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**Admission Hypothermia and Neonatal Mortality: A cross sectional
study of prospectively collected data**

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Admission Hypothermia and Neonatal Mortality: A cross sectional study of prospectively collected data

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Approval sheet

This is to certify the thesis prepared by Dr. Kullehe Haddis entitled “Admission Hypothermia and Neonatal Mortality: A cross sectional study of prospectively collected data in a Tertiary Teaching Hospital in Addis Ababa, Ethiopia ” and submitted in partial fulfillment of requirements for completion of fellowship program in Neonatology complies with regulations of the university and meets the accepted standards with the respect to originality and quality.

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Table of Contents

Table of Contents.....	i
Acronym	ii
Abstract	iii
1. Introduction	1
2. Methodology	2
3. Operational Definitions	4
4. Results	6
5. Discussion	16
6. Conclusion.....	19
7. References	20
Annex	23

Acronym

NBW -	Normal birth weight
LBW -	Low Birth weight
VLBW -	Very Low Birth Weight
ELBW -	Extremely Low Birth Weight
SGA -	Small for gestational age
AGA -	Appropriate for gestational age
ENN -	Ethiopian Neonatal Network
VON -	Vermont Oxford Network

Abstract

Background

According to a March 2024 WHO report, 2.3 million deaths occurred in newborns less than 28 days globally in 2022. Sub-Saharan Africa had the highest neonatal mortality rate, of 27 per 1000 live births [1]. Hypothermia is known to increase the risk of both morbidity and mortality. Thus maintaining a normal body temperature is one of the very important steps for survival of the newborns. Despite the different mechanisms proposed to prevent hypothermia, it remains a global problem especially for low-income countries like Ethiopia.

Objective

The objective of the study was to determine the effect of admission hypothermia on neonatal mortality across 20 Ethiopian hospitals discharged from neonatal units from January 1-December 31, 2021.

Methodology

This study is a secondary analysis of prospectively collected data. A total of twenty hospitals participating in the Ethiopian Neonatal Network (ENN) in the Vermont Oxford Network (VON) Global Health Database were included. All newborns whose temperature was recorded in one hour of birth were included in the study. The admission hypothermia was assessed in association with gestational age, birth weight, the environmental temperature, level of neonatal intensive care unit where the neonatal care provided, season of the year the newborn was born, and whether the newborn was born in the weekdays or weekends. Associations were tested for mode of delivery, birth weight, place of delivery and whether the newborn was term or preterm in relation to mortality. Effect modification by discharge diagnosis was considered. Associations were calculated using relative risk (RR) with a 95% CI. Data analysis was done using SAS 9.4.

Results

A total of 12,363 newborns were included in the study. The overall rate of hypothermia was 51.6%. Predictors for hypothermia and mortality included being part of a multiple birth, low birth weight and lower gestational age. The season of the month, mode of delivery or hospital environmental temperature did not have any impact in predicting hypothermia or death.

In unadjusted analyses, the risk of death increased more than five times [RR 5.65 (95% CI: 4.31, 7.41)] when the admission temperature was less than 33.9°C, more than four times [RR 4.25 (95% CI: 3.30, 5.49)] when the temperature was between 34 - 34.9°C. In a multivariable analysis with other confounding factors controlled, the risk of death increased by two times for body temperatures less than 36.5°C. Admission temperature was not an effect modifier in the associations between perinatal asphyxia, respiratory distress, or meconium aspiration syndrome and mortality. However, admission temperature was an effect modifier in the association between any sepsis and mortality.

Conclusion

Admission hypothermia is high in Ethiopia and is associated with a twofold increased risk of death. Lower gestational ages, low birth weight infants, septic patients, newborns with congenital anomaly and multiple births were associated with increased risk of death. Measures to improve admission hypothermia through the use of intensive quality improvement projects should be undertaken to improve the situation in the country.

1. Introduction

According to a March 2024 World Health Organization (WHO) report, globally 2.3 million deaths occurred in newborns less than 28 days in 2022. [1] Sub-Saharan Africa had the highest neonatal mortality rate, of 27 per 1000 live births. [1] The majority of the newborns (75%) died in the first 1 week of life and one million of those died in the first 24 hours of life. [1]

Maintaining a normal body temperature is one of the very important steps for survival of newborns. [2] The WHO defined hypothermia as a core body temperature less than 36.5 degrees Celsius (C). The degree of hypothermia has been classified as mild (36.4-36° C), Moderate (32-35.9°C) and Severe (< 32°C) [2,3]. Although it is known that hypothermia increases the risk of both mortality and morbidity, a direct relation has not been identified. [2,4,7,8]

Hypothermia remains a global problem despite the different mechanisms proposed to prevent it. [1,2,4,] According to Karsten Lunze et al, the global prevalence of hypothermia in hospitals ranged between 32% to 85% and that of home delivery was between 11% to 92%, even in tropical environments. [2,5] In another study, the body temperature of newborns less than 36°C in Nepal was found to be 85% in newborns delivered in a hospital within the first 2 hrs of life. [6] Similarly, in some parts of Sub-Saharan countries, an incidence of 65-85% has been documented. [7] The prevalence of hypothermia in preterm infants in 5 specialized hospitals of Ethiopia was found to be 79.5%. [8] As the degree of hypothermia worsened, the severity of morbidity and mortality increased. [8] For every one degree Celsius decrease in body temperature less than 36°C of very low birth weight infants, mortality rates have been shown to increase by 28%. [4,8]

There are a number of studies done about hypothermia in Ethiopia but most are single center observation or a localized area of a population. There has not been research done on 20 centers, most of which are community hospitals from all corners of the country. We used data from the Ethiopian Neonatal Network (ENN) to assess the prevalence of hypothermia on admission to the neonatal unit and its associations with mortality to give more reliable and generalizable data

about our country. The hospitals included are 15 general/community hospitals and 5 specialized referral hospitals which provide level II and level III neonatal specialized or intensive care.

