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Original Article

Association of Admission Temperature and Outcome among Neonates with Sepsis in a Tertiary Care Hospital

Basma Fatima[1], Muhammad Faisal Shafique[2], Masud Murad[2], Iqra Irfan[1], Adeel Mehmood[1], Tariq Nadeem[2], Muhammad Farrukh Habib[3]*

[1]Resident Pediatric Medicine, Combined Military Hospitals Kharian, Pakistan.
[2]Classified Pediatrician, Combined Military Hospitals Kharian, Pakistan.
[3]Department of Management Sciences, Shifa Tameer-E-Millat University Islamabad, Pakistan.
Corresponding Author: Muhammad Farrukh Habib; Email: muhammadfarrukhhabib@gmail.com

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ABSTRACT

Background: Neonatal sepsis is a leading cause of mortality in the neonatal period, particularly in low- and middle-income countries. Temperature at admission may provide valuable prognostic information for managing critically ill neonates.

Objective: This study aimed to determine the association between admission temperature and outcomes in neonates with sepsis, including mortality rates, length of hospital stay, and the requirement for intensive interventions.

Methods: This descriptive cross-sectional study was conducted from July 2022 to February 2023 in the Department of Paediatrics, Combined Military Hospital, Kharian. A total of 170 neonates diagnosed with sepsis were enrolled using non-probability, consecutive sampling. Informed, written consent was obtained from parents or guardians. Temperature was recorded at admission using a mercury thermometer in the axilla. Hypothermia was defined as a body temperature <36.5°C, hyperthermia as >37.5°C, and normothermia as 36.5-37.5°C. Blood and urine samples were collected for culture. Data were analyzed using SPSS version 25. Quantitative variables were expressed as mean ± standard deviation or median with interquartile range, and qualitative variables as frequencies and percentages. Comparisons were made using Chi-square, Fisher's exact test, ANOVA, and independent samples t-test, with a significance level of $p \leq 0.05$.

Results: Of the 170 neonates, 94 (55.3%) were male and 76 (44.7%) were female. Hypothermia was present in 50 (29.4%) neonates, normothermia in 35 (20.6%), and hyperthermia in 85 (50.0%). Blood culture positivity was highest in hyperthermic neonates (61.2%), followed by hypothermic (36.0%) and normothermic (17.1%) neonates ($p < 0.001$). The mean length of hospital stay was 13.1 ± 4.1 days for hyperthermic neonates, 9.1 ± 2.3 days for hypothermic, and 6.3 ± 2.9 days for normothermic neonates ($p < 0.001$). Mortality rates were 31.8% for hyperthermic neonates, 14.0% for hypothermic, and 5.7% for normothermic ($p = 0.002$).

Conclusion: Admission temperature in neonates with sepsis is significantly associated with clinical outcomes. Hyperthermic neonates have higher mortality rates, increased blood culture positivity, and longer hospital stays compared to normothermic and hypothermic neonates. Measuring body temperature at admission can aid in risk stratification and management decisions.

Keywords: Neonatal sepsis, admission temperature, hyperthermia, hypothermia, neonatal mortality, length of hospital stay, blood culture positivity, critical care, neonatology, predictive factors.

INTRODUCTION

Approximately four million babies die within the neonatal period every year, particularly in low- and middle-income countries (1). A significant proportion of these deaths are attributable to neonatal sepsis (2). This disorder is associated with severe complications such as septic shock, coagulopathy, and organ dysfunction (3). Early recognition and timely, appropriate treatment are the cornerstones of management; the ability to predict the severity of illness through various prognostic factors is invaluable in determining the required intensity of management (4). Prognostic factors such as lower gestational age at birth, low birth weight, low APGAR score at birth, thrombocytopenia, intrapartum fever, deliveries requiring induction, and non-oral/enteral feeding have all been associated with poorer outcomes in patients suffering from neonatal sepsis (5, 6). Temperature appears to be an important clinical parameter that may reflect the severity of sepsis, as a measure of the body's response to infection (7). Studies in adults have demonstrated that high body temperature at the time of admission to critical-care units is an independent risk predictor for

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mortality, not just during the hospital stay but also after discharge and over the long term. It may serve as an important variable in establishing risk, guiding management, and providing a clearer prognostic picture (8). Hypothermia is purported to be associated with an increased risk of death due to a higher likelihood of complications, while hyperthermia is thought to reflect the severity of the inflammatory response and is also associated with an increased risk of death (9, 10). However, the importance of admission body temperature is less clear in neonates: recent studies have shown that hypothermia in neonates is not associated with an increased risk of mortality, despite being linked with higher lactate levels (9), while others have reported that hypothermia is indeed associated with an increased risk of mortality (10).

