BMC Pregnancy and Childbirth

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Impact of postpartum maternal fever or hypothermia on newborn and early infant illness and death in Southwestern Uganda

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Abstract

Background Deaths occurring during the neonatal period contribute close to half of under-five mortality rate (U5MR); over 80% of these deaths occur in low- and middle-income countries (LMICs). Poor maternal antepartum and perinatal health predisposes newborns to low birth weight (LBW), birth asphyxia, and infections which increase the newborn's risk of death.

Methods The objective of the study was to assess the association between abnormal postpartum maternal temperature and early infant outcomes, specifically illness requiring hospitalisation or leading to death between birth and six weeks' age. We prospectively studied a cohort of neonates born at Mbarara Regional Referral Hospital in Uganda to mothers with abnormal postpartum temperature and followed them longitudinally through early infancy. We performed a logistic regression of the relationship between maternal abnormal temperature and six-week infant hospitalization, adjusting for gestational age and 10-minute APGAR score at birth.

Results Of the 648 postpartum participants from the parent study who agreed to enrol their neonates in the sub-study, 100 (15%) mothers had abnormal temperature. The mean maternal age was 24.6 (SD 5.3) years, and the mean parity was 2.3 (SD 1.5). There were more preterm babies born to mothers with abnormal maternal temperature (10%) compared to 1.1% to mothers with normal temperature (p=<0.001). While the majority of newborns (92%) had a 10-minute APGAR score > 7, 14% of newborns whose mothers had abnormal temperatures had APGAR score <7 compared to 7% of those born to mothers with normal postpartum temperatures ($P=0.02$). Six-week outcome data was available for 545 women and their infants. In the logistic regression model adjusted for gestational age at birth and 10-minute APGAR score, maternal abnormal temperature was not significantly associated with the composite adverse infant health outcome (being unwell or dead) between birth and six weeks' age (aOR = 0.35, 95% CI 0.07–1.79, $P=0.21$). The 10-minute APGAR score was significantly associated with adverse six-week outcome ($P<0.01$).

Conclusions While our results do not demonstrate an association between abnormal maternal temperature and newborn and early infant outcomes, good routine neonate care should be emphasized, and the infants should be observed for any abnormal findings that may warrant further assessment.

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Target journal BMC Pregnancy and Childbirth (https://bmcpregnancychildbirth.biomedcentral.com/).
Keywords Neonate, Mother, Pregnancy, Outcome, Africa

Background

Despite global efforts to improve child health outcomes, the under-5-mortality rate (U5MR) remains high; five million children below 5 years died in 2021 [1]. Deaths occurring during the neonatal period have persistently contributed close to half the U5MR [1–3]. Over 80% of neonatal deaths occur in less developed countries, especially low- and middle-income countries (LMICs) in sub-Saharan Africa and southern Asia [2, 4, 5]. In 2022 the neonatal mortality rate in sub-Saharan was 27 deaths per 1000 live births, which was the highest in the world while that of Uganda was 22 deaths per 1000 live births [6, 7]. While there is regional variation in the causes of neonatal deaths, globally the most common causes include prematurity (10.7%), intrapartum-related events (10.7%) and neonatal infections (6.8%) [5, 8, 9]. In Uganda, 60% of early neonatal deaths result from birth asphyxia followed by prematurity and septicaemia at 23% and 7% respectively [7]. Poor maternal antepartum and perinatal health can predispose newborns to low birth weight (LBW), birth asphyxia, and infections, all of which increase the risk of neonatal and early infant death [10–12].

In addition, infants born to mothers with infections or poor postpartum health may receive inadequate early neonatal care, leading to malnutrition, infections, and other illnesses. Postpartum infections including endometritis, bacteraemia, and urinary infections are common in many LMIC health facilities, including Mbarara Regional Referral Hospital (MRRH) in Uganda [13]. Pregnancy related sepsis contributes to approximately 10% of maternal deaths in Uganda [7]. Abnormal maternal temperature is a proxy indicator of infection, and maternal intrapartum and postpartum fever has been associated with neonatal sepsis and other adverse infant outcomes [14, 15]. Puerperal infections can present with fever and other features, and have been associate with early neonatal deaths in a secondary analysis of demographic health surveys of six countries from Asia, Central America and South America [16]. A recent study in Uganda in a national referral hospital found a high prevalence of maternal postpartum fever at 19% [17]. However, there are few published studies describing the impact of maternal postpartum temperature on neonatal and early infant health outcomes.

