# ORIGINAL ARTICLE

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

Mahfuza Shirin<sup>1</sup>, M Monir Hossain<sup>2</sup>, Manifa Afrin<sup>3</sup>

# **Abstract**

**Background:** Neonatal sepsis is one of the major causes of mortality in neonates. Hypothermia is also an important contributing factor of neonatal mortality. Neonates with sepsis can present with normal temperature, hypo or hyperthermia.

**Objectives:** This study was design to find out the pattern of temperature on admission and its association with mortality among neonates admitted with sepsis.

Methods: This cross-sectional study was conducted from September 2017 to April 2018 in the Department of Neonatal Medicine and NICU, Dhaka Shishu (Children) Hospital. Neonates up to thirty days of age, diagnosed as probable sepsis were enrolled. On admission, axillary temperature was recorded for 3 minutes and neonates were categorized according to the recorded temperature. Neonates were classified as early onset sepsis (EOS) and late onset sepsis (LOS) according to the age of onset of the sepsis. Outcome was also recorded. Statistical analysis was done by SPSS program version 25. Chi-square ( $\chi^2$ ) test was done to determine the association and p value, <0.05 was taken as significant.

**Results:** Among 493 enrolled neonates, 41.2% neonates were with early onset sepsis (EOS) and 58.8% were with late onset sepsis (LOS). Out of 493 neonates, 89(18.1%) died. Among the enrolled neonates, 54.4% had normal temperature, 16.6% had mild hypothermia, 14.6% had moderate hypothermia and 14.4% had hyperthermia. It was found that mild and moderate hypothermia were significantly more in EOS(p<0.05). Mortality was significantly high in neonates with mild and moderate hypothermia (p<0.05).

**Conclusion**: This study found that mortality was associated with mild and moderate hypothermia in neonates admitted with sepsis.

**Keywords:** Neonate, sepsis, temperature.

Correspondence to: Dr. Mahfuza Shirin, Associate Professor, Department of Neonatal Medicine & NICU, Bangladesh Institute of Child Health (BICH), Dhaka Shishu (Children) Hospital. Cell:01819220582, E-mail: mahfuzashirin@gmail.com Received: 13 August 2019; Accepted: 11 September 2019

<sup>1.</sup> Associate Professor, Department of Neonatal Medicine & NICU, Bangladesh Institute of Child Health (BICH), Dhaka Shishu (Children) Hospital, Dhaka.

<sup>2.</sup> Professor, Department of Neonatal Medicine & NICU, Bangladesh Institute of Child Health (BICH), Dhaka Shishu (Children) Hospital, Dhaka.

<sup>3.</sup> Assistant Professor, Department of Paediatrics, BISH General Hospital.

# Introduction

Neonatal period is the most critical time for child survival. Globally around 2.6 million deaths occurred during neonatal period. In Bangladesh, under-five and infant mortality rate have decreased significantly over the last 3 decades, but neonatal mortality (23/1000 live birth) remains high. Sepsis is an important cause of neonatal mortality and account for approximately one-third of the global burden of neonatal deaths. Most of these deaths occur in the developing world.

Signs and symptoms of infection in neonates are subtle and non-specific and may clinically be indistinguishable from those occurring in noninfectious conditions, including almost every sign of neonatal distress.<sup>5</sup> Neonates with sepsis may be presented with either fever or hypothermia and even with normal temperature. Hypothermia is common and a major contributor of significant morbidity and mortality in developing countries.<sup>6-8</sup> Febrile neonates are at risk for bacterial infection, including meningitis, bacteremia, and urinary tract infections. Schwartz et al<sup>9</sup> and Marom et al<sup>10</sup> reported that the rate of serious bacterial infections was 4 to 28% among those neonates who were presented with fever during admission. Voora et al reported on a prevalence of fever of 1% in term newborns with 10% of these febrile newborns having sepsis. 11 It was reported that fever is the presenting symptom of bacterial infection in term neonates whereas preterm neonates were more likely presented with hypothermia. 12

There were studies reported the incidence and outcome of hypothermia at the time of admission among neonates with different diagnoses. <sup>13,14</sup> As sepsis is one of the major causes of neonatal mortality, it is necessary to evaluate the association of temperature on admission with mortality as in many cases fever or hypothermia is an important presentation of sepsis in neonates. So, this study was designed to find out the pattern of temperature on admission and its relation with mortality among neonates with sepsis.

