approaches to better maintain body temperature, recent studies have noted that a significant proportion of preterm infants in high-resource countries have failed to maintain normothermia after delivery [1, 9–11]

Neonatal hypothermia is associated with a fivefold increased risk of death within the first five days of life [14]. Studies have shown that a decrease of one degree Celsius in a newborn's body temperature increases the risk of death by 80% [15]. Furthermore, neonatal hypothermia in extremely preterm infants is linked to severe neurodevelopmental impairment [16].

Neonatal hypothermia is a condition that is caused by pathological, physiological, environmental, and behavioral factors in newborns [15, 16]. To reduce neonatal mortality, the World Health Organization (WHO) has added thermal care as the primary component of the essential newborn care package [5].

Neonatal hypothermia is potentially preventable, and its prevention will be reflected in neonatal mortality and morbidity rates. Therefore, this study aimed to determine the incidence and risk factors of neonatal hypothermia on NICU admission and its impact on mortality and short-term morbidities in neonates.

2. Methods

2.1. Study design and participants

This prospective cohort observational study was executed at the Neonatal Intensive Care Unit (NICU), Benha University Hospitals, from January 2022 to July 2022. Benha University Hospital NICU is a tertiary care unit with average admission of 50–60 neonates per month. All neonates, either born in or transferred early to the hospital, were registered for the study during the study duration. Neonates with congenital anomalies, those without recorded admission temperature or with temperature measured beyond 15 minutes of admission, those referred to other hospitals, and those without informed consent were excluded.

The research ethics committee, Benha Faculty of Medicine, approved this study. Before enrollment, informed consent was acquired from parents. All neonates underwent the following; (a) Detailed history taking, including gestational age, sex, mode delivery, gestational age, and Apgar Score at 1 and 5 minutes; (b) Prenatal history, including maternal risk factors during pregnancy, such as chronic medical illness, infection, premature rupture of membrane, multiple gestations; (c) The leading cause of NICU admission.

2.2. Assessment of temperature

Axillary temperatures were recorded using digital thermometers in Celsius degrees within 15 minutes of NICU admission. Once the baby transferred to NICU by transport incubator, we manage him at warmer, and his initial temperature measured at this time before transferring him to the NICU incubator.

Because the WHO classification of moderate hypothermia includes a large range of temperature (32.0°C–35.9°C) and severe hypothermia (<32.0°C) is extremely rare, we divided included infants into 5 groups according to their admission temperature: <35.0°C, 35.0°C–35.9°C, 36.0°C–36.4°C, 36.5°C–37.5°C (normal temperature), and >37.5°C (hyperthermia).

All neonates were followed up until discharge or death with their length of stay, need and duration of respiratory support, and morbidities, such as necrotizing enterocolitis, intraventricular hemorrhage, and pulmonary hemorrhage, being recorded.

2.3. Statistical analysis

Version 25 of SPSS was used for statistical analysis (IBM, Armonk, New York, United States). Means and standard deviations were employed to summarize numerical data. Numbers and percentages were employed to represent categorical data. The one-way ANOVA test was employed to compare quantitative data between various temperature grades. The Fisher's exact or Chi-square tests were used to com-

pare categorical data. The performance of body temperature in predicting mortality in the examined neonates was evaluated using ROC analysis. The optimal cutoff point, diagnostic indices, and the area under the curve with a 95% confidence interval were calculated. Multivariate logistic regression analysis was done to predict hypothermia. The odds ratios were calculated along with the 95% confidence intervals. There were two sides to every single statistical test. Significant P values were defined as those less than 0.05.

3. Results

Gestational age, weight, singleton, antenatal steroid use, and PROM significantly differed between neonatal admission temperatures. In contrast, sex and mode of delivery, maternal DM, maternal HTN, maternal UTI, previous abortion, consanguinity, and order did not significantly differ (Table 1).

As shown in Table 2, Pulmonary hemorrhage, sepsis, IVH, NEC, mortality, and duration of hospital stay significantly differed between neonatal admission temperatures.

ROC analysis was done to evaluate the performance of body temperature to predict mortality in the studied neonates. The AUC was 0.863 (95% confidence interval: 0.810–0.917, $P < 0.001$). At a cutoff point <35.6°C, the sensitivity was 80.3%, and the specificity was 74% Fig. 1.

In univariate analysis, gestational age, sex, age, weight, ANS, and PROM were significant independent predictors of hypothermia with Odds ratios of 0.762, 20.191, 0.763, 0.343, 0.545, and 140.084, respectively. In contrast, order, diabetes mellitus, hypertension, twins, and infection were insignificant predictors of hypothermia.