To determine whether abnormal postpartum maternal temperature is associated with adverse early infant health outcomes, we prospectively studied a cohort of neonates born at MRRH to mothers with abnormal postpartum temperature and followed them longitudinally through early infancy. Therefore, we aimed to determine the impact of abnormal postpartum maternal temperature on early infant outcomes, specifically illness requiring hospitalisation or leading to death between birth and six weeks' age. We hypothesized that abnormal maternal postpartum temperature is associated with higher risk of adverse outcomes during the first six weeks of life.

Methods

Study design, site and population

This is a prospective cohort study of neonates delivered to women with abnormal temperatures while admitted to MRRH during the immediate postpartum period between April and September 2015. Maternal temperature was measured every 6–8 h during admission for delivery, beginning within six hours after delivery. MRRH is located in Mbarara city and is the referral hospital for the mainly rural southwestern region of Uganda whose population is estimated at 473,000 and a density of 98.6 inhabitants/km^2. MRRH is the teaching hospital for the Medical School of Mbarara University of Science and Technology. It is a 350-bed hospital with a bed occupancy rate of over 200%. It has an outpatient department, and inpatient services including but not limited to obstetrics and gynaecology unit and a paediatric unit with resuscitation equipment, incubators and oxygen as well as various diagnostic laboratories. The obstetrics unit of MRRH delivers up to 10,000 pregnant women annually.

Sample size and sampling procedure

All infants born to mothers enrolled in the parent prospective maternal sepsis cohort were enrolled in this substudy upon ethical clearance. The parent study aimed to define the epidemiology, microbiology, and outcomes of maternal infection on the maternity ward of MRRH during the study period [13, 18, 19]. In the maternal study, potential 'cases' of maternal infection were postpartum women who developed fever or hypothermia while admitted to hospital after delivering their baby. Fever was defined as temperature of $>38.0^0$ C and hypothermia $<36.0^0$ C. Additional maternal enrolment criteria and sample collection are described elsewhere [13, 18, 19]. Neonates born to participants with altered mental status who had no surrogate/family member to give consent were excluded. Surrogates were only approached for consent when the mother was critically ill and unable to participate in the consent process.

Parent study participants were approached by two trained research assistants, a doctor and a nurse and informed of the sub-study on child outcomes. After obtaining written informed consent, their newborns were

enrolled. Clinical assessment, including history, review of maternal records, and neonatal examination, was performed, and information was recorded on a standardized questionnaire. While hospitalized at MRRH, neonates were monitored every 12 h for any signs of ill health including fever or hypothermia, defined as temperatures of $\geq 38.0^0$ C or $< 35.5^0$ C, respectively; respiratory distress, feeding difficulties, lethargy, hypotonia, seizures, bulging fontanels, bleeding, and others. Ill neonates were handed over to the neonatologists on the paediatric ward of MRRH for further care. All infants who were alive at discharge were followed-up remotely at two weeks' age by telephone call, and by an in-person visit at six weeks' age. For infants who were not brought for the six-week visit, child vital status and hospitalisation information was obtained from the parent study, who collected the same outcomes data via telephone call at two- and six-weeks' age. If no outcome data was available from the parent study, a telephone call was made to determine the infant's health status.

Study outcomes

The primary outcome was a composite adverse infant health outcome, defined as being dead or unwell enough to require hospitalisation at any time during the first six weeks of life. Pre-specified secondary outcomes included vital status at birth, premature birth, and low birth weight (LBW), defined as weight less than 2500 g measured within 48 h of birth [20, 21].

