

Disclaimer/Publisher's Note: The statements, opinions, and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions, or products referred to in the content.

Risk Factors for Neonatal Hypothermia at Arba Minch General Hospital, Ethiopia

Tegenu Tento¹, Tilahun Asena^{*2}, Meseret Alemayehu³ and Asmare Wube⁴

¹Department of Statistics, College of Natural Sciences, Jinka University, Ethiopia

²Department of Statistics, College of Natural Sciences, Arba Minch University, Ethiopia

³Pawe General Hospital, Department of Pediatrics, Pawe, Ethiopia

⁴Ethiopian Public Health Institute, Addis Ababa, Ethiopia

*¹Corresponding Author

Email: feredetilahun14@gmail.com

Abstract

Background: The first few minutes after birth are the most dangerous for the survival of an infant. Babies in neonatal intensive care units are either under heated or overheated, and hypothermic infants remain hypothermic or develop a fever. As a result, special attention must be paid to monitoring and maintaining the time of recovery from hypothermia states. Despite numerous studies, only a few have examined the transition from neonatal hypothermia and associated risk factors in depth. A multi-state model will be used in the current study to assess risk factors for newborns transitioning from hypothermic states at Arba Minch General Hospital in Ethiopia.

Method: A retrospective observational study was conducted to track axillary temperatures taken at the time of neonatal intensive care unit admission, which were then tracked every 30 minutes until the newborn's temperature stabilized. All hypothermic neonates admitted to the neonatal intensive care unit between January 2018 and December 2020 was included in the study. Temperature data were available at birth and within the first three hours of admission for 391 eligible hypothermic neonates. The effect of factors on the transition rate in different states of hypothermia was estimated using a multi-state Markov model.

Result: The likelihood of progressing from mild to severe hypothermia was 5%, while the likelihood of progressing to normal was 34%. The average time spent in a severe hypothermia state was 48, 35, and 24 minutes for three different levels of birth weight, and 53, 41, and 31 minutes for low, moderate, and normal Apgar scores, respectively. Furthermore, the mean

sojourn time in a severe hypothermia state was 48, 39, and 31 minutes for three different levels of high, normal, and low pulse rate, respectively.

Conclusion: Very low birth weight, low Apgar, and high pulse rate had the strongest association with hypothermia and took the longest to improve/recover for hypothermic survivors within the first three hours of life. As a result, there is an urgent need to train all levels of staff dealing with the maintenance of neonatal hypothermia recovery time.

Keywords: Mean sojourn time, Multi-state Markov model, Transition rate

1. Background

Neonatal hypothermia is defined as a core body temperature of less than 36.5°C. Because it is the transitional period from intrauterine to extra uterine life, the first few minutes after birth are the most dangerous for infant survival [1]. Sustained body temperature decrease increases the metabolic demands of the neonate and has been linked to sepsis, asphyxia, respiratory distress syndrome, and mortality [2]. As a result, caregivers must work hard to prevent neonatal hypothermia in the first few minutes after birth.

According to WHO, when a baby's heat loss exceeds his or her ability to produce heat, the baby's body temperature falls below the normal range (36.5°C - 37.5°C). The newborns are suffering from mild hypothermia, with temperatures ranging from 36.0°C to 36.4°C, which should be cause for concern. A body temperature of 32.0°C to 35.9°C is considered moderate hypothermia. A newborn with a temperature of less than 32.0°C is considered to be suffering from severe hypothermia and should be treated as soon as possible [1]. Infant rewarming after birth should be optimized and time allotted for it to reduce the presence of hypothermia after birth even before undergoing procedures at the neonatal intensive care unit [3].

Thermal care is essential for reducing newborn morbidity and mortality. The monitoring system, however, is insufficient, and sensors occasionally detach or are not observed by health professionals, babies in neonatal intensive care units are under heated or overheated, and infants with hypothermia at birth and admission remain hypothermic or develop fever [4]. Neonatal hypothermia, regardless of climate, is a major cause of neonatal death and health impairment [5].

Because of their high surface area per unit of body weight, newborns are unable to fully maintain their body temperature. A neonate's skin temperature can drop at a rate of 0.1°C to 0.3°C per minute if no action is taken immediately after birth [6]. As a result, special precautions must be taken in neonatal intensive care units to monitor and maintain newborns' time of recovery from hypothermia.

The prevalence of hypothermia at the hospital ranged from 32% to 85%, with rates varying even in tropical environments [7]. Approximately 81,000 babies die in Ethiopia during their first four weeks of life. This accounts for 42% of all deaths among children under the age of five. Ethiopia had a prevalence of postnatal hypothermia of 69.8% [8]. Infants with birth weights ranging from 1000 to 1499 grams and mild hypothermia (36.0°C-36.5°C) died at a rate of 40.8%, while those with temperatures below 34.0°C died at a rate of 56.8% [2]. Risk factors are inextricably linked to newborn health, and illness has a significant impact on neonate health and survival [10].