This study aims to determine the association of admission temperature with outcomes in patients admitted to the critical-care setting. Specifically, we aimed to investigate the relationship between admission temperature and mortality rates, as well as other important outcomes such as the length of hospital stay and the requirement for more intense interventions like mechanical ventilation and inotropic support. By doing so, we hoped to provide clinicians with valuable insights into the role of admission temperature in managing neonatal sepsis and inform future research directions in this area.

MATERIAL AND METHODS

This descriptive cross-sectional study was conducted from July 2022 to February 2023 in the Department of Paediatrics, Combined Military Hospital, Kharian, involving 170 pediatric patients diagnosed with neonatal sepsis. Informed, written consent was obtained from the parents or guardians of all participants prior to their enrolment. Study participants were selected via non-probability, consecutive sampling. Ethical approval was obtained from the hospital's ethical review board (reference letter no. 1103/Administration). The sample size was calculated using the World Health Organization (WHO) sample size calculator, with a confidence level (1-α) of 95%, absolute precision (d) of 0.05, and an anticipated population proportion (P) of 12.6%, based on the percentage of pediatric patients who died from neonatal sepsis, as reported by Ahmad et al. (11).

The inclusion criteria encompassed all neonates of both genders suffering from neonatal sepsis, defined by clinical signs and symptoms of sepsis such as irritability, lethargy, poor feeding, dyspnoea, pyrexia, hypothermia, and/or hypotension, accompanied by a positive culture from blood or urine. Alternatively, culture-negative patients with a white blood cell (WBC) count >30,000/µL or C-reactive protein (CRP) levels >6µg/mL were also included (11). Exclusion criteria comprised neonates diagnosed with metabolic disorders, congenital anomalies, chromosomal abnormalities, hypoxic-ischaemic encephalopathy, and respiratory distress syndromes, as well as patients who had received interventions to control body temperature, such as NSAIDs, or those suspected of having hospital-acquired infections.

Participants diagnosed before the age of 72 hours were classified as suffering from early-onset sepsis. At the time of enrollment, neonatal and pregnancy features such as gender, birth weight, gestational age at birth, and mode of delivery were documented. Temperature was measured in the axilla using a control-tested mercury thermometer, ensuring the axilla was dried and the bulb of the thermometer was placed in direct contact with the skin, with the arm adducted for three minutes. All patients underwent phlebotomy, and samples were sent for complete blood counts (XP-300 Automated Hematology Analyzer, Sysmex; Kobe, Japan), as well as for blood and urine cultures at the time of admission. Follow-up continued for one month to monitor for mortality. A body temperature <36.5°C was defined as hypothermia, >37.5°C as hyperthermia, and temperatures between these two values as normothermic (11).

Data were analyzed using the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, version 25, IBM Corp; Armonk, USA). Mean and standard deviation or median and interquartile range were calculated for quantitative variables, including gestational age at birth, birth weight, body temperature on admission, WBC counts, platelet counts on admission, and length of hospital stay. Qualitative variables such as gender, mode of delivery, type of sepsis, category of temperature, status of blood and urine cultures, requirement for mechanical ventilation, requirement for inotropic support, and mortality occurrence were recorded in terms of frequency and percentage. Patients were grouped based on the occurrence of mortality, and qualitative variables were compared across groups using the Chi-square test or Fisher's exact test, while quantitative variables were compared using one-way ANOVA or independent samples t-test, as appropriate. A p-value of ≤0.05 was considered statistically significant.

The study adhered to the ethical principles outlined in the Declaration of Helsinki. Data collection was performed meticulously to ensure accuracy, and all analyses were conducted with rigorous attention to detail to uphold the study's integrity and reliability.