# **Materials and Methods**

This cross-sectional observational study was conducted from September 2017 to April 2018 in the Department of Neonatal Medicine and NICU, Dhaka Shishu (Children) Hospital. Neonates up to thirty days of age, diagnosed as probable sepsis with any

3 or more of the following sign/symptoms: 15 poor feeding, lethargy, hypo/hyperthermia, abdominal distension, bradycardia (HR<100/min), tachycardia (HR >200/min), respiratory distress, apnoea, tachypnea, cyanosis, CRT >3 sec and neonates age <72hrs having one or more maternal risk factors: foul smelling liquor, antepartum / intrapartum maternal fever, prolonged or premature rupture of membranes ≥18 hours, offensive vaginal discharge, single unclean vaginal examination(s) during labour were enrolled in this study after taking informed consent from the parents. Neonates with congenital heart diseases, congenital anomalies, hypoxic ischemic encephalopathy, respiratory distress syndromes and did not give consent were excluded from the study.

Those neonates with onset of sepsis within 72 hours of age were classified as early onset sepsis (EOS)<sup>16</sup> and neonates with onset of sepsis at >72 hours of age were classified as late onset sepsis (LOS).

Temperature was recorded in axilla by using clinical mercury in glass thermometer. Before measuring the temperature, it was confirmed that axilla was dry, and then the thermometer was placed high up in the middle of the axilla and the arm was pressed against the side of chest to prevent air pockets between skin and thermometer. Thermometer was kept in this position for 3 minutes. The thermometer was disinfected by using chlorhexidine-soaked cotton after every axillary temperature measurement. In this study recorded temperature was classified according to WHO criteria as: Normal temperature 36.5°C to 37.5°C, hypothermia <36.5°C and hyperthermia >37.5°C. Hypothermia was subclassified into: mild (36.0°C to 36.5°C), moderate  $(32.0^{\circ}\text{C to}35.9^{\circ}\text{C})$  and severe  $(<32.0^{\circ}\text{C})$ .  $^{17}$ 

Blood samples of all the patients were obtained for complete blood count (CBC), CRP and blood culture, after enrollment and collected blood samples were send to microbiology and pathology department of Dhaka Shishu (Children) Hospital.

At the time of enrollment, for each neonate, information including gender, gestational age, age, weight, birth history was recorded in a questionnaire. Recorded temperature with category, investigation reports and outcome were also recorded. All enrolled neonates received supportive care and appropriate antibiotics according to unit protocols.

Statistical analysis was done by SPSS program version 25. To determine the association between categorical variables, Chi-square ( $\chi^2$ ) test was done. P value, <0.05 was taken as significant.

# Results

Out of 493 enrolled neonates, 70.6% were male with male to female ratio of 2.4:1, mean age of admission was 9.2±6.7 days with mean admission weight was 2337.2±732.04 gm. Mean gestational age was 36.4±2.7 week with 42% were preterm. All the enrolled neonates were out born; 70.8% were born at hospital and 60.6% delivered by normal vaginal delivery. Early onset sepsis (EOS) was present in 203 (41.2%) cases and late onset sepsis (LOS) in 290 (58.8%) cases. Among 493 study cases, 404 (81.9%)

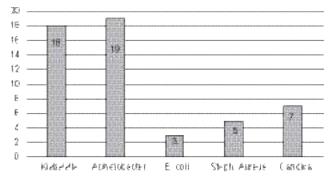


Fig 1 Isolated organisms in blood culture (N=52)

patients were discharged and 89 (18.1%) died (Table I). Among 493 neonates, 52 (10.5%) had growth of single organism in blood culture. Out of those 52 culture positive samples, highest isolated organism was gram negative bacteria, Acinetobacter (19/52) (Fig 1).

The mean axillary temperature was 36.66±0.72°C with minimum and maximum axillary temperatures were 35.0°C and 38.9°C respectively. Among the enrolled neonates, 54.4% had normal temperature, 16.6% had mild hypothermia, 14.6% had moderate hypothermia and 14.4% had hyperthermia (Table II). Among the neonates who had normal temperature at the time of admission, 37.3% (100/ 268) and 62.7% (168/268) were suffering from EOS and LOS respectively. It was found that mild and moderate hypothermia were significantly associated with EOS (p <0.05). Hyperthermia was relatively more in neonates suffering from LOS than EOS (69.1% vs. 30.9%), though the difference was not statistically significant (p > 0.5) (Table III). Mild and moderate hypothermia were associated with mortality (p <0.05) (Table IV). The mortality was also related to gestational age and was significantly high in preterm neonates (p=<0.05) (Table V).

