

A multicentre study on admission hypothermia in very low-birth weight preterm infants in China: distribution, causes and risk factors

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Abstract

Background Neonatal hypothermia, defined as a temperature $< 36.5^{\circ}\text{C}$, is a major contributor to neonatal mortality and morbidity. Hypothermia in preterm infants remains a challenge in the neonatal intensive care unit (NICU) for many reasons.

Objective To investigate the incidence of admission hypothermia (AH) in very low-birth weight (VLBW) infants in multiple NICUs in Shandong Province, China, and to provide clinical evidence for the implementation of quality improvement practices to reduce the incidence of AH in NICU.

Methods This retrospective, observational study was carried out over a period of 12 months, from January 1, 2018 to December 31, 2018. The correlations between hypothermia preventive measures and the incidence of AH were analysed by descriptive statistical methods and a Spearman analysis. The associations between AH and maternal and neonatal variables were tested with bivariate analyses, followed by stepwise logistic regression. $P < 0.05$ was considered statistically significant.

Results A total of 1639 in-born infants who were born at a weight less than 1500 g were enrolled in the study on their day of birth. Among them, 1295 VLBW infants fulfilled the inclusion criteria. The incidence of AH was 87.9% in VLBW infants among the 28 NICUs. We investigated whether team training and education, such as monthly chart reporting on hypothermia in preterm infants on admission to the NICU, which was associated with 10.7% of all the cases, could decrease the rate of AH. Indeed, transport with a heated transport incubator was associated with 9.3% of the cases. here was a negative correlation between the incidence of AH and the number of quality improvement measures implemented to prevent hypothermia ($r = -0.242$, $p < 0.05$). A low birth weight, intubation in the delivery room, and a low 5-min Apgar score were significantly associated with AH.

Conclusion: The incidence of AH was high. There was a negative correlation between the incidence of AH and the number of quality improvement measures implemented to prevent hypothermia. It is important to monitor for AH in newborns who have a low birth weight, who have a low Apgar score at 5 min and who require intubation in the delivery room.

Background

Because of the immature physiological development of preterm infants, they are susceptible to heat loss, potentially leading to hypothermia, especially very low-birth weight (VLBW) infants and extremely low-birth weight (ELBW) infants [1]. The incidence of hypothermia on admission to the neonatal intensive care unit (NICU) in VLBW preterm infants is 31%–78% [2, 3]. Admission hypothermia (AH) is a vital risk factor for neonatal mortality and morbidity in preterm infants [4, 5].

Maintaining normothermia in infants has been shown to improve survival and outcomes [6, 7]. In a multicentre study, Caldas et al. [8] reported that AH was significantly associated with early neonatal death regardless of hospital performance. In Korea, Lee et al. [9] reported that 74.1% of 5860 VLBW preterm

infants (< 33 weeks of gestational age) with AH were admitted to neonatal units, and AH was associated with high mortality and several notable morbidities. Wilson et al. [10] reported that hypothermia occurred in 53.4% of 5697 infants born at <32 weeks of gestational age in a population-based study with samples from 11 European countries, and AH after very preterm birth was a significant factor associated with an increased risk of early and late neonatal mortality. Lyu et al. [11] showed that the rates of the composite outcome, severe neurological injury, severe retinopathy of prematurity (ROP), necrotizing enterocolitis (NEC), bronchopulmonary dysplasia (BPD), and nosocomial infection had U-shaped relationships with admission temperature, and the lowest rates of adverse outcomes were associated with admission temperatures between 36.5°C and 37.2°C.

To reduce the rates of these complications, many clinical studies have suggested various measures to prevent hypothermia, including plastic wrapping without drying [12, 13, 14], the use of incubators [15], and the use of chemical mattresses [16]. Despite the knowledge and development of new approaches to better maintain infant body temperatures, recent studies have noted that a significant proportion of VLBW infants in undeveloped countries are not kept sufficiently warm immediately after birth [10, 17].

The aim of this study was to investigate the distribution, causes and risk factors of AH in VLBW infants in multiple NICUs in China.