In Multivariate analysis, sex, age, weight, ANS, and PROM were significant independent predictors of hypothermia with odds ratios of 10.846, 0.729, 0.247, 0.372, and 280.767, respectively (Table 3).

4. Discussion

The management of newborn health and well-being is a crucial aspect of pediatric treatment, and several factors can influence neonatal outcomes. Hypothermia is a prevalent disorder that can affect infant health. While known risk factors such as prematurity and low birth weight play a significant role, ensuring the awareness of healthcare personnel and the availability of appropriate technical equipment in the delivery room and neonatal care settings are also essential for preventing adverse outcomes associated with neonatal hypothermia [17].

Regarding the general and clinical characteristics of the studied neonates according to admission temperature, the current study is consistent with Tessema et al., who found no significant association between sex or mode of delivery and neonatal admission temperature [17]. However, the study revealed that gestational age, weight, and singleton status significantly differed according to neonatal admission temperatures, which is in line with Gidi et al. and Fneish et al., who reported that lower gestational age and birth weight are associated with a higher risk of neonatal hypothermia [18, 19].

Furthermore, the current study indicated that antenatal steroid use significantly higher in the normothermic infants. Other studies and recent meta-analysis reported no significant effect of antenatal steroids on the admission hypothermia [19–21]. A multicenter Chinese study reported higher incidence of hypothermia in neonates whom mothers received antenatal steroids but the authors after subgroups analysis stated that the statistical significance of antenatal steroids has no clinical significance [22]. The interpretation of this variable requires special care as the significance was between normothermic infants and infants with temperature <35.0°C. but not with the other groups with milder hypothermia. Also, the obstetrics department policy to give antenatal steroids for elective CS in late preterm pregnant mothers.

Moreover, the current study revealed that premature rupture of membranes (PROM) was significantly higher in neonates with admission temperatures less than 35.0°C compared to the other temperatures. This finding is supported by a study demonstrating that PROM is associated with an increased risk of neonatal hypothermia [17]. The fetus is prone to heat loss and cold stress because to the rupture of the protective amniotic fluid barrier by PROM. In addition, PROM is usually linked with premature birth, which raises the risk of neonatal hypothermia due to underdeveloped thermoregulatory systems and reduced subcutaneous fat stores in preterm neonates. Prolonged PROM or oligohydramnios may prolong exposure to a cool intrauterine environment, generating physiological responses including vasoconstriction and shivering, which can deplete energy reserves and raise the risk of hypothermia [23, 24].

Table 1
General and clinical characteristics of the studied neonates according to admission temperature

		Temperature								
		<35.0°C		35.0°–35.9°C		36.0°–36.4°C		36.5°–37.5°C		
		N = 58	%	N = 70	%	N = 62	%	N = 95	%	*P*-value
Sex	Male	26	44.8	34	48.6	28	45.2	62	65.3	0.073
	Female	32	55.2	36	51.4	34	54.8	33	34.7	
Gestational age (wks)	Mean ± SD	31.5 ± 3.5		34.3 ± 3.2		35.3 ± 2.8		36.3 ± 2.5		<0.001*
Weight (kg)	Mean ± SD	1.6 ± 0.6		2.2 ± 0.8		2.4 ± 0.7		2.9 ± 0.9		<0.001*
Mode of delivery	CS	34	58.6	38	54.30	45	72.6	65	68.4	0.17
	NVD	24	41.4	32	45.7	17	27.4	30	31.6	
Singleton	Single	46	79.3	53	75.7	54	87.1	83	87.4	0.04*
	Multiple	12	20.7	17	24.3	8	12.9	12	12.7	
Antenatal Steroid	Negative	27	46.6	13	18.6	18	29.0	19	20.0	0.002*
	Positive	31	53.4	57	81.4	44	71.0	76	80.0	
Maternal DM	Yes	2	3.4	5	7.1	11	17.7	7	7.4	0.058
Maternal HTN	Yes	5	8.6	3	4.3	4	6.5	6	6.3	0.87
PROM	Yes	4	6.9	17	24.3	3	4.8	0	0.0	<0.001*
Maternal UTI	Yes	3	5.2	3	4.3	2	3.2	7	7.4	0.76
Previous abortion	Yes	6	10.3	7	10.0	5	8.1	11	11.6	0.93
Consanguinity	Yes	16	27.6	18	25.7	17	27.4	28	29.5	0.09
Order	1st	13	22.4	25	35.7	19	30.6	33	34.7	0.74
	2nd	16	27.6	14	20.0	15	24.2	22	23.2	
	3rd	17	29.3	14	20.0	18	29.0	25	26.3	
	4th	5	8.6	11	15.7	3	4.8	9	9.5	
	5th	4	6.9	4	5.7	2	3.2	3	3.2	
	6th	3	5.2	2	2.9	5	8.1	3	3.2	

CS: Cesarean section, NVD: Natural vaginal delivery, SD: Standard deviation, DM: diabetes mellitus, HTN: Hypertension, PROM: Premature rupture of membranes, UTI: Urinary tract infection, *: significant as *P*-value <0.05.