Statistical analysis

We described continuous variables using means and standard deviations (SD); and used frequencies and proportions for categorical variables. We first assessed the unadjusted relationship between each variable and the six-week composite adverse infant health outcome. We then performed a logistic regression of the relationship between maternal abnormal temperature and six-week infant hospitalization (Table 1), adjusting for gestational age (in weeks) and 10-minute APGAR score at birth (categorized as <7versus ≥7). Because a high proportion (15.9%) of participants were missing six-week outcome data, we ran multiple sensitivity models, creating models for both extremes, e.g. considering those with missing data as being alive and well in one model, and considering those participants with missing outcomes as being dead in a second model. In addition, we compared maternal demographics (age, sex, parity, socioeconomic and marital stats), and medical characteristics (HIV status, presence of maternal sepsis) between the groups with missing infant outcome data and those without missing infant outcome data.

Results

Baseline characteristics

Supplement material 1 represents enrolment and follow-up of the participants enrolled in this prospective cohort sub-study. Overall, 648 postpartum participants from the parent study agreed to enrol their neonates in the sub-study. Of these, the overall mean maternal age was 24.6 (SD 5.3) years and mean parity was 2.3 (SD 1.5). Mean gestational age at birth was 39.1 (SD 1.6) weeks and a mean birth weight was 3.2 (SD 0.5) kilograms. Baseline characteristics were similar by infant 6-week outcome (Table 2).

Neonatal outcomes

Overall, 100/648 (15.4%) of the mothers had abnormal temperature (Table 1). Vital status differed significantly by maternal temperature group, with more preterm deliveries and fresh stillbirths in the abnormal maternal temperature group (Table 1). The vast majority of newborns (92.2%) had a 10-minute APGAR score>7. Twice as many neonates born to mothers with abnormal temperatures than those born to mothers with normal

Table 1 Health status of the neonate at birth and infant at six weeks' age in relation to maternal temperature (*N* = 648 for birth outcomes, *N* = 545 for six-week outcomes)

Child outcome	Total *n* (%) *N* = 648	Abnormal maternal postpartum temperature *n* (%) *n* = 100	Normal maternal postpartum temperature *n* (%) *n* = 548	*P*-value
Vital status at birth				< 0.001
Live, term (≥36 weeks' gestational age)	605 (93.4)	83 (83.0)	522 (95.3)	
Live, preterm (< 36 weeks' gestational age)	16 (2.5)	10 (10.0)	6 (1.1)	
Macerated stillbirth	7 (1.1)	1 (1.0)	6 (1.1)	
Fresh stillbirth	18 (2.8)	7 (7.0)	11(2.0)	
10-minute APGAR score < 7	50 (7.7)	14 (14.0)	36 (6.6)	0.02
Six-week infant outcome*				0.15
Dead or unwell	25 (3.9)	3 (3.0)	22 (4.0)	
Alive and well	520 (80.2)	88 (88.0)	432 (78.8)	
Unknown	103 (15.9)	9 (9.0)	94 (17.2)	

*Six-week outcome data was available for only 545 of the 648 enrolled infants (84.1%)

Table 2 Maternal and newborn characteristics and their association with adverse infant health outcome (being unwell or dead) at six weeks of age (*N* = 545)

Characteristic	Alive and well *n* = 520	Dead or unwell *n* = 25	*P*-value
Maternal age in years, mean (SD)	24.6 (5.2)	25.3 (5.4)	0.51
Parity, mean (SD)	2.3 (1.5)	2.7 (1.6)	0.16
Gestational age in weeks, mean (SD)	39.1(1.6)	38.6 (1.9)	0.16
Delivery mode			0.38
Vaginal, *n* (%)	235 (45.2)	15 (60.0)	
Caesarean, *n* (%)	279 (53.7)	10 (40.0)	
Operative vaginal, *n* (%)	5 (1.0)	0 (0.0)	
Maternal abnormal temperature, *n* (%)	88 (16.9)	3 (12.0)	0.78
Apgar < 7 at 10 min, *n* (%)	20 (3.8)	12 (48.0)	< 0.001
Infant fever at birth or within 6 weeks of age, *n* (%)	18 (3.5)	0 (0.0)	< 0.001
Birth weight in kg, mean (SD)	3.1(0.5)	3.0(0.5)	0.05

Table 3 Logistic regression model of the association between maternal postpartum abnormal temperature and adverse infant health outcome (being unwell or dead) at six weeks of age, adjusted for gestational age at birth and APGAR score (*N* = 545)

Variable	Unadjusted OR* (95% CI)	Unadjusted *P*-value	Adjusted OR (95% CI)	Adjusted *P*-value
Maternal abnormal temperature	0.67 (0.19, 2.29)	0.52	0.35 (0.07, 1.79)	0.21
Gestational age at birth (weeks)	0.80 (0.58, 1.09)	0.17	0.76 (0.54, 1.07)	0.12
APGAR score > 7 at 10 min after birth	0.0.04 (0.0.01, 0.09)	< 0.001	0.04 (0.01, 0.13)	< 0.001

*OR = odds ratio

postpartum temperatures had an APGAR score of <7 (14.0 vs. 6.6%, *P*-value 0.02, Table 2).