Methods

Study design and time period

This retrospective, observational study was carried out over a period of 12 months, from January 1, 2018, to December 31, 2018, to investigate the incidence of AH in VLBW infants in multiple NICUs in Shandong Province, China.

Study setting

Shandong is located on the western shore of the Pacific; it has 3345 kilometres of coastline and borders on the Bohai Sea and the Yellow River, and its 158,000 square kilometres of landmass is home to over 100 million people. The study was conducted in twenty-eight public hospitals in Shandong, China, that have their own NICU. East Hospital of Shandong Provincial Hospital Affiliated to Shandong University has its own NICU, with an average NICU admission rate of 75 neonates per month. Qilu Hospital of Shandong University has an average NICU admission rate of 121 neonates per month. Shandong Provincial Maternity and Child Health Care Hospital has an average NICU admission rate of 83 neonates per month. Qianfo Shan Hospital Affiliated to Shandong University has an average NICU admission rate of 79 neonates per month. Jinan Maternity and Child Health Care Hospital has an average NICU admission of 180 neonates per month. Yantai Yuhuangding Hospital has an average NICU admission rate of 162 neonates per month. Weifang Maternity and Child Health Care Hospital has an average NICU admission rate of 326 neonates per month. Linyi People's Hospital has an average NICU admission rate of 349

neonates per month. Linyi Women's and Children's Hospital has an average NICU admission rate of 370 neonates per month. The Affiliated Hospital of Weifang Medical College has an average NICU admission rate of 56 neonates per month. Taian Central Hospital has an average NICU admission rate of 171 neonates per month. Liaocheng People's Hospital has an average NICU admission rate of 253 neonates per month. Binzhou Medical University Hospital has an average NICU admission rate of 193 neonates per month. Zaozhuang Maternity and Child Health Care Hospital has an average NICU admission rate of 185 neonates per month. Taian Maternity and Child Health Care Hospital has an average NICU admission rate of 153 neonates per month. Dongying People's Hospital has an average NICU admission rate of 202 neonates per month. Affiliated Hospital of Jining Medical College has an average NICU admission rate of 530 neonates per month. The Second Affiliated Hospital of Shandong First Medical University has an average NICU admission rate of 100 neonates per month. Jinan Second Maternity and Child Health Care Hospital has an average NICU admission rate of 96 neonates per month. Tengzhou Central Hospital has an average NICU admission rate of 177 neonates per month. Zibo Maternity and Child Health Care Hospital has an average NICU admission rate of 161 neonates per month. The People's Hospital of Linzi District, Zibo, has an average NICU admission rate of 56 neonates per month. Central Hospital of Shandong Provincial Affiliated to Shandong University has an average NICU admission rate of 68 neonates per month. Ju County People's Hospital has an average NICU admission rate of 109 neonates per month. Heze Municipal Hospital has an average NICU admission rate of 51 neonates per month. Liaocheng Second People's Hospital has an average NICU admission rate of 72 neonates per month. Jinan Central Hospital has an average NICU admission rate of 49 neonates per month.

Data measurement, data collection and data quality control procedures

The admission temperature was defined as the infant's axillary or rectal temperature measured on admission to the NICU within one hour after birth, in accordance with local routines. Since January 1, 2018, homogeneous neonatal cooperative research platforms have been established. The admission temperatures, mortality incidence and morbidity data of VLBW infants born in 28 level-III NICUs in Shandong Province were collected prospectively. The database provided maternal, delivery, and neonatal data until the first NICU discharge, and the data were collected by trained staff using a standardized operating procedure [18]. The entered data were analysed for statistical adjustment of possible confounders with a multivariate analysis.

Population

Study population

The study population included all VLBW infants who were admitted to the NICUs of 24 level-III hospitals in Shandong Province, China, from January 1, 2018, to December 31, 2018, and their mothers.

Exclusion criteria

VLBW infants who were out-born, families who rejected treatment, and infants with missing temperature data were excluded.

Study variables

Dependent variable

The dependent variable was AH.