RESULTS

The study analyzed the characteristics and outcomes of 170 neonates diagnosed with sepsis, with a focus on the association between admission temperature and various clinical parameters. Of the study population, 94 (55.3%) were males and 76 (44.7%) were females. The gestational age at birth for males was 37.9 ± 1.8 weeks, while for females it was 37.8 ± 1.7 weeks. Regarding the mode

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of delivery, 71 (75.5%) males and 56 (73.7%) females were born via vaginal delivery, whereas 23 (24.5%) males and 20 (16.3%) females were delivered via Caesarean section. Birth weights were similar between genders, with males averaging 3037.5 ± 526.7 grams and females 3013.7 ± 501.8 grams.

Table 1. Patient Characteristics/Study Results According to Gender (n=170)

Variable	Males (n=94)	Females (n=76)
Gender	94 (55.3%)	76 (44.7%)
Gestational Age at Birth (weeks)	37.9 ± 1.8	37.8 ± 1.7
Mode of Delivery		
Vaginal	71 (75.5%)	56 (73.7%)
Caesarean Section	23 (24.5%)	20 (16.3%)
Birth-Weight (g)	3037.5 ± 526.7	3013.7 ± 501.8
Type of Sepsis		
Early-Onset	57 (60.6%)	37 (48.7%)
Late-Onset	37 (39.4%)	39 (51.3%)
Temperature on Admission (°C)	37.3 ± 1.4	37.7 ± 1.4
Temperature Category		
Normal	21 (22.3%)	14 (18.4%)
Low	33 (35.1%)	17 (22.4%)
High	40 (42.6%)	45 (59.2%)
Blood Culture Positivity	42 (44.6%)	34 (44.7%)
Urine Culture Positivity	19 (20.2%)	13 (17.1%)
Requirement for Mechanical Ventilation	22 (23.4%)	26 (34.2%)
Requirement for Inotropic Support	17 (18.1%)	16 (21.1%)
Length of Hospital Stay (days)	10.5 ± 4.3	10.7 ± 4.6
Occurrence of Mortality	15 (16.0%)	21 (27.6%)

Table 2. Study Results According to Temperature Status (n=170)

Variable	Low (n=50)	Normal (n=35)	High (n=85)	p-value
Gender				0.084
Male	33 (66.0%)	21 (60.0%)	40 (47.1%)	
Female	17 (34.0%)	14 (40.0%)	45 (52.9%)	
Gestational Age at Birth (weeks)	37.5 ± 1.6	38.1 ± 1.7	37.9 ± 1.8	0.228
Mode of Delivery				0.296
Vaginal	34 (68.0%)	29 (82.9%)	64 (75.3%)	
Caesarean Section	16 (32.0%)	6 (17.1%)	21 (24.7%)	
Birth-Weight (g)	2940.7 ± 486.2	3126.0 ± 478.2	3036.7 ± 541.5	0.256
Type of Sepsis				0.502
Early-Onset	25 (50.0%)	22 (62.9%)	47 (55.3%)	
Late-Onset	25 (50.0%)	13 (37.1%)	38 (44.7%)	
White Cell Count (x 10^3/µL)	18.3 (IQR: 15.6)	24.4 (IQR: 15.5)	21.8 (IQR: 17.3)	0.283
Platelet Count (x 10^3/µL)	21.4 (IQR: 19.9)	23.6 (IQR: 18.3)	26.6 (IQR: 20.8)	0.166
Blood Culture Positivity	18 (36.0%)	6 (17.1%)	52 (61.2%)	<0.001
Urine Culture Positivity	5 (10.0%)	5 (14.3%)	22 (25.9%)	0.055
Requirement for Mechanical Ventilation	11 (22.0%)	7 (20.0%)	30 (35.3%)	0.121
Requirement for Inotropic Support	6 (12.0%)	5 (14.3%)	22 (25.9%)	0.099
Length of Hospital Stay (days)	9.1 ± 2.3	6.3 ± 2.9	13.1 ± 4.1	<0.001
Occurrence of Mortality	7 (14.0%)	2 (5.7%)	27 (31.8%)	0.002