2. Methodology

A total of twenty hospitals in the Ethiopian Neonatal Network (ENN) were involved in the study. The ENN was established in 2018 in collaboration with Vermont Oxford Network (VON), Ethiopian Pediatric Society (EPS) and the Ethiopian Federal Ministry of Health. VON is a voluntary worldwide community of practice dedicated to improving the quality, safety, and value of newborn care through a coordinated program of data-driven quality improvement, education, and research. The goal of the ENN is to establish data driven quality improvement among member hospitals. The ENN constitutes 6 hospitals from Addis Ababa, three hospitals from Oromia (from western part of the country), two hospitals from Amhara region (Northern part of Ethiopia), three from Somali region (Southeast), 1 hospital each from Tigray (North) Benishangul Gumuz (Northwest), Diredawa (East), Gambella (Southwest), Central Ethiopia and Sidama (South) regions. The different hospitals are classified based on the level of care that they provide according to the Ethiopian Ministry of Health classification of levels of NICU care. There are 15 general/community hospitals and 5 specialized hospitals with 16 level II and 4 Level III NICUs.

The study is a secondary analysis of prospectively collected data from the ENN database for all infants discharged from a neonatal unit from January 1, 2021 to December 31, 2021 (Western calendar). Data were entered by the local staff using standardized definitions. The data tool was explained well to the data collectors and they were well versed with the tools used. The body temperatures were taken from the axilla using a digital thermometer. All infants whose temperature was recorded within the first hour of birth and whose outcomes were known were included in the study. The exclusion criteria included patients transferred to other hospitals and patients with no information about temperature at admission.

The admission hypothermia was assessed in association with the environmental temperature, level of neonatal care provided, season of the year the newborn was born, and the day the patient was born (weekday or weekend). Associations were also tested for mode of delivery, birth

weight, place of delivery and whether the newborn was term or preterm. The levels of the hospitals and NICUs were made based on the Ethiopian ministry of health classification system and the environmental temperatures were classified based on the average annual environmental temperature of the site where the hospitals are located in the country. Common discharge diagnosis recorded in the database were selected to assess effect modification between admission hypothermia and mortality.

Risk ratios (RR) and 95% confidence intervals (95% CI) were estimated in univariable and multivariable analysis using generalized estimating equation logistic regression models with a log link to control for clustering of infants within hospitals. Only variables with statistically significant associations in univariable analyses were entered into the multivariable analysis. We assessed whether admission temperature was an effect modifier with perinatal asphyxia, respiratory distress, late onset sepsis, or meconium aspiration syndrome, and mortality; a P-value of <0.05 indicated an interaction. All analyses were done using SAS 9.4.

3. Operational Definitions

Hypothermia - Axillary Body Temperature less than 36.5° C

Mild Hypothermia - Body temperature between 36.4°C - 36°C

Moderate Hypothermia - Between 32°C - 35.9°C

Severe Hypothermia - Less than 32°C

Hyperthermia - More than 37.5°C

Preterm - Newborns born earlier than 37 weeks' gestational age

Normal birth weight (NBW) - Weight between 2500 – 4000 grams

Low Birth weight (LBW) - Weight between 1500 - 2500 grams

Very Low Birth Weight (VLBW) - Weight between 1000- 1500 grams

Extremely Low Birth Weight (ELBW) - Weight less than 1000 grams

Inborn - Newborns delivered in the same hospital as the neonatal unit they were admitted to.

Outborn - Newborn delivered outside the hospital and transferred to admitting NICU.

Warm (hot) areas - Environmental temperature >25° C [28]

Cold areas - Environmental temperature <25° C [28]

Seasons of the year in Ethiopia [25,26]

- Dry season - January, February, March, April, May, September, October, November, December
- Wet season - June, July, August

Ethiopian Levels of Neonatal Care [27]

Level I : Well Newborn Nursery. Provide basic care for healthy infants.

Stabilize and provide care for infants born at 35 to 37 weeks' gestation provides care to all sick newborns (except for those requiring advanced care including transfusions, assisted ventilation or major surgery). Perform essential newborn care, Neonatal Resuscitation, Evaluate and provide postnatal care of healthy and sick newborn infants

Level II : Special care nursery. Provide care for moderately ill or premature infants.

Provide care to infants born at more than 32 weeks' gestation and weighing more than 1500 g who have physiologic immaturity such as apnea of prematurity, inability to maintain body temperature, or inability to take oral feedings; who are moderately ill with problems that are expected to resolve rapidly and are not anticipated to need sub specialty services on an urgent basis; or who are convalescing from intensive care.

Level III : Neonatal intensive care unit (NICU). Provide comprehensive care for critically ill or very premature infants.