Several studies have been conducted to determine the prevalence and causes of hypothermia. However, few have thoroughly addressed the transition from a hypothermic state and the risk factors that accompany it. Iranian researchers discovered a link between some hypothermia risk factors, such as birth weight and Apgar score, but no link between environmental temperature and hypothermia [11]. The other study looked into whether keeping newborns in a suitable thermal environment accelerated the transition from hypothermia to normalcy [12].

Despite this, the study took temperature measurements in the first two hours, did not take into account neonatal observation transitions to the severe hypothermia state in the first three hours, and included some other risk factors such as pulse rate, respiratory rate, and oxygen saturation. Concerns about the scarcity of long-term studies on the transition from hypothermia prompted the researchers to look into the subject. A patient's experience in a survival study can be thought of as a two-state process with one possible transition from a 'live' to a 'dead' state [9]. In this study, however, the "hypothermia" state was divided into two transient states, each of which corresponded to a different stage of the illness. When a newborn is in one of a set of discrete states at any given time, multi-state models can be used to model state transitions. It should be noted that the majority of research on neonatal hypothermia transition has concentrated on risk factors. The ability to quantify disease dynamics, such as the time it takes to reach a specific

state or the likelihood of movement, may lead to more effective disease prevention, management, and treatment. We wanted to look at a shorter time span with observed covariates. As a result, the goal of this study was to bridge that gap by analyzing data from hypothermic neonates at Arba Minch General Hospital, as well as to identify other risk factors associated with the rate of transition between different states of neonatal hypothermia.

2. Methods

2.1. The data

Retrospective data were obtained from Arba Minch General Hospital for the period from January 2018 to December 2020. The longitudinal measurement data on the record of neonate patient care follow-up cards were used in this study at regular time intervals. The standardized clinical recommendations for maintaining an infant's normal body temperature, which is one of the fundamental components of neonatal care, are to take temperature measurements every 30 minutes [1].

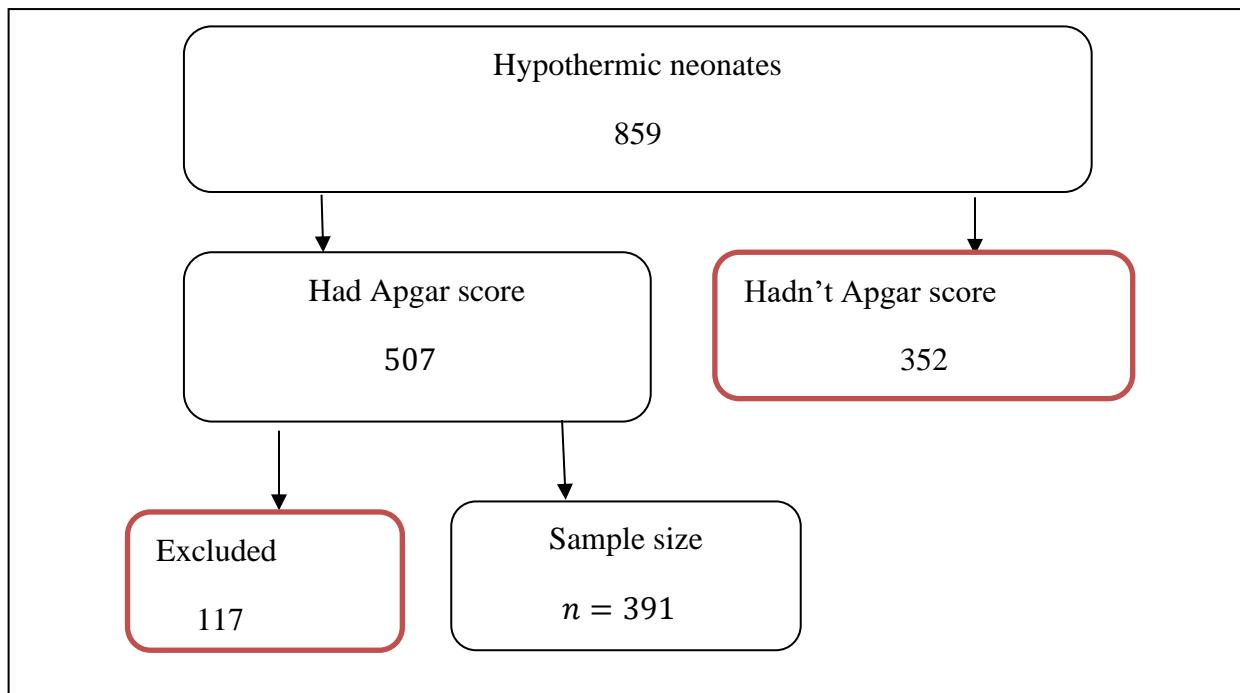
Study Design

This retrospective study examined newborns with up to seven surveillance scans in critically ill babies at the neonatal intensive care unit. Before data collection began, the institutional review board approved the study protocol. Data was extracted from the cards of hypothermic neonates by identifying the neonates' cards using their respective Medical Record Numbers from the medical center, and the data extraction was completed in the card room per the researcher's agreement. Following data extraction, data entry, editing, coding, and organization were completed. R software version 4.1.1 was used to conduct descriptive statistics. MSM (Version 1.6.8) was used in R to perform inferential statistics.