Table I  Baseline characteristics of enrolled neonates (N=493)			
Variables	Number (%)		
Age on admission (day) mean±sd (min-max)	9.2±6.7 (1-28)		
Weight on admission (gm) mean±sd(min-max)	2337.2±732.04 (800-4600)		
Gestational age (week) mean±sd (min-max)	36.4±2.7 (26-42)		
Preterm	207 (42.0)		
Term	286 (58.0)		
Gender			
Male	348 (70.6)		
Female	145 (29.4)		
Place of delivery			
Home	144 (29.2)		
Hospital	349 (70.8)		
Mode of delivery			
Normal	299 (60.6)		
LUCS	194 (39.4)		
Diagnosis			
EOS	203 (41.2)		
LOS	290 (58.8)		
Outcome			
Died	89 (18.1)		
Cured	404 (81.9)		

Table II  Category of neonates according to recorded axillary temperature ( $N$ =493)			
Recorded temperature category (°C)	Number (%)		
Normal (36.5-37.5)	268 (54.4)		
Mild hypothermia (36-36.4)	82 (16.6)		
Moderate hypothermia (<36-32)	72 (14.6)		
Hyperthermia (>37.5)	71 (14.4)		
Total	493 (100.0)		
Mean±sd (min-max) °C	36.66±0.72 (35.0 - 38.9)		

Table III  Association of temperature pattern with EOS and LOS ( $N$ =493)					
Temperature Category (°C)	Total	EOS n (%)	LOS n (%)	p* value	
Moderate hypothermia (<36-32)	72	39 (54.2)	33 (45.8)	0.015	
Mild hypothermia (36-36.4)	82	42 (51.2)	40 (48.8)	0.031	
Hyperthermia (>37.5)	71	22 (30.9)	49 (69.1)	0.080	
Normal (36.5-37.5)	268	100 (37.3)	168 (62.7)	0.070	
Total	493	203	290		

<sup>\*</sup>Chi square test  $(\chi^2)$ 

Table IV Association of mortality with admission temperature (N=493)					
Temperature category (°C)	Total	Died	Cured	p* value	
Moderate hypothermia (<36-32)	72	20 (27.8)	52 (72.2)	0.017	
Mild hypothermia (36-36.4)	82	22 (26.8)	60 (73.2)	0.023	
Hyperthermia (>37.5)	71	7 (9.9)	64 (90.1)	0.077	
Normal	268	40 (14.9)	228 (85.1)	0.063	
Total	493	89	404		

<sup>\*</sup>Chi square test  $(\chi^2)$ 

Table V Association of mortality with gestational age (N=493)					
Gestational age	Number	Died	Survived	p* value	
		n (%)	n (%)		
Preterm	207	53 (25.6)	154 (74.4)	0.000	
Term	286	36 (12.6)	250 (87.4)		
Total	493	89	404		

<sup>\*</sup>Chi square test  $(\chi^2)$ 

#### **Discussion**

This study was conducted to identify the pattern of temperature on admission among neonates with sepsis and its relation with mortality. In this study, 36.1% neonates had early onset sepsis and 63.9% neonates had late onset sepsis respectively. But Getabelew et al<sup>18</sup> found 65% and 35% of neonates developed early onset neonatal sepsis and late onset neonatal sepsis, respectively, which was opposite to our findings. We found that the rate of isolation of single organism was about 10.5%. In a previous study reported from Bangladesh, the culture positivity rate was 36%. <sup>19</sup> Studies from different countries shown that culture positivity rate varies from 16%-54%. <sup>20-22</sup>