Provide care to newborn infants with differing degrees of complexity and risk. All newborn infants with extreme prematurity or extremely low birth weight or who have severe and/or complex illness are in the highest risk group and have the most specialized needs. Contains a broad range of pediatric medical subspecialists and pediatric surgical specialists, highly skilled nursing and respiratory care staff, advanced respiratory support and physiologic monitoring equipment, laboratory and imaging facilities, parenteral nutrition (TPN), nutrition and pharmacy support with pediatric expertise, social services, including high dependency unit.

Hospitals with Environmental Temperature <25° C: Tikur Anbessa Specialized Hospital, St. Paul Hospital & Millennium Medical College, Zewditu Memorial Hospital, Gandhi Hospital , Tirunesh Beijing Hospital , Alert Hospital , Ambo Hospital, Nekemte Hospital, Debrebirhan Hospital, Gondar Hospital , Hawassa Hospital, NigistEleni Memorial Hospital, Arbaminch General Hospital, Ayder Comprehensive Specialized Hospital.[25,26]

Hospitals with Environmental Temperature >25° C: Gambella Hospital, Assossa Hospital, Karamara Hospital, Degehabour Hospital , Jijiga Hospital , DilChora Hospital.[25,26]

Level II Hospitals: Gandhi Hospital, Tirunesh Beijing Hospital , Alert Hospital, Ambo Hospital, Nekemte Hospital, Debrebirhan Hospital , Gondar Hospital, Hawassa Hospital, NigistEleni

Memorial Hospital , Assosa Hospital , Gambella Hospital , Karamara Hospital, Degehabour Hospital, Jijiga Hospital, Dil Chora Hospital, Arbaminch General Hospital[27]

Level III Hospitals: Tikur Anbessa Specialized Hospital, St. Paul Hospital & Millennium Medical College, Zewditu Memorial Hospital, Ayder Comprehensive Specialized Hospital.[27]

Ethical Approval and Informed Consent

Ethical clearance was obtained from the Pediatrics and Child Health Department's Research and Publications Committee of the School of Medicine, college of Health Sciences and Addis Ababa University and Vermont Oxford Network (VON) which intern has memorandum of understanding from each hospital in the system. Since this is a retrospective analysis, specific ethical clearance was not required from the mothers/parents/ and data will be analyzed anonymously.

4. Results

Socio-demographic Characteristics

From the total 12,363 infants included in the study, 3494/12363 (28.3%) of the infants were preterm (< 37 weeks), 4367/12360 (35.3%) of the infants had low birth weight (≤ 2500 grams), and 870/12363 (7%) of the infants had very low birth weight (≤ 1500 grams). More than half of the population (57.3%) of the infants were male and 7.9% of the deliveries were multiple births. Maternal age was 26-35 years for 6194/12359 (50.1%) of the cases.

Table 1. Maternal and Infant Characteristics		
Total=12,363 Infants	Cases	%
Maternal Age		
<18 years	65	0,5
18-25 years	5411	43,8
26-35 years	6194	50,1
>35 years	689	5,6
Gestational Age		
<30 weeks	431	3,5
31-33 weeks	983	8
34-36 weeks	2080	16,8
37-39 weeks	6204	50,2
>=40 weeks	2665	21,6
Birth Weight		
<1500 grams	870	7,0
1500-1999 grams	1712	13,9
2000-2499 grams	1785	14,4
2500-2999 grams	2768	22,4
3000-3499 grams	3142	25,4
>=3500 grams	2080	16,8
Male Sex	7081	57,3
Multiple Birth	980	7,9
Congenital Anomaly	861	7,0

Degree of Admission Temperature

The most frequent admission body temperature was normal body temperature (36.5-37.5°C) at 40.7% followed by body temperatures of 36.0-36.4°C (21.2%) and 35.0-35.9°C (20.6%) while 34.0-34.9°C and <33.9°C admission body temperatures were recorded in 7.2% and 2.6% of the infants, respectively. Hyperthermia (Temperature>37.5°C) was recorded in 7.7% of the infants (Figure 1).

Figure 1 - Bar graph showing degree of admission temperature in the twenty hospitals, 2021