Sampling Design

The study protocol was approved by the institutional review board before data collection began. Data was extracted from hypothermic neonates' cards by identifying the neonates' cards using their respective Medical Record Numbers from the medical center, and the extraction was completed in the card room per the researcher's agreement. Data extraction was followed by data

entry, editing, coding, and organization. To conduct descriptive statistics, R software version 4.1.1 was used. Figure 1 shows the conceptual framework of sampling procedure.



[Figure 1](#) the conceptual framework of sampling procedure

Inclusion and exclusion criteria

The newborn babies diagnosed with hypothermia at birth, observed at a minimum of three different time points, had an Apgar score recorded, and inborn admitted to NICU on the same day were included but outborn babies, newborns babies who remain hypothermic for more than three hours and who died without gaining temperature within three hours were excluded. An exit criterion was the infant getting to a normal state.

Variables in the Study

Hypothermia severity was classified as severe (32.0°C), moderate ($32.0\text{-}35.9^{\circ}\text{C}$), mild ($36.0\text{-}36.4^{\circ}\text{C}$), and normal ($36.5\text{-}37.5^{\circ}\text{C}$) [1]. In this study, the first two groups were combined and classified as severe hypothermia (state I), mild hypothermia (state II), and normal body temperature (state III) [12]. Gender (male, female), birth weight (very low birth weight

(1500gram), low birth weight (1500-2500gram), normal birth weight (>2500 gram) [1]), Apgar score at 5 minute (low (0-3), moderate (4-6), normal (>2500 gram) [1]) were independent variables (7-10) [13]) Pulse rate (lower rate (80 bpm), normal rate (80-160 bpm), higher rate (>160 beats per minute) [14]), Respiratory rate (lower rate (30 bpm), normal (30-60 bpm), faster (>60 birth per minute) [1]) and newborn oxygen saturation (low (90%), normal (90-95%), high ($>95\%$) saturation [1]). The explanatory variables were chosen from the literature and were all included in the models.

Operational definitions

Hypothermia: an axillary temperature of a newborn baby less than 36.5°C

The respiratory rate: is the rate at which breathing occurs

Pulse/heart rate: is the wave of blood in the artery created by contraction of the left ventricle during a cardiac cycle

Oxygen saturation is the fraction of oxygen-saturated hemoglobin relative to total hemoglobin in the blood.

2.2. Data Analysis Method

We employed a discrete time method, to represent movement between hypothermia states, a multi-state Markov model with constant transition rates is used. The normal state was thrilling because it does not allow for exits. We focused on the first occurrence of the normal state ("first hitting time") due to the short duration of the study and ignored further potential recovery. Severe and mild hypothermia were both transient conditions.

Longitudinal data consisted of observations of the disease process at arbitrary times. The exact times at which state transitions occurred were not known although the underlying process evolved continuously in time. Kalbfleisch & Lawless (1985) introduced the analysis of panel data under a Markov assumption where movements between disease states are governed by transitional intensities $q_{ij}(t, z(t))$ with $i, j = 1, 2, 3$ (the three possible states) and depend on time t and individual level or time-dependent explanatory variables at time t , denoted $z(t)$ [15]. In our

case, the q_{ij} forms a (3x3) matrix Q whose rows sum to zero so that the diagonal entries are defined by $q_{ij} = -\sum_{i \neq j} q_{ij}$. Since it is not possible to move from state III to either state I or state II, then in the transition intensity matrix, $q_{31} = q_{32} = q_{33} = 0$.

Marshall and Jones (1995) introduced a new class of models by restricting the number of parameters, allowing all progressive or all regressive transitions to have the same regression

coefficients, that is, $q_{ijl}(t) = \begin{cases} q_{ij}(0) e^{\beta_p z_l} & j = i + 1 \\ q_{ij}(0) e^{\beta_r z_l} & j = i - 1 \end{cases}$ An even more restrictive

model can be introduced by setting the regression coefficients to $\beta_p = -\beta_r = \beta$ [16]. Using the technique of regression, many covariates can be incorporated such as time varying covariates [17]. Details of the model description is found at supplementary file