Six-week outcome data was missing for 103/648 infants (15.9%). There was no difference in baseline maternal characteristics between infants missing six-week outcome data and those without missing outcomes data, including age, gestational age at birth, HIV serostatus, asset index (a measure of wealth), income, marital status, or employment ($P > 0.05$ for all).

Our primary regression analysis included data from the 545 women and their infants with non-missing six-week outcome data. In a logistic regression model adjusted for gestational age at birth and 10-minute APGAR score, maternal abnormal temperature was not significantly associated with the composite adverse infant health outcome (being unwell or dead) between birth and six weeks' age, (adjusted odds ratio [aOR] 0.35, 95% CI 0.07–1.79, $P = 0.21$, Table 3), though 10-minute APGAR score > 7 was protective against adverse six-week outcomes after adjusting for gestational age at birth ($P < 0.01$, Table 3). In sensitivity analyses counting missing six-week infant outcomes as all adverse (dead or unwell) or favourable (alive and well), there was no change in the association between maternal abnormal temperature and the six-week composite adverse infant outcome (*P*-value > 0.05 for the association in all models).

Discussion

We aimed to determine the impact of abnormal postpartum maternal temperature on early infant outcomes. We hypothesized that infants born to mothers with abnormal postpartum temperature would have a higher risk of illness or death between birth and six weeks' age than those born to mothers with normal postpartum temperatures. Our primary analysis found no association between abnormal maternal postpartum temperature and six-week infant outcome, while adjusting for gestational age at birth and APGAR score. Our estimate of the effect of maternal temperature at birth on six-week outcome had a narrow confidence interval, indicating we likely had a sufficient sample size to evaluate the association in this convenience sample. Due to few overall adverse outcomes, we were unable to adjust for additional covariates that might affect this relationship, including delivery mode, maternal age, or maternal parity. However, none of these variables were statistically significantly related with the outcome in bivariate analysis.

Our results are similar to some other studies, including a study in Korea that found no evidence of increased neonatal mortality nor sepsis in the setting of maternal fever [14, 22]. A second study found increased neonatal intensive care unit admission rates for neonates born to febrile mothers but no increased risk of neonatal infections [23]. In contrast, higher rates of adverse short- and long-term infant outcomes have been reported in the setting of maternal fever in pregnancy [24–27], and a systematic review of studies carried out in sub-Saharan Africa identified intrapartum fever as a risk factor for neonatal sepsis (OR 2.28, 95% CI 1.18 to 4.39) [28].

In our study, maternal temperature was measured every 6–8 h, beginning within six hours postpartum. Most other previous studies evaluated infant infection

risk related to antepartum or intrapartum fever, making our study amongst the first to evaluate the relationship between postpartum temperature and child health outcomes. The different timing of temperature measurement in our study could indicate different causes of fever, including some that began postpartum and therefore did not impact neonatal outcomes. However, fevers developing within 24 h postpartum could result from antepartum factors, including endometritis, bacteraemia, urinary infections, premature and prolonged rapture of membranes, and unhygienic birth conditions, all of which could predispose to adverse newborn and infant outcomes. In another large retrospective study, three out of four neonates with bacteraemia were delivered to mothers who developed fever postpartum [14]. In our study, the lack of association between maternal abnormal temperature and adverse neonatal outcomes could have also resulted from routine intraoperative and postoperative antibiotic administration to people delivering by caesarean, which is common practice in our setting [18]. Since a large proportion (50%) of the children in our study were delivered by caesarean, maternal antibiotics could have passed into neonatal circulation, decreasing infection incidence. Another reason for the lack of association could have been the inclusion of hypothermic women, many of these may have had non-infectious causes of hypothermia, diluting any effect of maternal fever on child health outcomes.