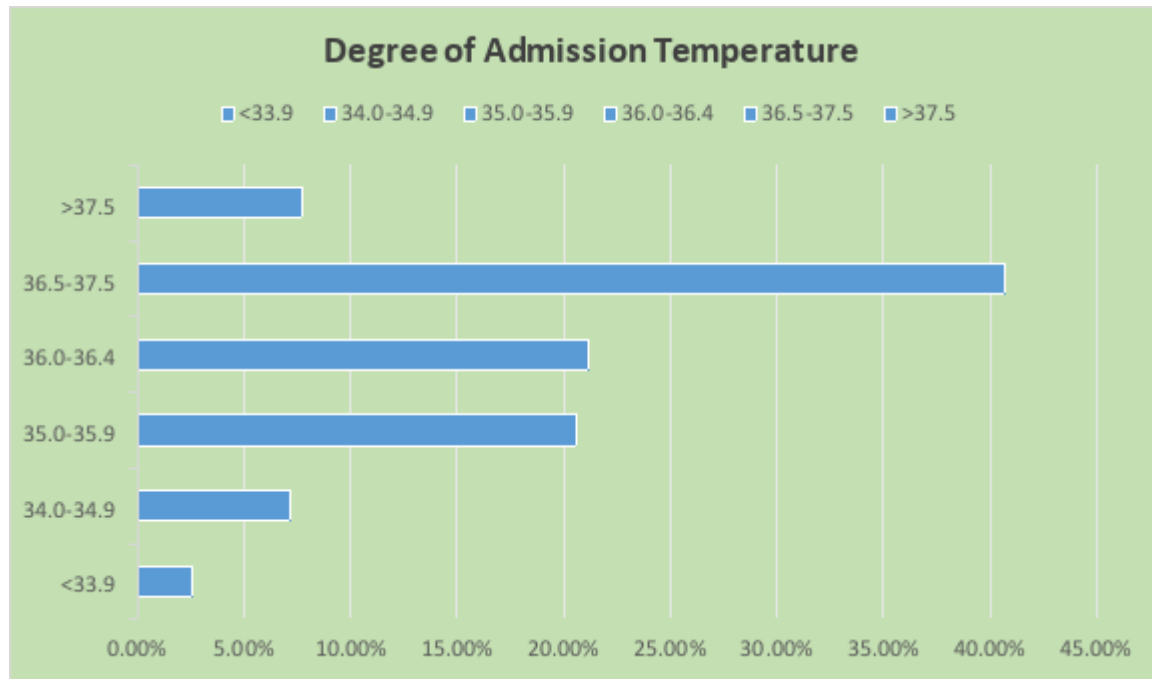


Table 2 depicts risk factors for hypothermia and admission temperature. Predictors of hypothermia included being inborn (81.5% hypothermic versus 76.2% normothermic) as well as being part of a multiple birth (10.7% vs 5.5%). Infants born before 37 weeks (39.1% vs 18.3%) or born less than 2500 grams (46.2% vs 25.4%) were more likely to be hypothermic. Additionally, infants born at level 3 units were more likely to be hypothermic (40.5% vs. 27.4%).

The hypothermia rates were similar across the dry and wet seasons. In addition, there were no real differences by type of delivery, presence of congenital anomaly, the hospital's environmental temperature, or whether the infant was born during the week or on the weekend.

Table 2. Risk factors for hypothermia by admission temperature

	Temperature 36.5-37.5 (N=5029)		Temperature < 36.5 (N=6385)	
	No.	%	No.	%
Mode of Delivery				
Vaginal	3574	71.1	4399	69.0
Cesarean	1454	28.9	1977	31.0
Place of Delivery				
Outborn	1195	23.8	1182	18.5
Inborn	3829	76.2	5200	81.5
Gestation (weeks)				
<30	73	1.5	346	5.4
31-33	243	4.8	726	11.4
34-36	601	12	1425	22.3
>=37	4112	81.8	3888	60.9
Birth Weight (grams)				
<1500	179	3.6	682	10.7
1500-1999	498	9.9	1171	18.4
2000-2499	596	11.9	1089	17.1
>=2500	3756	74.7	3438	53.9
Type of Birth				
Multiple	277	5.5	685	10.7
Singleton	4748	94.5	5695	89.3
Congenital Anomaly				
Yes	370	7.4	389	6.1

No	4651	92.6	5984	93.9
Environmental				
Temperature				
<25	4337	86.2	4959	77.7
>25	692	13.8	1426	22.3
Level of Unit				
3	1376	27.4	2584	40.5
2	3653	72.6	3801	59.5
Month of				
Birth				
Wet Season	1256	25	1430	22.4
Dry Season	3773	75	4955	77.6
Date of Birth				
Weekday	3696	73.5	4683	73.3
Weekend	1333	26.5	1702	26.7

Independent risk factors for mortality are depicted in table 3. The risk of death increased more than five times [RR 5.65 (95% CI: 4.31, 7.41)] when the admission temperature was less than 33.9°C, more than four times [RR 4.25 (95% CI: 3.30, 5.49)] when the temperature was between 34 - 34.9°C, close to three fold when the temperature was between 35-35.9°C [RR 2.83 (95% CI: 2.16, 3.71)] and two times when the temperature was between 36 - 36.4°C [RR 1.83 (95% CI: 1.43, 2.33)] as compared to those with normal temperature. There was no increased risk associated with hyperthermia. Other predictors of mortality included lower gestational age, lower birth weight, multiple birth, and presence of a congenital anomaly. Inborn infants had reduced risk of mortality. Level of NICU, environmental temperature, season of the year or whether the newborn was born on a weekday or weekend were not significantly associated with mortality.

Table 3. Independent risk factors for mortality

	Survived (N=11091)		Did (N=1272)	Not	Survive
	No.	%	No.	%	Risk Ratio (95% CI)
Mode of Delivery					
Cesarean	3328	30	335	26.3	0.84 (0.71, 1.01)
Vaginal	7753	70	937	73.7	reference
Place of Delivery					
Outborn	2360	21.3	373	29.3	1.46 (1.16, 1.84)
Inborn	8721	78.7	899	70.7	reference
Gestation					
<30 w	183	1.6	248	19.5	9.87 (7.99, 12.20)
31-33 w	702	6.3	281	22.1	4.90 (3.77, 6.37)
34-36 w	1854	16.7	226	17.8	1.86 (1.45, 2.39)
>=37 w	8352	75.3	517	40.6	reference
Birth Weight					
<1500 g	443	4	427	33.6	9.57 (7.92, 11.55)
1500-1999 g	1443	13	269	21.2	3.06 (2.37, 3.95)
2000-2499 g	1620	14.6	165	13	1.80 (1.46, 2.23)
>=2500 g	7580	68.4	410	32.3	reference
Type of Birth					
Multiple	808	7.3	172	13.6	1.82 (1.45, 2.30)
Singleton	10279	92.7	1095	86.4	reference
Congenital Anomaly					
Yes	674	6.1	187	14.7	2.30 (1.60, 3.30)
No	10398	93.9	1084	85.3	reference
Environmental					
Temperature	9014	81.3	1027	80.7	0.97 (0.59, 1.61)