In multi-state models, data are considered as series of observations $x_{i0}, x_{i1}, \dots, x_{in}$ and at times $t_{i0}, t_{i1}, \dots, t_{in}$ which is the product of $X(t)$ process. In this process the amount of $1, \dots, I$ states is $i = 1, \dots, N$ for each newborns, with covariate vectors z_l and model parameters θ , the log-likelihood under a Markov assumption can be expressed as [18] $L(\theta) = \sum_{i=1}^N \sum_{j=1}^{n_i} \log (p_{x_{i(j-1)}x_{ij}}(t_{i(j-1)}, t_{ij}; z_l, \theta))$ where, $p_{ij}(t_0, t_1, \theta) = p(x(t_1) = j | x(t_0) = i; \theta)$ and (i, j) Entry of $I \times I$ matrix is the transition probability which can be found by solving Kolmogorov Forward equation [19]. Details of the model description is found at supplementary file

Model Comparisons

For these models, the Akaike's Information Criterion (AIC) Akaike (1987) was used for model selection: $AIC = -2 \ln(\text{likelihood}) + 2p$ where p is the number of parameters in the model and n is the number of subjects in the data or sample size. Detailed description is found as supplementary file

Model Diagnostics

The likelihood ratio test statistic was also used to assess the models' time inhomogeneity [20] Aguirre-Hernandez and Farewell (2002) developed the Pearson-type goodness-of-fit test for the hypothesis that longitudinal data was generated by a fitted Markov model [21].

Ethical Consideration

An official letter of cooperation was written by the Arba Minch University College of Natural Sciences Department of Statistics to the administrators of Arba Minch General Hospitals (Ref. No. stat/519/2012). The administrators granted permission for this study to use the neonates' data. Medical professionals reviewed based on their admission and registration number. There were no links with neonates for the sake of confidentiality, and all data had no personal identifier. Ethical clearance was obtained from Arba Minch General Hospitals Ethical Review Board (Ref. No. AMGH/11309/13) and Arba Minch University.

3. Results

The study included 391 neonates with hypothermia in total. There were 187 female infants and 204 male newborns in this sample (52.2%). There were 120 newborns with normal birth weight, 246 (60.3 percent) with low birth weight, and 35 with extremely low birth weight, according to the diagnoses of newborns admitted to the hospital. There was a difference between stays of one and twenty-one days. For neonates admitted to the NICU, the average, typical, and median length of stay were, respectively, 6, 4, and 5. It was 3.14 for the standard deviation. 27 (6.9 percent) of the newborns admitted to the NICUs died before being released from the hospital, while 45 were sent to other hospitals and discharged against medical recommendation. 3919 of the babies brought to the NICUs recovered and were sent home, while 27 (6.9 percent) passed away before leaving the hospital and 45 were sent to other hospitals and released against medical recommendation (self-discharges). Table 1 shows the stages of hypothermia in infants at seven different observational time points. As demonstrated in Table 1, 176 neonates suffer severe or moderate hypothermia at birth, while 215 babies (55%) have mild hypothermia.

Table 1 The states of hypothermia among newborns at Arba Minch General Hospital, Ethiopia, 2018-2020

Observation time in minute	States of hypothermia		
	Severe state	Mild state	Normal state
1	176	215	0
30	105	178	108
60	60	136	87
90	40	81	75
120	26	59	36
150	15	10	60
180	0	0	25

3.1. State transition between different possible states

Table 2 shows the 1883 longitudinal observations from the 391 babies admitted to the NICU who recovered from hypothermia in the first three hours as part of the trial. On 85 times, severe hypothermia led to normal states, while mild hypothermia in 306 cases led to normal states. On 137 occasions, observations of severe hypothermia were recorded, then those of mild hypothermia. There were 46 instances of moderate hypothermia seen followed by severe hypothermia. The exclusion of several transitions based on how long it took to return to the normal state, such as the transition from the normal state to mild hypothermia for fewer than three hours after recovery, was supported by this finding.

Table 2 shows the transitions probability matrix computed from data with various states of neonatal hypothermia in the first three hours.

From \ To	Severe	Mild	Normal
Severe	376 (63%)	137 (23%)	85 (14%)
Mild	46 (5%)	542 (61%)	306 (34%)
Normal	0 (0%)	0 (0%)	391 (100%)

3.2. The estimated transition intensities on the covariates

The transition intensities between neonatal hypothermia states from severe to moderate hypothermia and from mild hypothermia to normal state were calculated to be 0.027 and 0.020 per minute, respectively, using a fitted multi-state Markov model with three covariates.

According to this, the change from severe to moderate hypothermia happened faster than the change from mild to normal hypothermia.

The transition intensities between neonatal hypothermia states from severe to moderate hypothermia and from mild hypothermia to normal state were calculated to be 0.027 and 0.020 per minute, respectively, using a fitted multi-state Markov model with three covariates. According to this, the change from severe to moderate hypothermia happened faster than the change from mild to normal hypothermia.