Table 2
Outcome of the studied groups according to admission temperature

		Temperature								
		<35.0°C		35.0°–35.9°C		36.0°–36.4°C		36.5°–37.5°C		
		N = 58	%	N = 70	%	N = 62	%	N = 95	%	*P*-value
Pulmonary hemorrhage		28	48.3	7	10.0	3	4.8	0	0.0	<0.001*
Sepsis		30	51.7	40	57.1	28	45.2	12	12.6	<0.001*
IVH		9	15.5	5	7.1	0	0.0	0	0.0	<0.001*
NEC		7	12.1	4	5.7	2	3.2	0	0.0	0.002*
Mortality		38	65.5	14	20.0	6	9.7	3	3.2	0.001*
Duration of hospital stay (d)	Median	7		14		18		4		0.001*
	Range	1–49		2–78		2–61		2–43		

IVH: Intraventricular hemorrhage, NEC: Necrotizing enterocolitis, *: significant as *P*-value <0.05.

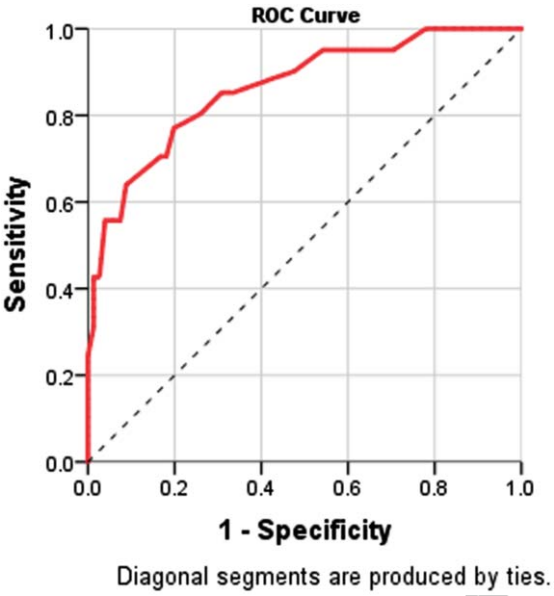

Fig. 1. ROC analysis for the performance of body temperature to predict mortality.

In contrast, maternal factors, including diabetes mellitus, hypertension, urinary tract infection, previous abortion, consanguinity, and birth order, did not significantly differ between neonatal admission temperatures. This finding aligns with Mullany et al., who concluded that there is no significant association between maternal factors and neonatal hypothermia [25].

According to the current study, significant associations were reported between neonatal hypothermia and adverse outcomes, such as pulmonary hemorrhage, sepsis, intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), mortality, and duration of hospital stay. These findings are consistent with Lee et al., who demonstrated that hypothermia at admission was associated with pulmonary hemorrhage, sepsis, IVH, NEC, and mortality in preterm infants [1]. Our results also align with Silverman et al. [26].

The association between hypothermia and adverse outcomes in neonates could be explained by disruption of normal physiology, leading to increased vulnerability to infections, poor perfusion, and compromised organ function. Additionally, hypothermia can disrupt the neonatal capacity to maintain stable blood glucose levels, thereby elevating the risk of adverse outcomes [27].

The current study demonstrated that hospital stay significantly differed according to neonatal admission temperatures, which is consistent with a study reporting that hypothermic neonates have longer hospital stays than normothermic neonates. Prolonged hospital stay increases healthcare costs and poses additional risks to neonates, such as an increased risk of nosocomial infections and developmental delay [28].

In this study, ROC analysis determined the performance of body temperature as a predictor of mortality in neonates. It revealed a significant area under the curve (AUC) of 0.863 with a 95% confidence interval of 0.810–0.917. The optimal cutoff point was <35.6°C, with a sensitivity of 80.3% and specificity of 74%. These findings suggest that body temperature might be a valuable predictor of mortality in neonates. Earlier research has reported an association between hypothermia and increased mortality risk in neonates [17, 19].