Our study is strengthened by the prospective nature of data collection and the heterogeneous population studied, including both rural and urban dwellers, increasing the generalizability of our findings. We also studied a relatively large sample of 648 participants, but it is possible that despite this large sample size, our study was too small to detect a significant association between maternal abnormal temperature and adverse infant outcomes, though our narrow confidence intervals in logistic regression models suggest a sufficiently large sample size to detect an association. Furthermore, we were unable to measure all potential confounders of the relationship between maternal abnormal temperature and the six-week infant outcome, which is a limitation of our analysis. Another weakness of our study is a high proportion of infants with missing outcomes data. However, our sensitivity analyses suggest that the data are missing at random, and our results are likely to be valid. In addition, APGAR<7 at 10 min after birth was significantly associated with the composite adverse six-week infant health outcome even after adjusting for gestational age at birth, though it is an intermediary step between adverse birth outcomes and adverse six-week outcomes. A low APGAR score after delivery is an indication that the baby is not doing well after delivery, resulting from in utero or delivery insults or prematurity, many of which are also associated with adverse infant outcomes. Thus, the significant association between low neonatal APGAR score and adverse infant outcome should be interpreted with caution.

Conclusions

Abnormal postpartum maternal temperature was not associated with an increased risk of death or being unwell within six weeks of birth. While our results do not suggest a need for more aggresive management of neonates whose mothers develop postpartum fever or hypothermia, good routine neonate care should be emphasized and the infants should be observed for any abnormal findings that may warrant further assessment.

Abbreviations

LBW	Low birth weight
LMICs	Low- and middle-income countries
MRRH	Mbarara Regional Referral Hospital
SD	Standard deviations
U5MR	Under-five mortality rate

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12884-024-06775-7.

Supplementary Material 1

Acknowledgements

The authors are grateful to all study participants, study staff of the main (UPIM) and the neonatal sub studies in particular Dr Sam Oloya and Brian Mwanga, and Mbarara Regional Referral Hospital Maternity ward staff.

Author contributions

Conceptualization: JMA, YB, LMB. Data curation: JMA, JA, RA, JN, DN, PO, LMB. Formal analysis: JA, LMB, JMA, RA. Funding acquisition: JMA, YB, LMB. Investigation: JMA, LMB, JN, PO, YB, DN. Methodology: JMA, RA, LMB, JN, DN, YB, JA. Main manuscript writing: JMA, JA, LMB. Manuscript review: All authors.

Funding

This work was supported by the Einhorn Foundation, Sweden to JMA, research training grants from the National Institutes of Health -grant numbers R25TW009337 and T32AI007433 to LMB, a grant from the Harvard Global Health Institute to LMB, the Harvard University Center for AIDS Research National Institutes of Health/National Institute of Allergy and Infectious Diseases grant number P30AI060354 to LMB, and by a KL2/Catalyst Medical Research Investigator Training award from Harvard Catalyst (The Harvard Clinical and Translational Science Center grant number KL2TR002542) to LMB, the charles H. Hood Foundation to LMB, a career development award from the National Institute of Allergy and Infectious Diseases grant number K23AI138856 to LMB, and the American Society of Tropical Medicine and Hygiene Burroughs Wellcome Postdoctoral Fellowship in Tropical Infectious Diseases to LMB. The sponsors had no role in study design, data collection, analysis or interpretation, writing the report, or decision to submit the article for publication. The content is solely the responsibility of the authors and does not necessarily represent the official views of Harvard Catalyst, Harvard University and its affiliated academic healthcare centers, the National Institutes of Health, or other funders. None of the authors have a commercial or other association that might pose a conflict of interest.

Data availability

Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments and was approved by the institutional ethics review boards at Mbarara University of Science and Technology (08/10–14), Partners Healthcare (2014P002725/MGH), and the Uganda National Council of Science and Technology (HS/1729). All methods were carried out in accordance with relevant guidelines and regulations. All participants provided written informed consent.

Competing interests

The authors declare no competing interests.

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Received: 29 March 2024 / Accepted: 21 August 2024
Published online: 27 August 2024

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