The hazard ratio was 0.98, or 2% lower risk for the normal condition compared to mild hypothermia, with a 95 percent confidence interval spanning from 0.82 to 1.17. The hazard ratio was 1.50, or 50% higher risk for mild hypothermia compared to severe hypothermia. Accordingly, neonates with normal birth weights have a higher chance of changing their condition than newborns with extremely low birth weights. With a 95% confidence interval of 1.06 to 1.59 and 1.14 (14% higher risk for moderate hypothermia against severe hypothermia), respectively, the hazard ratio for different levels of Apgar score was 1.30 or 30% higher risk for normal state than mild hypothermia. Accordingly, neonates with normal Apgar scores had a higher likelihood of changing states than newborns with low Apgar scores. At various pulse rate levels, the hazard ratio was calculated to be 1.03 or 3% higher risk for normal state compared to mild hypothermia and 0.48 (51%) lower risks for severe hypothermia states compared to mild hypothermia states, with a 95 percent confidence range spanning from 0.24 to 0.97. According to this, infants with greater heart rates were less likely to experience state changes than infants with lower heart rates.

3.3. Estimated average time spent in transient state

Table 3 shows that for neonates with very low birth weights, the average duration spent in severe and mild hypothermia was roughly 48 and 40 minutes, respectively, depending on the effect of weight on the transition rate from severe to mild hypothermia. Infants with low Apgar scores spent about 53 and 46 minutes, respectively, sojourning in severe and mild hypothermia, according to the effect of Apgar scores on transition rates from mild hypothermia to normal state.

The average time spent in severe and mild hypothermia for neonates with higher heart rates who were at higher risk was 48 and 34 minutes, respectively, according to the effect of pulse rate on transition rate from mild to severe hypothermia. This shows that the average time in transient states may be longer for one group than the other, depending on the risk factors and the hypothermic neonates.

Table 3 shows the estimated average times spent in severe and mild hypothermia for each group of newborns based on birth weight, Apgar score, and pulse rate.

Covariate name	Covariate levels	Estimated average times spent in severe hypothermia(minute)	Estimated average times spent in mild hypothermia(minute)
Birth Weight	VLBW	48	40
	LBW	35	38
	Normal	24	36
Apgar score at 5 minutes	Low	53	46
	Medium	41	42
	Normal	31	36
Pulse rate of newborns	Lower	31	34
	Normal	39	40
	Higher	48	42

3.4. Results for model comparison

The covariate model's maximum likelihood of the unknown parameters had a lower AIC score of 2118.98, which was better. The measurements' results demonstrated that, given that it best matches the available data, the selected covariates model can forecast future observations.

3.5. Model diagnostic check

Figure 2 shows the estimated probability of a state's duration in comparison to the typical lengths of time spent in mild and severe hypothermia, respectively (bottom). Infants who suffered from mild hypothermia recovered from it more quickly than those who suffered from severe hypothermia. Figure 2 shows that with severe hypothermia, the likelihood of recovery after 60 minutes was approximately 0.6 and with mild hypothermia, 0.4. This data implies that when

treating severely hypothermic infants, moderate rewarming rather than quick rewarming increased the risk of mild hypothermia persisting.

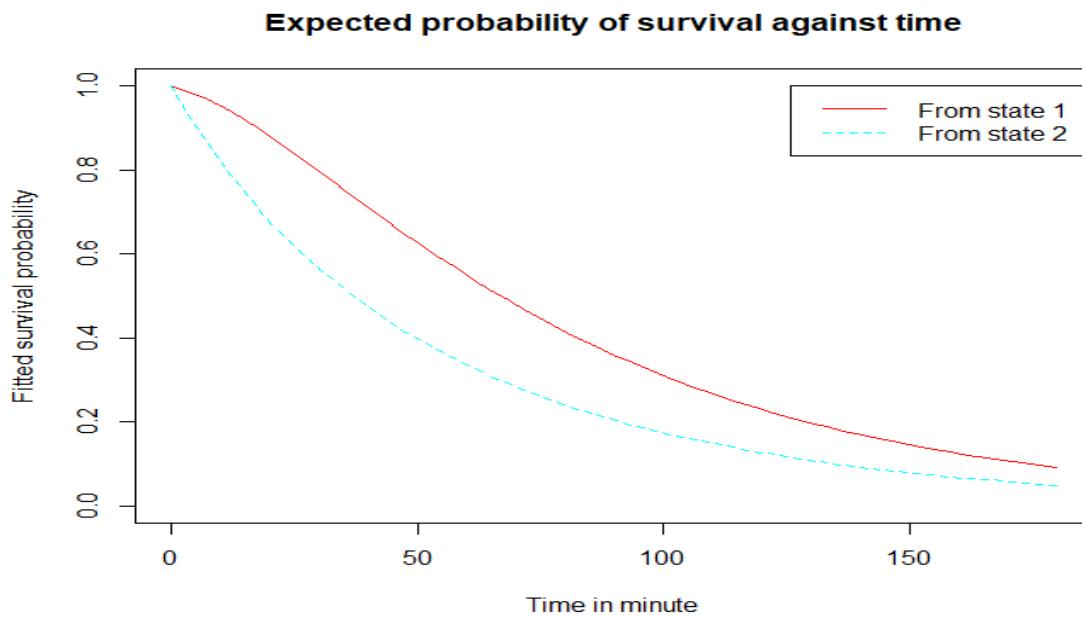


Figure 2: Time-plot of the anticipated likelihood of staying in a particular state.