Independent variables

The following obstetric and neonatal variables were considered independent variables: diabetes, maternal hypertension, premature rupture of the membranes (PROM) (>24 hours), and caesarean section. The following neonatal variables were considered independent variables: multiple birth (twins or more), sex, gestational age (GA), birth weight (BW), small for gestational age (SGA) (defined as growth below the 10th percentile), Apgar scores at 1 min and 5 min, and intubation in the delivery room. Data on the implementation of measures to prevent hypothermia were collected using a retrospective questionnaire. The measures to prevent hypothermia were based on a review of the medical literature [19], best practice recommendations from the California Perinatal Quality Care Collaborative (CPQCC) [20], evidence-based principles from the Neonatal Resuscitation Program [21, 22], and recommendations by the World Health Organization (WHO) on ambient air temperatures in the delivery room [23]. The implementation of the measures to prevent hypothermia are described in Table 1.

Operational definitions

Hypothermia: an axillary temperature of less than 36.5°C, as defined by the WHO [23]: cold stress or mild hypothermia, 36.0°C to 36.4°C; moderate hypothermia, 32.0°C to 35.9°C; and severe hypothermia, below 32°C.

Normothermic: a body temperature of 36.5°C to 37.5°C.

Out-born: the newborn was delivered at a site other than the study hospital.

Statistical analysis

Demographic data are expressed as means (\pm standard deviations (SDs)) or percentages. The correlation between the hypothermia preventive measures and the incidence of AH was analysed by descriptive

statistical methods and Spearman analysis. Associations between perinatal variables and hypothermia were tested with a bivariate analysis, followed by stepwise logistic regression. Separate models were constructed for combined moderate/severe and mild hypothermia. We also studied the potential contribution of hypothermia to the risk factors. Separate models were constructed for risk factors in which severe/moderate or mild hypothermia was the independent variable. $P < 0.05$ was considered statistically significant. The statistical analyses were conducted using SPSS v. 25.0 (SPSS Inc., Chicago, Illinois).

Results

The 28 recruited hospitals included 20 general hospitals and 8 maternal and child health care hospitals, with an average of 59 and 40 beds in the neonatology departments and NICUs, respectively. A total of 1639 in-born infants born at a weight less than 1500 g were enrolled in the study on their day of birth; 97 infants were excluded because they were out-born. Additionally, 135 infants with families who ceased treatment and 94 infants who had missing temperature data were excluded. The remaining 1295 infants were included in this analysis (Fig. 1). The final cohort had a mean (\pm SD) BW and GA of 1225 ± 205 g and 29.7 ± 2.1 weeks, respectively.

Hypothermia

The mean (SD) admission temperature was 35.8°C (0.6°C), with a range of 32°C to 37.5°C . Only 12% of the study population had an admission temperature in the WHO recommended range of 36.5°C to 37.5°C . A total of 87.9% of infants had an admission temperature lower than 36.5°C , including 567 infants (43.8%) in the mild hypothermia group and 572 infants (44.2%) in the moderate/severe hypothermia group. No hyperthermia ($> 37.5^\circ\text{C}$) infants were identified. The distributions of infants across the range of admission temperatures according to BW are reported in Fig. 2.

Cause of hypothermia

Quality improvement methodologies such as Pareto charts were used to identify and prioritize the contributing reasons for AH (Fig. 3). We investigated whether team training and education could decrease the rate of AH, including monthly chart reporting on hypothermia in preterm infants on admission to the NICU, which was associated with 10.7% of all the cases. Indeed, transport with a heated transport incubator was associated with 9.3% of the cases. In addition, 8.8% of the cases of hypothermia were associated with no measured and recorded body temperature 10 min after birth. There was a negative correlation between the incidence of AH and the number of quality improvement measures implemented to prevent hypothermia ($r = -0.227$, $p < 0.05$). (Fig. 4).