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Temperature on admission showed a noteworthy pattern, with males having an average of 37.3 ± 1.4°C and females 37.7 ± 1.4°C. When categorized by temperature, 21 (22.3%) males and 14 (18.4%) females were normothermic, 33 (35.1%) males and 17 (22.4%) females were hypothermic, and 40 (42.6%) males and 45 (59.2%) females were hyperthermic. Blood culture positivity was nearly identical between genders, with 42 (44.6%) males and 34 (44.7%) females testing positive. Similarly, urine culture positivity was observed in 19 (20.2%) males and 13 (17.1%) females. The requirement for mechanical ventilation was noted in 22 (23.4%) males and 26 (34.2%) females, while the need for inotropic support was seen in 17 (18.1%) males and 16 (21.1%) females. Length of hospital stay was comparable, with males averaging 10.5 ± 4.3 days and females 10.7 ± 4.6 days. However, mortality rates were higher among females, with 21 (27.6%) females compared to 15 (16.0%) males (Table 1).

The analysis of outcomes based on temperature status revealed significant associations. Among the 50 hypothermic neonates, 33 (66.0%) were male and 17 (34.0%) female. In the normothermic group of 35 neonates, 21 (60.0%) were male and 14 (40.0%) female, whereas in the hyperthermic group of 85 neonates, 40 (47.1%) were male and 45 (52.9%) female, showing a higher incidence of hyperthermia among females. Gestational age at birth did not differ significantly across temperature categories, with hypothermic neonates averaging 37.5 ± 1.6 weeks, normothermic neonates 38.1 ± 1.7 weeks, and hyperthermic neonates 37.9 ± 1.8 weeks. Mode of delivery also did not show significant variation with 68.0% of hypothermic, 82.9% of normothermic, and 75.3% of hyperthermic neonates born vaginally, and the remainder via Caesarean section.

Birth weights were slightly lower in the hypothermic group (2940.7 ± 486.2 grams) compared to the normothermic (3126.0 ± 478.2 grams) and hyperthermic groups (3036.7 ± 541.5 grams). Early-onset sepsis was present in 50.0% of hypothermic, 62.9% of normothermic, and 55.3% of hyperthermic neonates. White cell counts and platelet counts did not show significant differences across the groups, with white cell counts being 18.3 (IQR: 15.6) x 10^3/µL in hypothermic, 24.4 (IQR: 15.5) x 10^3/µL in normothermic, and 21.8 (IQR: 17.3) x 10^3/µL in hyperthermic neonates, and platelet counts being 21.4 (IQR: 19.9) x 10^3/µL, 23.6 (IQR: 18.3) x 10^3/µL, and 26.6 (IQR: 20.8) x 10^3/µL respectively.

Blood culture positivity was significantly higher in hyperthermic neonates (61.2%) compared to hypothermic (36.0%) and normothermic (17.1%) groups, with a p-value of <0.001. Urine culture positivity also tended to be higher in hyperthermic neonates (25.9%) compared to hypothermic (10.0%) and normothermic (14.3%) groups, although this did not reach statistical significance (p = 0.055). The requirement for mechanical ventilation was observed in 22.0% of hypothermic, 20.0% of normothermic, and 35.3% of hyperthermic neonates. The need for inotropic support followed a similar trend, being required in 12.0% of hypothermic, 14.3% of normothermic, and 25.9% of hyperthermic neonates. Length of hospital stay was significantly longer for hyperthermic neonates (13.1 ± 4.1 days) compared to hypothermic (9.1 ± 2.3 days) and normothermic neonates (6.3 ± 2.9 days), with a p-value of <0.001. Mortality was also significantly higher in hyperthermic neonates (31.8%) compared to hypothermic (14.0%) and normothermic (5.7%) groups, with a p-value of 0.002 (Table 2).

DISCUSSION

The findings of this study suggested that admission temperature could potentially predict mortality and guide the intensity of management in critically ill neonates. Hyperthermia on admission was associated with an increase in blood culture positivity, a longer length of hospital stay, and a higher frequency of mortality compared to normothermic neonates. Although hypothermia also showed an association with these adverse outcomes, the effects were less pronounced.