The null hypothesis of the models' temporal inhomogeneity was disproved by the likelihood ratio test (p -value = 0.00016), and the covariate model offered a considerable improvement over the null model. The Pearson-type test did not reject the null hypothesis that longitudinal data fit the Markov property, and the chi-square statistics (34.71) and p values (0.53) show that these models offer a good overall fit. It would be predicted that a design that enabled factors to influence transition intensities would offer a better fit.

4. Discussions

The average time spent in a hypothermic state is determined by risk factors and hypothermic neonates. The neonatal risk factors of very low birth weight, low Apgar score, and high pulse rate increased the mean sojourn time of newborns who remained hypothermic for the first three hours after birth. This research supports previous findings that neonatal hypothermia increases morbidity and hospital stay [23]. Neonatal hypothermia is associated with an increased risk of

long-term morbidity [24]. This demonstrates that all newborn care providers should continue to consider temperature regulation during the first three hours of postnatal life to be a neonatal risk factor. We focused on the first occurrence of normal state ("first hitting time") within three hours in this study, and we ignored any subsequent potential recovery/loss. The chance of developing mild to severe hypothermia was 0.05. There were no severe hypothermia transitions [11, 12, and 22]. The small sample size of newborn babies with severe hypothermia could explain the disparity.

We confirmed previous research findings that hypothermia causes clinical irreversible damage ranging from metabolic problems to neonatal death; therefore, a rapid transition from hypothermia is critical. The transition from severe to mild hypothermia occurs more quickly than the transition from mild to normal hypothermia [12, 22]. This could be because the World Health Organization recommends that healthcare providers consider rapid rewarming for severely hypothermic newborns and slow rewarming for mildly hypothermic newborns returning to normal [1]. We also found a link between risk factors that accelerate this transition and a positive step toward preventing post-hypothermic problems.

The average length of time spent separately in mild hypothermia for newborns with very low, low, and normal birth weight was 40,38,36 minutes in this study versus 38,29,22 minutes in Iran [12, 22]. The difference could be explained by weight having a significant effect on the rate of transition from mild hypothermia to a normal state, as well as the first hitting time of a normal state occurring within two hours.

The Apgar score influenced the transition from mild hypothermia to normal states in this study. Low Apgar newborns were more likely to die from hypothermia than normal Apgar newborns. In contrast, the Apgar score was not a risk factor for neonatal hypothermia transition [12, 22]. In the majority of studies [11, 24, 25, 26, 27, 28], the Apgar score has been identified as a risk factor for neonatal hypothermia. Low Apgar score newborns spend more time in hypothermic states due to increased resuscitation efforts, prolonged management time in the delivery room, or increased inherent illnesses in these newborns. This could imply that preventing neonatal hypothermia during the first three hours after birth should be prioritized.

In this study, pulse rate had a significant effect on the rate of transition from mild to severe hypothermia. Hypothermia occurred at a lower rate in high pulse rate newborns than in low pulse rate newborns. A few studies have found that the newborn pulse rate is a risk factor for neonatal hypothermia. The most common symptom of hypothermia, on the other hand, is a decrease in the infant's pulse rate [29]. The heart cannot function normally when the body temperature drops. Assessing newborn infant pulse rates after birth is critical for directing recovery efforts in the right direction.

In this study, we include several risk factors for transitioning from hypothermic states and focus on estimating several quantities that can assist caregivers in reducing the risk of transitioning from neonatal hypothermia. The temperature of the NICU environment where the hypothermic newborns were born was not recorded. An earlier study suggested looking into the effect of birth temperature on the transition from hypothermia states. Their findings revealed that neonates born at temperatures higher than 28°C spend less time in hypothermia [12, 22]. Furthermore, due to the abrupt change in ambient temperature, newborns are vulnerable to hypothermia [1].

A multi-state Markov model was used to investigate the transition rate and risk factors for transitioning from neonatal hypothermia states in several studies [12, 22]. However, the majority of studies have been cross-sectional or prevalence studies. This model may provide researchers with a better understanding of the illness's process, allowing them to better understand how the disease evolves [9].