Risk factors for hypothermia

The univariate analysis of the risk factors of severe/moderate hypothermia indicated that BW, caesarean section, low 5-min Apgar scores, intubation in the delivery room, maternal hypertension, and SGA were associated with AH (Table 2). After adjusting for risk factors using a logistic regression analysis, BW [adjusted *OR* 0.999, 95% *CI* (0.998–1.000); $p < 0.05$], intubation in the delivery room [adjusted *OR* 1.982, 95% *CI* (1.078–3.318); $p < 0.05$], and a low 5-min Apgar score [adjusted *OR* 2.159, 95% *CI* (1.071–4.352); $p < 0.05$] remained significantly associated with moderate/severe hypothermia.

Discussion

This is the first large national cohort study to investigate the incidence of AH and its association with in-hospital mortality and morbidity in the eastern region of China. Neonates regulate their body temperature much less efficiently than adults, and both hypothermia and hyperthermia can easily occur. Despite measures that were established in 2010 according to the recommendations of the Neonatal Resuscitation Program guidelines [21] to maintain normothermia in the delivery room, the incidence of AH is still high in China, occurring in 87.9% of VLBW infants. Mank et al. [24] reported that in 93% of infants, hypothermia occurred within the first three hours after admission. The proportion of infants with normal temperature ranges on NICU admission (12.0%) is much lower in China than in other developed countries, such as US infants less than 29 weeks (52.9%) [25], Canadian infants less than 33 weeks (57.2%) [11] and European infants less than 32 weeks (42.2%) [10].

The most notable infant characteristics that were associated with hypothermia were a low BW, intubation in the delivery room and a low Apgar score at 5 min. A low BW is associated with a large surface area-to-body mass ratio, a low amount of subcutaneous fat, an increased body water content, immature skin leading to increased evaporative water and heat losses, a poorly developed metabolic mechanism for responding to thermal stress and the delayed development of skin blood-flow control, reducing the ability to maintain heat by vasoconstriction [3, 4, 5], all of which may lead to hypothermia. Similar to our study, Laptok et al. [26] reported associations between BW and intubation in the delivery room and hypothermia. In addition, Lee et al. [9] reported that a low Apgar score at 5 min was a risk factor for hypothermia at admission. This may be related to the inadequate implementation of thermal protection measures during resuscitation.

The results of the correlation analysis indicated that the incidence of AH was effectively reduced with an increased number of hypothermia prevention measures, as there was a negative correlation between the incidence of AH and the number of implemented intervention measures. A retrospective study from the Vermont Oxford Network's (VON) VLBW database showed that the use of chemical warming packs in addition to routine care may be a useful intervention in achieving normothermia during the transition from delivery to admission to the NICU [27]. Recent studies reported that the use of plastic wrapping without drying reduced the rate of AH [12, 13, 14]. Wilson et al. [28] investigated the different strategies used in 11 European countries to prevent hypothermia. The results of the study showed that very preterm infants had a reduced risk of hypothermia at NICU admission if the unit used systematic prevention

strategies and that all the strategies had similar effects, possibly due to implementation rather than a strategy's specific efficacy.

In addition, a retrospective analysis of the practices to prevent hypothermia revealed that team training and education, including monthly chart reporting on hypothermia in preterm infants on admission to the NICU and transportation with a heated transport incubator, were key drivers of change. Although special space for the implementation of these interventions is not required, the reluctance to implement such measures may be associated with poor awareness by medical staff, a lack of infrastructure or funding, and so on. Based on these findings, implementing interventions to prevent hypothermia and enhancing team building were identified as key drivers of change. Based on recent studies in developed countries, after initiating quality improvement projects [29, 30, 31, 32], the incidence of AH dramatically declined. Thus, we need to implement evidence-based practices for improving quality (EPIQ) to reduce the incidence of AH in VLBW infants.

Our study had several limitations. We investigated only the incidence of AH and studied the association between AH and risk factors; we could not conduct a quality improvement project considering VLBW infants. Based on the results of this study, our next research project will be to carry out a multicentre quality improvement project to reduce the incidence of AH according to international EPIQ.