<25					
>25	2077	18.7	245	19.3	reference
Level of Unit					
3	3758	33.9	457	35.9	1.08 (0.72, 1.64)
2	7333	66.1	815	64.1	reference
Month of Birth					
Wet Season	2585	23.3	280	22	0.94 (0.81, 1.09)
Dry Season	8506	76.7	992	78	reference
Date of Birth					
Weekend	2976	26.8	333	26.2	1.03 (0.91, 1.17)
Weekday	8115	73.2	939	73.8	reference
Admission Temperature					
<33.9	225	2	97	7.6	5.65 (4.31, 7.41)
34 to 34.9	689	6.2	202	15.9	4.25 (3.30, 5.49)
35 to 35.9	2167	19.5	385	30.3	2.83 (2.16, 3.71)
36 to 36.4	2365	21.3	255	2	1.83 (1.43, 2.33)
36.5 to 37.5	4761	42.9	268	21.1	reference
> 37.5	884	8	65	5.1	1.29 (0.91, 1.81)

In the multivariable analysis, with other confounding factors controlled (place of birth, birth weight, mode of delivery, gestational age and type of birth), the risk of death increased by more than twice [RR 2.34 (95% CI: 1.60, 3.43)] when the infant admission temperature was less than 33.9°C or when between 35-35.9°C [RR 2.00 (95% CI: 1.46,2.75)], 2.4 times [RR 2.44 (95% CI: 1.85, 3.20)] when the temperature was between 34 - 34.9°C , and 1.6 times [RR 1.60 (95% CI: 1.24, 2.06)] when the temperature was between 36-36.4°C (table 4). Birth weight and presence of a congenital anomaly also increased risk of mortality, while being inborn decreased risk (Table 4).

Table 4. Multivariable analysis of risk factors for mortality

	<i>Risk Ratio (95% CI)</i>
Mode of Delivery	
Vaginal	1.18 (0.97, 1.43)
Cesarean	reference
Place of Delivery	
Outborn	1.35 (1.11, 1.64)
Inborn	reference
Birth Weight	
<1500 g	8.45 (6.99, 10.21)
1500-1999 g	2.88 (2.29, 3.61)
2000-2499 g	1.66 (1.35, 2.04)
>=2500 g	reference
Type of Birth	
Multiple	0.90 (0.73, 1.11)
Singleton	reference
Congenital Anomaly	
Congenital Anomaly	
Yes	2.69 (2.02, 3.59)
No	reference
Admission Temperature	
<33.9	2.34 (1.60, 3.43)
34 to 34.9	2.44 (1.85, 3.20)
35 to 35.9	2.00 (1.46, 2.75)
36 to 36.4	1.60 (1.24, 2.06)
36.5 to 37.5	reference
>37.5	1.41 (0.99, 2.00)

We investigated whether admission temperature was an effect modifier in the association between specific discharge diagnoses and mortality (Table 5) by assessing the interaction between admission temperature and the diagnosis. Admission temperature was not an effect modifier in the associations between perinatal asphyxia, respiratory distress, or meconium aspiration syndrome and mortality. However, admission temperature was an effect modifier in the association between any sepsis and mortality. Infants who were hypothermic on admission and developed sepsis had higher risk of mortality [RR 1.94 (95% CI: 1.42, 2.67)] than infants who were normothermic [RR 1.47 (95% CI: 0.95, 2.27)].

Table 5. Effect modification of admission temperature on risk of mortality for specific discharge diagnoses

Temperature 36.5-37.5 (N=5029)					
	Survived (N=4761)		Did Not Survive (N=268)		Risk Ratio (95% CI)
	No.	%	No.	%	
Perinatal Asphyxia - Yes	176	3.7	7	2.6	0.71 (0.25, 2.05)
Perinatal Asphyxia - No	4579	96.3	260	97.4	reference
Respiratory Distress - Yes	1909	40.1	186	69.4	3.18 (2.14, 4.72)
Respiratory Distress - No	2851	59.9	82	30.6	reference
Sepsis - Yes	3452	72.6	214	79.9	1.47 (0.95, 2.27)
Sepsis - No	1306	27.4	54	20.1	reference
Meconium Aspiration Syndrome - Yes	750	15.8	49	18.3	1.18 (0.79, 1.77)
Meconium Aspiration Syndrome - No	4008	84.2	219	81.7	reference

Temperature < 36.5 (N=6385)

	Survived (N=5446)		Did Not Survive (N=939)		Risk Ratio (95% CI)
	No.	%	No.	%	
Perinatal Asphyxia - Yes	193	3.5	28	3	0.86 (0.58, 1.28)
Perinatal Asphyxia - No	5247	96.5	910	97	reference
Respiratory Distress - Yes	2839	52.1	732	78	2.79 (2.05, 3.78)
Respiratory Distress - No	2606	47.9	207	22	reference
Sepsis - Yes	4088	75.1	811	86.6	1.94 (1.42, 2.67)
Sepsis - No	1354	24.9	126	13.4	reference
Meconium Aspiration Syndrome - Yes	965	17.7	159	17	0.95 (0.65, 1.41)
Meconium Aspiration Syndrome - No	4473	82.3	778	83	reference