The analysis indicated no significant difference in gestational age at birth (p=0.228) or birth weight (p=0.256) among neonates with different admission temperatures. While other studies have reported that lower gestational age and birth weight are associated with poor temperature regulation and increased risk of hypothermia (Kato et al., Fneish et al.), our findings differed likely due to the population studied, which consisted predominantly of term or near-term neonates. This observation aligns with Merazzi et al., who also found no significant effect of gestational age or birth weight on body temperature in term or near-term neonates (Merazzi et al.).

Male neonates in our study exhibited a higher incidence of hypothermia, although this did not reach statistical significance (p=0.084). Previous studies, such as those by Lubkowska et al. and Merazzi et al., have found no significant difference in body temperature between male and female neonates, suggesting that gender may not play a significant role in temperature regulation at birth (Lubkowska et al., Merazzi et al.). Further research focusing on septic neonates is needed to draw more definitive conclusions on this aspect.

The mode of delivery, whether vaginal or Caesarean section, did not significantly affect admission temperature status (p=0.296). This is consistent with findings from Lubkowska et al., who reported no significant difference in trunk temperature between neonates delivered vaginally and those delivered by Caesarean section, although a difference in forehead temperature was noted (Lubkowska et al.). Further investigation is required to determine if these observations apply to septic neonates.

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Early-onset sepsis was slightly more common than late-onset sepsis in our study, with no significant impact on temperature status at admission (p=0.502). This finding was in line with the conclusions of Giannoni et al., who found similar frequencies of early-onset and community-acquired late-onset sepsis (Giannoni et al.). However, Ogundare et al. noted a higher incidence of hypothermia in early-onset sepsis, potentially confounded by the predominance of preterm neonates in their sample (Ogundare et al.).

Blood cultures were positive in approximately half of the patients, with a significantly higher frequency in hyperthermic and hypothermic neonates (p<0.001). This observation is supported by Kayange et al., who found a higher frequency of positive blood cultures in hypothermic neonates with sepsis (Kayange et al.). Das et al. also reported an association between temperature dysregulation and increased incidence of positive blood cultures in septic neonates (Das et al.).

Approximately a quarter of the neonates required mechanical ventilation, with no significant association with temperature status at admission (p=0.121). Although direct comparisons are limited due to the scarcity of studies focusing on this aspect in neonates, Wynn et al. reported a high requirement for mechanical ventilation in infants with fulminant sepsis (Wynn et al.), while Razzaque found a high requirement in older children with septic shock (Razzaque).

The mean length of hospital stay was significantly longer in hyperthermic and hypothermic neonates compared to normothermic neonates (p<0.001). This contrasts with the findings of Sisay et al., who reported no significant effect of fever on the length of hospital stay (Sisay et al.). More research is needed to explore this relationship further.

Mortality occurred in approximately one-fifth of the neonates, with hyperthermic neonates showing the highest mortality rates, followed by hypothermic neonates (p=0.002). This is consistent with the findings of Ahmed et al., who also reported higher mortality in neonates with temperature disturbances, although they found a higher frequency of death in hypothermic neonates compared to hyperthermic ones (Ahmed et al.). The difference may be due to variations in the study populations, particularly the higher incidence of early-onset sepsis and preterm births in their study. Cavallin et al. also noted increased mortality rates in neonates with temperature dysregulation (Cavallin et al.).

The study had several limitations. It did not account for the specific events leading to admission to critical care, which varied widely and may have influenced mortality and hospital stay. There was also the possibility of unreported interventions to control body temperature or medications affecting temperature regulation. The single-center nature of the study and the specific population of armed forces personnel's wards may limit the generalizability of the findings. Future multicenter studies involving more diverse populations are needed to validate these results.

CONCLUSION

In conclusion, measuring body temperature at the time of admission in neonates with sepsis provided valuable prognostic information. Hyperthermia was associated with increased mortality, higher blood culture positivity, and longer hospital stays, while hypothermia also had similar but less severe associations. Further research should investigate interventions to mitigate the impact of temperature dysregulation on clinical outcomes in neonatal sepsis.

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