Conclusions

The incidence of AH was high. There was a negative correlation between the incidence of AH and the number of quality improvement measures implemented to prevent hypothermia. It is important to monitor for AH in newborns who have a low BW, who have a low Apgar score at 5 min and who require intubation in the delivery room.

Abbreviations

VLBW, very low-birth weight; NICU, neonatal intensive care unit; AH, admission hypothermia; OR, odds ratio; CI, confidence interval; SGA, small for gestational age; PROM, premature rupture of the membranes.

Declarations

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Availability of data and materials

The data that support the findings of this study are available from the corresponding authors upon reasonable request.

Ethics approval and consent to participate

Ethical approval with ethics approval number of LCYJ: NO. 2019–004 was obtained

from the Institutional Review Board of Shandong Provincial Hospital Affiliated with Shandong University. In our study, verbal informed consent was obtained from all participants. The Institutional Review Board of Shandong Provincial Hospital Affiliated with Shandong University considered the project exempt from written informed consent because this study was retrospective and observational study.

Consent for publication

Not applicable.

Authors' contributions

YYH, the corresponding author, designed the study, trained and supervised the data collectors, interpreted the results and revised the manuscript. The first authors, namely, WL, played a role in the analysis and interpretation of the data and in preparing and drafting the manuscript. The co-first authors, namely, LW, HL, WLL, FXF, WFQ, ZCL, SXM, LM, ZYFYG, LC, ZGY, ZXF, YZY, CT, RXY, LJ, QBP, NSP, ZRX, CY, GYL, ZRM, DLP, PFD, and BMR, participated in the design of the study, the collection and interpretation of the data and writing the manuscript. All authors listed on the manuscript approved the submission of this version of the manuscript and take full responsibility for the manuscript. The second authors, namely, DXY, played a role in the collection of the data.

Competing interests

The authors declare that they have no conflicts of interest.

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Tables

Table 1 Implementation measures to prevent hypothermia

Numerical order	Intervention
	Predelivery preparation
01	Ambient temperature at 25°C and the resuscitation bed on manual control with maximum heat output
02	Pre-warmed hat and blanket prepared
03	Polyethylene wrap prepared
	Birth
04	Infant immediately wrapped with a polyethylene wrap without drying
05	Infant wrapped in a pre-warmed blanket wrap after the umbilical cord is cut
06	Infant quickly weighed after being placed in a pre-warmed blanket
07	A pre-warmed hat is placed on the head
08	Body temperature measurement and recording 10 min after birth
	Before and at NICU admission
09	Infant transported with a heated transport incubator
10	All surfaces that the infant will contact are pre-warmed
11	Infant is immediately placed in the admission bed (e.g. Giraffe OmniBed)
12	Infant's body temperature is measured within 1 hour after birth
13	Infant receives hypothermic rewarming
14	The time of admission temperature $\geq 36.5^{\circ}\text{C}$ is recorded
	Team training and education
15	Both nursing and medical operations implemented
16	Monthly chart reporting on hypothermia in preterm infants on admission to the NICU
17	Temperature measurement standardized
18	Training and assessments on temperature measurement for nurses
19	Implementing quality improvement projects to reduce hypothermia in preterm infants on admission to the NICU

Table 2 Risk factors for moderate/severe hypothermia

	Moderate/severe hypothermia (%)	Mild hypothermia (%)	Normothermia (%)	<i>p</i>
GA, mean (SD), wk	29.6 (2.1)	29.8 (2.0)	29.8 (2.1)	0.835
BW, mean (SD), g	1200 (219)	1241 (194)	1270 (180)	0.004
SGA	162 (28.3)	113 (19.9)	28 (17.9)	0.001
Sex (boy)	297 (51.9)	286 (50.4)	84 (53.8)	0.664
Caesarean section	435 (76.0)	410 (72.3)	106 (67.9)	0.026
Multiple birth (twins or more)	109 (19.1)	113 (19.9)	25 (16.0)	0.547
Apgar score at 1 min < 7	212 (37.1)	197 (34.7)	44 (28.2)	0.119
Apgar score at 5 min < 7	100 (17.5)	68 (12.0)	11 (7.1)	0.001
Intubation in the delivery room	146 (25.5)	110 (19.4)	19 (12.2)	0.001
Maternal hypertension	259 (45.3)	225 (39.7)	49 (31.4)	0.005
Diabetes	64 (11.2)	62 (10.9)	19 (12.2)	0.909
PROM	147 (25.7)	169 (29.8)	40 (25.6)	0.258