The retrospective observational design is one of the study's major limitations. Our findings should be interpreted in terms of a combination of severe and moderate hypothermia due to the small number of severe hypothermic newborns in our study. As a result, large numbers of severely hypothermic babies must be included in the study and analyzed separately. The use of a large number of newborns may allow for the detection of significant differences between hypothermia states to be more accurate. More research is required to determine the effect of risk factors on the progression of severe hypothermia to moderate hypothermia. Other study limitations included the exclusion of newborns who were persistently hypothermic or died, as well as the time interval between admission and recovery at the NICU within the first 24 hours.

4.1. Conclusion and recommendations

The exclusion of persistently hypothermic and deceased newborns limits these findings to less sick newborns. For hypothermic survivors within the first three hours of life, very low birth weight, low Apgar, and high pulse rate had the strongest association with hypothermia and took the longest to improve/recover.

These findings suggested that there is an urgent need to train all levels of staff dealing with monitoring and maintaining the time of recovery from neonatal hypothermia, particularly neonates with very low birth weight, low Apgar scores, and higher heartbeat. Future research should concentrate on deceased and persistent hypothermia, as well as the sickest newborns who were excluded.

Declarations

Consent for Publication

Not applicable

Availability of Data and Materials

The datasets generated and analyzed during the current study are available as supplementary file.

Competing interests

The authors declare that they do not have any competing interests.

Funding

The authors received no specific funding for this work.

Authors' Contributions

This project was collaboratively carried by all of the authors. TT, TA, MA and AW came up with the concept for the paper. TT analyzed the data and drafted the first draft of the paper. TT,

TA, MA and AW revised the paper even more to improve it. The final manuscript was approved by all authors.

Acknowledgements

This study would not have been possible without the permission of Arba Minch University's Statistics Department. The official letter of cooperation referred as stat/519/2012 with subject, To Whom It May Concern was issued. The authors gratefully acknowledge the Neonatal Intensive Care Unit Department at Arba Minch General Hospital for allowing us to use their data in this study. We are grateful to the nurses who volunteered their time to collect data for our study.

Authors' Information

[Tegenu Tento, M.Sc](#)

Jinka University, Department of statistics, 165, Jinka, Ethiopia

[Tilahun Asena, PhD](#)

Arba Minch University, Department of Statistics, 21, Arba Minch, Ethiopia

[Meseret Alemayehu, MD](#)

Department Pediatrics, Pawe General Hospital, Pawe, Ethiopia

[Asmare Wube, M.Sc](#)

Ethiopian Public Health Institute, Addis Ababa, Ethiopia

Corresponding author: Tilahun Asena

Abbreviations

AIC Akaike's Information Criterion

APGAR Appearance Pulse Grimace Activity Respiration

CSA Central Statistics Agency of Ethiopia

LBW	Low Birth Weight
MSM	Multi State Model
NICU	Neonatal Intensive Care Unit
VLBW	Very low Birth Weight
WHO	World Health Organization

References

- [1] World Health Organization, (1997). *Thermal protection of the newborn: a practical guide* (No. WHO/RHT/MSM/97.2). World Health Organization.
- [2] Demtse, A. G., Pfister, R. E., Nigussie, A. K., McClure, E. M., Ferede, Y. G., TazuBonger, Z., ... &Muhe, L. M. (2020). Hypothermia in preterm newborns: impact on survival. *Global Pediatric Health*, 7, 2333794X20957655.
- [3] Dubbink-Verheij, G. H., van Westerop, T. A., Lopriore, E., &Te Pas, A. B. (2021). Hypothermia during umbilical catheterization in preterm infants. *The Journal of Maternal-Fetal & Neonatal Medicine*, 34(1), 87-92.
- [4] McEllis, E.M., Leonard, A.R., Thornton, K.A., Voos, K.C. (2019). Improving thermal support in very and extremely low birth weight infants during interfacility transport. *PediatrQualSaf*. 4:e170.
- [5] McCall, E., Alderdice, F., Hi. H., Vohra, S., Johnston, L., (2018). Interventions to prevent hypothermia at birth in preterm and / or low birth weight infants (Review). *Cochrane Collab*. 20:18-98.
- [6] Farhadi, R., Rezai, M. S., &Nakhshab, M. (2014). Incidence of neonatal hypothermia at birth in hospitals of Islamic Republic of Iran: A review. *Journal of Pediatrics Review*, 2(2), 21-30.
- [7] Lunze, K., Yeboah-Antwi, K., Marsh, D. R., Kafwanda, S. N., Musso, A., Semrau, K., ...&Hamer, D. H. (2014). Prevention and management of neonatal hypothermia in rural Zambia. *PloS one*, 9(4), e92006.

[8] Demissie, B.W., Abera, B.B., Chichiabellu, T.Y., Astawesegn, F.H., (2018). Neonatal hypothermia and associated factors among neonates admitted to neonatal intensive care unit of public hospitals in Addis Ababa. *Ethiopia BMC Pediatr.* 18(1):263.