5. Discussion

This study found that the rate of admission hypothermia was 51.6% in this sample of infants admitted to a neonatal unit in Ethiopia, and neonatal mortality increased by two times for temperature less than 36.5°C. A number of studies have been done on hypothermia in different regions of the country at different times with a limited sample size. This study used data from the ENN and included 20 hospitals distributed all over the country with different geographic and cultural structures. As far as we know, there has not been research done with a bigger sample size and considering the different levels of NICU care in the country. We believe the large sample size used with representation from all corners of the country gives more generalizable information about the situation of admission hypothermia in Ethiopia.

The rate of hypothermia in our study is close to a systemic review and meta-analysis done by Biruk et al in 2020 where Ethiopia had a prevalence of 55%[9] and similar to a Ugandan study done in 2021 where the prevalence of hypothermia is 51%. [10] Similarly our result lies in the range of the percentages mentioned in a systematic review done by Lunze et al where the prevalence of hypothermia in low and middle income countries was determined to be ranging between 32-85%. [5]

We confirmed that being part of multiple births, low birth weight, having a lower gestational age at birth were associated with lower admission temperatures which is consistent with a number of studies. [4,8,10,11,12,13].

Inborn infants were more likely to be hypothermic than outborn infants in our study. This result is different from a study done in Nigeria [13] where the rate of hypothermia was more in the outborn (64.4% vs 58.3%) and in a previous study in Ethiopia by Demtse et al [8] where the outborns had a higher percentage of hypothermia even though it was not statistically significant as compared to inborns. However, our finding has a similar higher prevalence of hypothermia in inborn infants in a study done in Ghana [12] although the rate is lower than our value (68.9%). The higher percentage in inborn infants might be due to the poor follow up of the warm chain, lack of knowledge, lack of warm intra-facility transport and sub optimal essential newborn care

practices done in the hospitals, in addition to lack of adequate equipment for maintaining normothermia. [3,4,7,11,14,] The hypothermia rate in level III hospitals was also higher although there was no significant association between hospital level and mortality as compared to Level II centers. The higher rate of hypothermic babies in level III hospitals might be due to the fact that the level III hospitals are referral centers which give care for the most sick, preterm, and low birth weight babies who also have an increased risk to become hypothermic. [4,8]

In our twenty hospitals, there was no increased risk of being hypothermic when born in either different seasons of the year or different environmental temperatures. Our result is different from studies done by Kumar et al where a review was done in neonatal hypothermia in low resource settings [6] and another study in Ghana [11], where the rate of hypothermia was low during dry seasons as compared to wet seasons. However, our finding is similar to other studies done which state that hypothermia is still a problem in tropical climates. [3,5,7,16,17] In addition, our study did not show any difference in hypothermia rate between vaginal or cesarean section deliveries unlike a research done in Indonesia where newborns born vaginally were having a 1.5 times lower risk of hypothermia as compared to cesarean section deliveries [16] and in Ghana where the newborns born vaginally had 40% less risk of developing hypothermia. [11] However, our result is similar to a study in high and middle income countries where the hypothermia rate was not affected by the mode of delivery. [4] A similar hypothermic rate might be due to a low delivery room temperature and cold operation theatre as well as poor practice of skin to skin in both of the delivery situations which will affect thermoregulation in the baby. [4,7,17,18]

When we take admission hypothermia as an independent risk factor, we found that as the degree of admission hypothermia decreased by 1°C, the mortality rate increased by two to five folds as compared to those with a normal temperature. This result is consistent with a study done in Brazil where admission temperature in a range of 32.0°C-35.9°C was associated with a threefold increase in neonatal death (AOR=3.5, 95% CI: 3.2- 3.8) [19]. Our finding also goes with the research done by Mullany et al [21] where the risk of death from hypothermia varied by 2-3 times depending on the degree of hypothermia. Similarly, in multivariate analysis, with the different degrees of hypothermia and other factors controlled, the risk of death increased by two times for every temperature group which is similar to other studies. In addition, we observed that

the classification of moderate hypothermia by WHO is wide and is difficult to predict which temperature range is associated with severity of outcomes and mortality. Sub classifying the moderate hypothermia group might help in predicting severity as suggested by previous authors. [8,21]

Newborns with a birth weight less than 1500 grams had ten times [RR 9.57 (95% CI: 7.92, 11.55)] increased risk of death as compared to newborns with a birth weight greater than 2500 grams in unadjusted analyses. This result was comparable to a population-based cohort study done in the USA which showed the risk of mortality increased by 10 times in the very low birth weight group compared to a higher birth weight. [8] In addition, in the multivariate analysis, we found that patients with birth weights less than 2500 grams had a two to eight times increased risk of mortality compared to those born with weight greater than 2500 grams. Our result is comparable to research done by Demtse et al where the risk of neonatal death increased 2-4 times in newborns with birth weight less than 2000 grams. [4,8] This finding confirms an inverse response relation between birth weight and mortality. [8,21]

We also confirmed that patients with a congenital malformation or being a part of multiple birth were associated with increased risk of mortality. (4,8,21) Being inborn was associated with decreased risk of mortality as compared to outborn newborns which might be explained by a relatively rapid management of any complication or morbidity as the patient is being managed in the same hospital.