Abbreviations: SGA, small for gestational age; PROM, premature rupture of the membranes

Table 3 Risk factors for the WHO criteria of moderate/severe hypothermia and mild hypothermia as determined by logistic regression models

	Adjusted <i>OR</i> * (95% <i>CI</i>)		
	Moderate/Severe hypothermia	Mild hypothermia	Normothermia
BW, mean (SD), g	0.999(0.998-1.000) ^a	1.000(0.999-1.001)	1
Caesarean section	1.256(0.810-946)	1.111(0.725-1.702)	1
Apgar score at 5 min<7	2.159(1.071-4.352) ^a	1.562(0.770-3.169)	1
Intubation in the delivery room	1.982(1.078-3.318) ^a	1.513(0.861-2.657)	1
Maternal hypertension	1.393(0.906-2.141)	1.349(0.881-2.065)	1
SGA	1.484(0.930-2.367)	0.917(0.572-1.471)	1

Abbreviations: OR, odds ratio; CI, confidence interval; SGA, small for gestational age; PROM, premature rupture of the membranes

*Adjusted for caesarean section, BW, SGA, Apgar score <7 at 5 min, and intubation in the delivery room.

^aodds ratios with $p < 0.05$

Figures

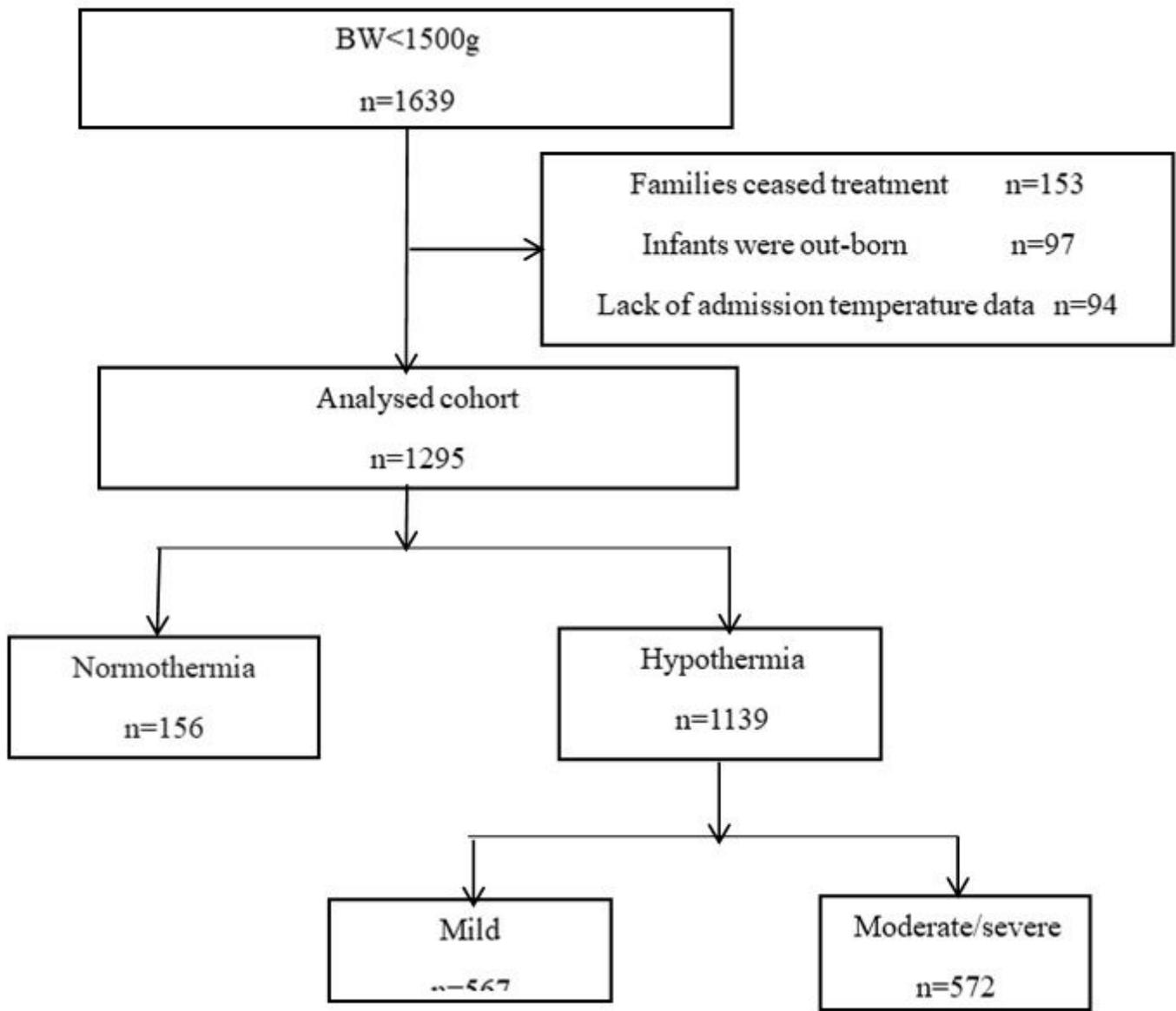


Figure 1

Flow diagram of the study population.

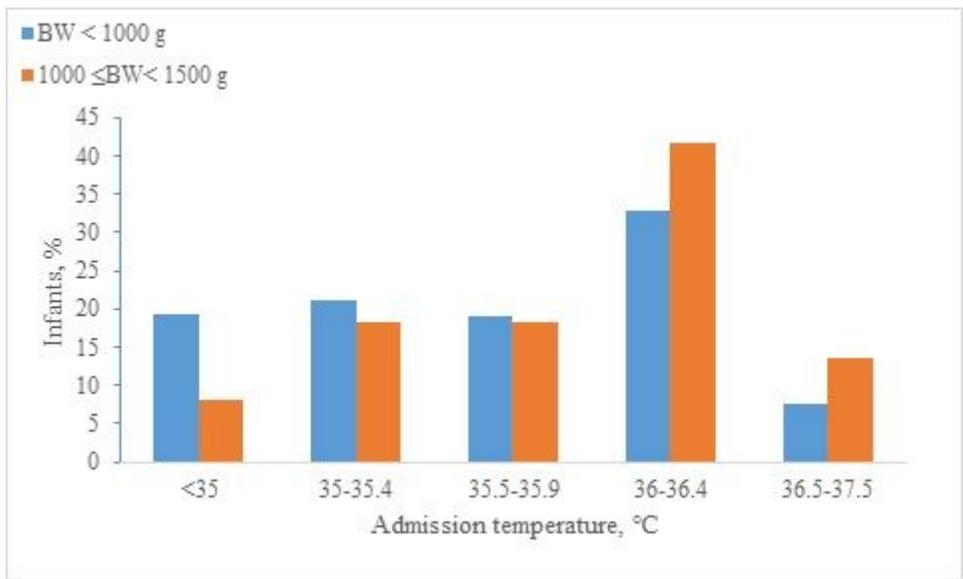


Figure 2

Temperature distribution according to birth weight.