[9] Meira-Machado, L., de Uña-Álvarez, J., Cadarso-Suárez, C., & Andersen, P. K. (2009). Multi-state models for the analysis of time-to-event data. *Statistical methods in medical research*, 18(2), 195-222.

[10] Central Statistical Agency, (2016). CSA/Ethiopia, ICF. Ethiopia Demographic and Health Survey 2016. Addis Ababa: CSA and ICF; 2017.

[11] Salmani, F., Abadi, A., Taheri, M., Alavimajd, H., Nayeri, F., (2016). The effects of risk factors on the improvement of neonatal hypothermia using fuzzy transition. *SDH* . 2(1):15-20.

[12] Jambarsang, S., Baghban, A. A., Nayeri, F., & Tajalli, V. (2016). Investigating the factors affecting the transition rates between states of neonatal hypothermia using markov model. *Asian Journal of Medical Sciences*, 7(2), 34-38.

[13] Burd, I., Andrikopoulou, M., Farzin, A., Bienstock, J., & Graham, E. (2014). Neonatal Encephalopathy and Neurologic Outcome: New Guidelines Update. *Topics in Obstetrics & Gynecology*, 34(18), 1-5.

[14] Jeremic, A., & Tan, K. (2008, March). Heart rate monitoring in Neonatal Intensive Care using Markov models. In *2008 IEEE International Conference on Acoustics, Speech and Signal Processing* (pp. 485-488). IEEE.

[15] Kalbfleisch, J.D., and Lawless, J.F., (1985). The analysis of panel data under a Markov assumption. *Journal of the American Statistical Association*. 80(392): 863-871.

[16] Marshall, G.,& Jones, R.H., (1995). Multi-state models and diabetic retinopathy. *Stat Med*, 14: 1975-1983.

[17] Christodoulou, G., and Taylor, G.J., (2001). Use of a continuous-time hidden Markov process, with covariates, to model bed occupancy of people aged over 65 years. *Health Care Manag Sc*, 4: 21-24.

[18] Titman, A.C.,(2009). Computation of the asymptotic null distribution of goodness of fit test for multi-state models. *Life data analysis*. 15(4):519-533.

[19] Cox, D.R., and Miller, H.D., (1965). The theory of stochastic processes. *Chapman & Hall*.

[20] Lawless, J.F. and Nazeri Rad, N. (2015). Estimation and assessment of markov multi state models with intermittent observations on individuals. *Lifetime Data Analysis*, 21(2), 160–179.

[21] Aguirre-Hernandez, R., Farewell, V., (2002). “A Pearson-Type Goodness-of-Fit Test for Stationary and Time-Continuous Markov Regression Models.” *Statistics in Medicine*, 21:1899–1911.

[22] Baghban, A.A., Jambarsang, S., Pezeshk, H., and Nayeri, F. (2012). The effects of temperature and birth weight on the transition rate of hypothermia in hospitalized neonates using Markov models. *Tehran University Medical Journal* 70:282–288.

[23] Nayeri F. and Nili F.,(2006). Hypothermia at birth and its associated complications in newborns: a follow up study. *Iranian J Publ Health*; 35(1):48-52.

[24] Elbaum, C., Beam, K. S., Dammann, O., &Dammann, C. E. (2021).Antecedents and outcomes of hypothermia at admission to the neonatal intensive care unit. *The Journal of Maternal-Fetal & Neonatal Medicine*, 34(1), 66-71.

[25] Ali, S.R., Mirza, R., Qadir, M., Ahmed, S., Bhatti, Z., Demas, S., (2012). Neonatal hypothermia among hospitalized high risk newborns in a developing country. *Pak J Med Sci*.28(1):49-53.

[26] Shanta, D. S., (2019). Incidence of neonatal hypothermia and its association with low birth weight, preterm delivery, APGAR score and nursing care. *Journal of Patan Academy of Health Sciences*. Dec;6(2):75-80.

[27] Shibesh, B. F., Yalew, W. A., Beyene, M. B., &Minyiwab, G. W. (2020). Determinants of neonatal hypothermia among neonates admitted to neonatal intensive care unit northwest, Ethiopia, case-control study. *The Journal of Maternal-Fetal & Neonatal Medicine*, 1-6.

[28] Tasew, H., Gebrekristos, K., Kidanu, K., Mariye, T., Teklay, G., (2018). Determinants of hypothermia on neonates admitted to the intensive care unit of public hospitals of central zone, Tigray, Ethiopia 2017: unmatched case–control study. *BMC Res Notes*. 11(1):576. 28.

[29] Newnam, K. M., &DeLoach, D. L. (2011). Neonatal hypothermia: a method to provide neuroprotection after hypoxic ischemic encephalopathy. *Newborn and infant nursing reviews*, 11(3), 113-124.