In the current study, univariate and multivariate analyses were employed to identify independent predictors of hypothermia in neonates. In the univariate analysis, gestational age, sex, age, weight, ANS, and PROM were significant predictors of hypothermia. This is consistent with previous studies, which indicated that gestational age, birth weight, PROM, and Apgar score were significant predictors of hypother-

Table 3
Univariate and Multivariate logistic regression analyses of various variables for prediction of hypothermia

	Univariate				Multivariate			
	OR	95%CI		*P*-value	OR	95%CI		*P*-value
GA	0.762	0.694	0.838	**<0.001***	–	–	–	
Sex	20.191	10.325	30.623	**0.002***	10.846	0.987	30.453	**0.055***
Age	0.763	0.654	0.89	**<0.001***	0.729	0.61	0.872	**<0.001***
Weight	0.343	0.245	0.478	**<0.001***	0.247	0.124	0.491	**<0.001***
Order	10.106	0.922	10.326	0.277	–	–	–	
ANS	0.545	0.303	0.98	**0.043***	0.372	0.184	0.756	**0.006***
DM	10.367	0.551	30.394	0.5	–	–	–	
HTN	10.039	0.378	20.857	0.941	–	–	–	
PROM	140.084	10.876	1050.731	**0.010***	280.767	20.903	2850.069	**0.004***
Twins	10.331	0.882	20.009	0.173	–	–	–	
Infection	0.575	0.202	10.633	0.299	–	–	–	

GA: gestational age, DM: diabetes mellitus, HTN: Hypertension, PROM: Premature rupture of membranes, OR: Odds ratio, CI: confidence interval, *: significant as *P*-value <0.05.

mia in neonates [17]. In the multivariate analysis, sex, age, weight, ANS, and PROM remained significant predictors of hypothermia.

The insignificant associations in the current study between hypothermia and other factors, such as birth order, diabetes mellitus, hypertension, twins, and infection, may be due to various causes, such as different sample sizes, study populations, and study designs.

The significant prevalence of newborn hypothermia indicated by our study necessitates a greater comprehension of the local variables that contribute to this problem as several factors at our setting may be contributing to the prevalence of hypothermia, including suboptimal temperature control during transport of outborn neonates to the NICU, insufficient environmental temperature regulation within the NICU, and limited access to thermal care resources for neonates. To effectively address this challenge, a multidisciplinary approach including healthcare professionals is necessary. Other preventative measures include establishing standard protocols for temperature control, providing extensive training to healthcare personnel, and implementing frequent monitoring and quality improvement measures. By addressing local concerns and adopting these preventive measures, we can reduce the incidence of infant hypothermia and improve the short-term outcomes and survival rates of at risk babies.

There are several limitations to be mentioned in this study First we did not compare between the in-born and out-born infants, this is because the low numbers of out-born infants (almost 5% of the cases) as the study hospital has a busy obstetrics department. Second, the study was conducted in a single center, limiting the generalizability of the findings. Additionally, the study design was observational, introducing the possibility of confounding biases. Third, temperature measurements were obtained on admission, and changes in body temperature during the NICU stay were not accounted for, which could potentially impact the findings. Fourth we concentrated on the maternal and neonatal risk factors for the neonatal hypothermia but not the Knowle and attitude of the obstetrics and neonatal teams about hypothermia, also their utilization and knowledge about the available resources like the transport incubator. We noticed that these causes are a major contributor to the problem and will be our future research.

Up to our knowledge, this is the first study evaluated the incidence of neonatal hypothermia in Egypt, Previous study evaluated the effect of polyethylene cap or wrap to prevent the hypothermia in preterm infant and reported higher incidence of hypothermia in control groups [29], Large prospective multicenter designs studies are needed to evaluate the magnitude of the neonatal hypothermia in Egypt could serve as a valuable tool to initiate quality improvement projects for prevention of neonatal hypothermia and its related morbidities and mortality.

5. Conclusions

Neonatal hypothermia on NICU admission has a high incidence. It is associated with lower gestational age, multiple births, PROM, prolonged need for respiratory support, higher rates of pulmonary hemorrhage, sepsis, IVH, and NEC, longer duration of hospital admission, and mortality. Body temperature is an excellent predictor of mortality. These findings highlight the importance of early detection and man-

agement of hypothermia in neonates admitted to the NICU and the need for strategies to prevent and manage hypothermia in this vulnerable population.

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Conflict of interest

There is none to be declared.

Human research statement

This observational study involved human subjects and was conducted in compliance with the Declaration of Helsinki and the IOS Press Use of Experimental Subjects Policy. Approval was obtained from the local Institutional Review Board, Faculty of Medicine, Benha University (Approval number:Ms.35.9.2021). Informed consent was obtained from the parents or legal guardians of all participating neonates.

Other disclosures

None to be declared.

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