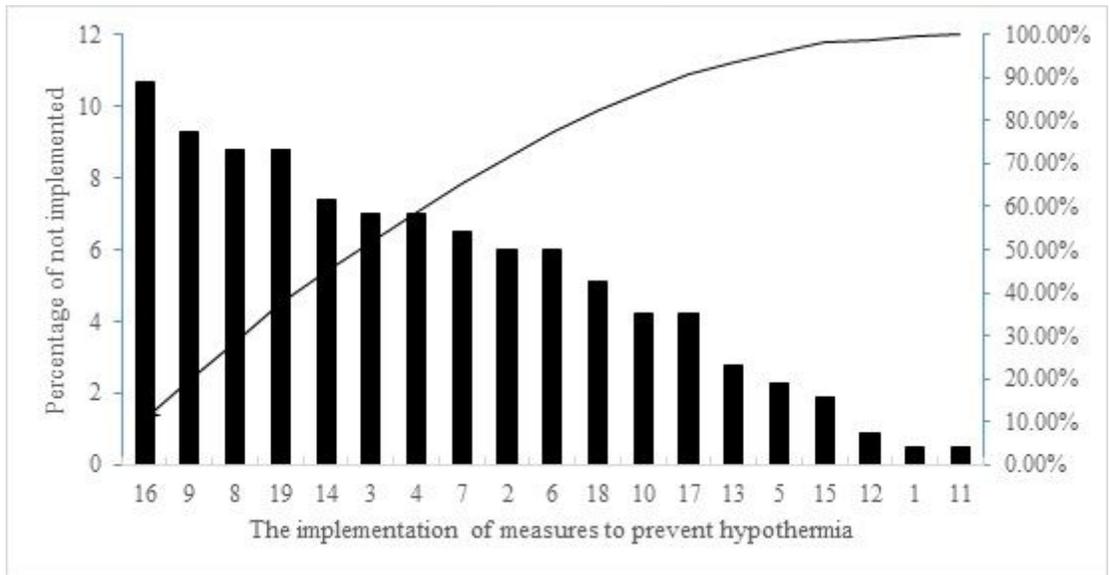


Figure 3

Pareto chart of the reasons for hypothermia.

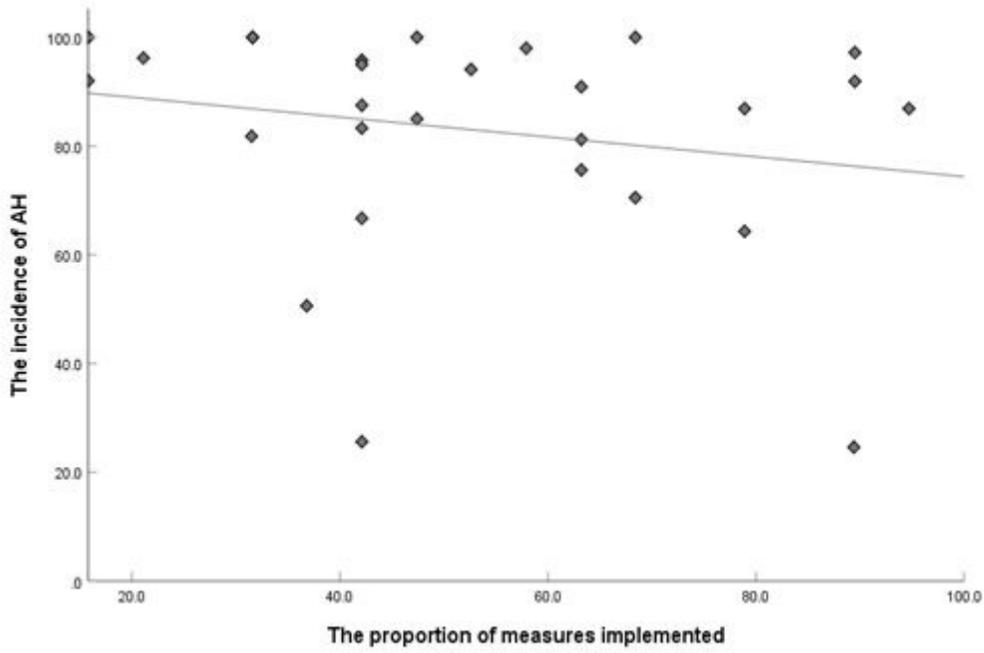


Figure 4

The correlation between the number of measures implemented and the incidence of AH.