In a multivariable analysis, admission hypothermia increased the risk of death by two fold with all other factors controlled. Our result is lower than the studies done in Guinea-Bissau and Iran which found that the risk of death increased by fivefold and threefold for neonatal hypothermia respectively. [22,23] The difference might be due to the classification of the hypothermia in the Guinea study at 34.5°C which is a much lower body temperature. [22]

In our study, we found that admission temperature was not an effect modifier in the associations between mortality and perinatal asphyxia, respiratory distress syndrome, or meconium aspiration syndrome. However, admission temperature was an effect modifier in the association between

sepsis and death. Infants who were hypothermic at admission and developed sepsis had a significantly increased risk of mortality; infants who were normothermic at admission and developed sepsis did not. This might be due to the fact that hypothermia influences the ability of the body to fight infections in its effect on compromising activity of white blood cells. Hypothermia also reduces the body's ability to produce and distribute surfactant and resultant pulmonary vasoconstriction will easily lead to being susceptible to infections and respiratory distress together with other multi system effects. [2,4,7,24]

Strengths of the Study

This study includes over 12,000 infants at 20 hospitals with varying levels of neonatal care. The data collectors used standardized definitions, and during this study period, data collection was supplemented with paid collectors, increasing the opportunities for quality data collection.

Limitations of the Study

The study only involved patients who were admitted to a neonatal unit in one of the 20 hospitals, were recorded in the data base, and had their temperature measured within 1 hour of birth. This study did not include all hospitals in Ethiopia, and did not include health centers or home births.

6. Conclusion

We found that admission hypothermia is high in our country and mortality is increased at least two times in newborns who had admission hypothermia after adjusting for confounding factors. Inborn babies and infants cared at level III NICU had a higher rate of hypothermia. We did not find any difference in mortality in patients cared at different levels of NICU, different environmental temperatures or whether newborns were inborn or outborn. To achieve a reduction in newborn mortality by 2030, quality improvement projects should be conducted in all facilities to improve the quality of care that is provided.

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Annex

VERMONT OXFORD NETWORK CORE DATASET
DEVELOPED IN PARTNERSHIP WITH AFRICAN NEONATAL ASSOCIATION

Infant Name _____ **Medical Record Number** _____

_____ **VON ID** _____

1a. Date of Birth: ____/____/____ (DD/MM/YYYY)

1b. Time of Birth ____:____ (HH:MM 24hr clock) ☐ Unk

2. Date of Admission: ____/____/____ (DD/MM/YYYY)

3. Date of Discharge or Death: ____/____/____ (DD/MM/YYYY)

4. Previously Discharged Home: ☐ Yes ☐ No

5. Place of Delivery: ☐ Inborn at Same Facility ☐ Other Hospital ☐ Health Center / Clinic ☐
Home ☐ In Transit ☐ Unk

6. Mode of Delivery: ☐ Vaginal ☐ Instrument-assisted vaginal ☐ Cesarean section ☐ Unk

7. Antenatal Care: ☐ None ☐ 1 to 3 Visits ☐ ≥ 4 Visits ☐ Unk

8. Maternal Age: ____ years ☐ Unk

9. Maternal Obstetric History: Gravida ____ ☐ Unk

Total Live Births ____ ☐ Unk

Total Living Children ____ ☐ Unk

10a. Maternal HIV status: ☐ Positive ☐ Negative ☐ Unk

10b If maternal HIV status is positive, did mother receive anti-retroviral therapy?

☐ Yes ☐ No ☐ Unk

10c. If maternal HIV status is positive, did infant receive prophylaxis for HIV?

☐ Yes ☐ No ☐ Unk

11. Receipt of Any Antenatal Corticosteroids: ☐ Yes ☐ No ☐ Unk

12. Gestational Age: ____ weeks ____ days ☐ Unk

13. Gestational Age Determined by Early Ultrasound: ☐ Yes ☐ No ☐ Not Applicable -
dates based on assisted reproductive technology ☐ Unk

14. Birth Weight: ____ grams ☐ Unk

15. Sex: ☐ Male ☐ Female ☐ Unk

16. Multiple Gestation: ☐ Yes ☐ No ☐ Unk

17. Delivery Room Interventions:

a) Delayed Cord Clamping

☐ Yes ☐ No ☐ Unk

d) Intubation

☐ Yes ☐ No ☐ Unk

b) Face Mask Ventilation

☐ Yes ☐ No ☐ Unk

e) Chest Compressions

☐ Yes ☐ No ☐ Unk

c) CPAP

☐ Yes ☐ No ☐ Unk

f) Epinephrine

☐ Yes ☐ No ☐ Unk

18. Apgar Score:

1 minute: ____ ☐ Unk

5 minutes: ____ ☐ Unk

19. Admission Assessment:

a) Temperature Within 1 hour

☐ Yes ☐ No ☐ Unk

b) *If yes*, list temperature

_____ Celsius ☐ Unk

c) Pulse Oximetry Recorded

☐ Yes ☐ No ☐ Unk

d) *If yes*, list saturation

_____ % ☐ Unk

e) Was admission assessment recorded above when infant was on oxygen/respiratory support? ☐

Yes ☐ No ☐ Unk

f) Objective Respiratory Assessment ☐ Yes ☐ No ☐ Unk

g) *If yes*, list assessment

☐ Downes ☐ Silverman-Andersen ☐ Other ☐ Unk

h) *If Downes or Silverman-Andersen*, list score (0-10) _____ ☐ Unk

20. Primary Reason for Admission (check only one):

☐ Prematurity/LBW ☐ Birth Asphyxia ☐ Suspected Infection ☐ Congenital Anomaly ☐

Jaundice ☐ Tetanus ☐ Suspected Need for Surgery

☐ Respiratory Distress ☐ Convulsions ☐ Hypothermia ☐ Pallor/Anemia ☐ Feeding Difficulty

☐ Risk for Hypoglycemia ☐ Birth Injury ☐ Other ☐ Unk

21. Interventions Received in the Neonatal Unit (answer all questions a through r):

a) Immediate Kangaroo Care (KMC) ☐ Yes ☐ No ☐ Unk

j) Antibiotics

☐ Yes ☐ No ☐ Unk

b) KMC Initiated After 2hrs

☐ Yes ☐ No ☐ Unk

k) Phototherapy

☐ Yes ☐ No ☐ Unk

c) Oxygen

☐ Yes ☐ No ☐ Unk

l) Blood Transfusion

☐ Yes ☐ No ☐ Unk

d) CPAP

☐ Yes ☐ No ☐ Unk

m) Exchange Transfusion

☐ Yes ☐ No ☐ Unk

e) Mechanical Ventilation

☐ Yes ☐ No ☐ Unk

n) Anticonvulsant Medication

☐ Yes ☐ No ☐ Unk

f) Methylxanthine Medication

☐ Yes ☐ No ☐ Unk

o) Active therapeutic Hypothermia ☐ Yes ☐ No ☐ Unk

g) Surfactant

☐ Yes ☐ No ☐ Unk

p) Surgery

☐ Yes ☐ No ☐ Unk

h) ROP examination

☐ Yes ☐ No ☐ Unk

q) Cranial Ultrasound

☐ Yes ☐ No ☐ Unk

i) *If yes*, Worst Stage of ROP (0-5):_____ ☐ Unk

r) *If yes*, Worst Grade of IVH (0-4):_____ ☐ Unk

22. Final Diagnoses (answer all questions a through s)

a) HIE

☐ Yes ☐ No ☐ Unk

k) Hypoglycemia

☐ Yes ☐ No ☐ Unk

b) Meconium Aspiration

☐ Yes ☐ No ☐ Unk

l) Hyperbilirubinemia

☐ Yes ☐ No ☐ Unk

c) Birth Injury

☐ Yes ☐ No ☐ Unk

m) Anemia

☐ Yes ☐ No ☐ Unk

d) Transient Tachypnea of Newborn ☐ Yes ☐ No ☐ Unk

n) Congenital Anomaly

☐ Yes ☐ No ☐ Unk

e) Pneumonia

☐ Yes ☐ No ☐ Unk

o) Congenital Infection

☐ Yes ☐ No ☐ Unk

f) Seizures/Convulsions

☐ Yes ☐ No ☐ Unk p) Early-onset Sepsis

☐ Yes ☐ No ☐ Unk

g) RDS

☐ Yes ☐ No ☐ Unk q) *If yes, Culture Confirmed* ☐ Yes ☐ No ☐ Unk

h) NEC

☐ Yes ☐ No ☐ Unk

r) Late-onset Sepsis

☐ Yes ☐ No ☐ Unk

i) Respiratory Support on Day 28

☐ Yes ☐ No ☐ Unk

s) *If yes, Culture Confirmed* ☐ Yes ☐ No ☐ Unk

j) Respiratory Support at 36 Weeks: ☐ None ☐ Nasal Cannula ≤ 2 L/min ☐ Nasal Cannula > 2 L/min or CPAP ☐ Mechanical Ventilation ☐ Unk

23. Discharge: ☐ Discharged Home Alive ☐ Absconded/Left Against Medical Advice ☐ Died in hospital ☐ Referred to Another Facility ☐ Unk

24. Discharge Weight: _____ grams ☐ Unk

25. If Discharged Alive or Referred, Feeding at Discharge: ☐ Human Milk Only ☐ Formula Only ☐ Combination ☐ None ☐ Unk

26. If Died, Primary Cause of Death (including presumed clinical diagnoses) (check only one):

Prematurity: ☐ RDS ☐ NEC ☐ IVH ☐ BPD ☐ Other _____

Infection: ☐ Probable Sepsis ☐ Culture-positive Sepsis ☐ Culture-positive Meningitis ☐ Pneumonia ☐ Tetanus ☐ Other _____

Intrapartum-related: ☐ Hypoxic Ischemic Encephalopathy ☐ Meconium Aspiration ☐ Birth Injury ☐ Other _____

Congenital Anomaly: ☐ Cardiac ☐ Chromosomal ☐ Neurological ☐ Abdominal/Pelvic ☐ Respiratory/Airway ☐ Other _____

Hyperbilirubinemia: ☐ Pathologic jaundice / Bilirubin-induced Neurologic dysfunction

☐ **Other Cause (Not Listed)** _____

27. If Died, Time of Death: ____:____ (HH:MM 24hr clock) ☐ Unk