Presentation of neonatal sepsis is usually subtle and non-specific. Hypothermia or fever is the common presentation. Hypothermia is a common problem in neonates and to identify this problem, studies were conducted in Bangladesh<sup>11</sup> and other countries.<sup>23,24</sup> The prevalence of hypothermia varies widely in those studied. Factors like age, weight, gestational age, place of birth, early bathing, APGAR scores, season and ambient temperature can alter the prevalence of hypothermia in neonates. 18,25-27 All those studies included neonates with different diagnoses. But very few studies were conducted to evaluate the relationship of hypothermia with sepsis.<sup>28,29</sup> This study was among those where we found, 31.2% of the neonates had hypothermia on admission. Similarly, Ahmad et al<sup>29</sup> found 28.9% of the study patients had hypothermia on admission. We found mild and moderate hypothermia was significantly associated with EOS (p=0.000). Similar findings were reported by Ahmad et al.<sup>29</sup>

Hypothermia is associated with increase rate of mortality in neonates suffering from various diseases. Ogunlesi et al<sup>30</sup> found that mortality rate of neonatal sepsis was 32.2%. In the present study all enrolled neonates were out born and mortality rate was 17.6%, which was much less than the finding of Ogunlesi et al<sup>30</sup> and similar to the finding of Ahmad et al.<sup>29</sup> Ahmad et al<sup>29</sup> found that neonates with hypothermia had higher mortality rate as compared to patients with normal temperature among neonates with sepsis. We also found that hypothermia was significantly associated with mortality.

Like hypothermia, neonates with sepsis might be presented with hyperthermia.<sup>28</sup> Usually neonate

with fever are at risk for bacterial infection. Approximately 10% of neonates with fever have a serious bacterial infection. In this study 14.4% neonates had hyperthermia, which was similar to the findings reported by Ahmad et al. 29

### Conclusion

This study concluded that mild and moderate hypothermia were associated with mortality among neonates admitted with sepsis. Early onset sepsis was associated with hypothermia.

### References

- World Health Organization. Neonatal mortality (Global health observatory data). World Health organization. Available from: http://www.who.int/ gho/child\_health/mortality/neonatal/en. [Last accessed on 2019 Mar 27].
- United Nations Inter-Agency Group for Child Mortality - UNICEF Data; 2018. Available from: https://data.unicef.org. [Last accessed on 2019 Mar 27].
- 3. Lawn JE, Wilczynska-Ketende K, Cousens SN. Estimating the causes of 4 million neonatal deaths in the year 2000. *Int J Epidemiol* 2006;**35**:706-18.
- Black RE, Cousens S, Johnson HL, Lawn JE, Rudan I, Bassani DG, et al. Global, regional, and national causes of child mortality in 2008: A systematic analysis. *Lancet* 2010;375:1969-87.
- Kurlat I, Stoll BJ, McGowan JE. Global, regional, and national causes of child mortality in 2008: A systematic analysis. Time to positivity for detection of bacteremia in neonates. J Clin Microbiol 1989;27:1068-71.
- Chang HY, Sung YH, Wang SM, Lung HL, Chang JH, Hsu CH, et al. Short- and long-term outcomes in very low birth weight infants with admission hypothermia. *PLoS One* 2015;10:e0131976. doi: 10.1371/journal.pone.0131976.
- Ogunlesi TA, Ogunfowora OB, Adekanmbi FA, Fetuga BM, Olanrewaju DM. Point-of-admission hypothermia among high-risk Nigerian newborns. BMC Pediatr 2008;8: 40.
- 8. Darmstadt GL, Bhutta ZA, Cousens S, Adam T, Walker N, De Bernis L. Evidence-based, cost effective interventions: how many newborn babies can we save? *Lancet* 2005;**365**:977-88.
- Schwartz S, Raveh D, Toker O, Segal G, Godovitch N, Schlesinger Y. A week-by-week analysis of the low-risk criteria for serious bacterial infection in

- febrile neonates. Arch Dis Child 2009;94:S287-S292.
- Marom R, Sakran W, Antonelli J, Horovitz Y, Zarfin Y, Koren A, et al. Quick identification of febrile neonates with low risk for serious bacterial infection: An observational study. Arch Dis Child Fetal Neonatal Ed 2007;92:F15-F18.
- 11. Voora S, Srinivasan G, Lilien LD, Yeh TF, Pildes RS. Fever in full-term newborns in the first four days of life. *Pediatrics* 1982;**69**:40-44.
- 12. Weisman LE, Stoll BJ, Cruess DF, Hall RT, Merenstein GB, Hemming VG, *et al.* Early-onset group B streptococcal sepsis: A current assessment. *J Pediatr* 1992;**121**:428-33.
- Akter S, Parvin R, Yasmeen BHN. Admission hypothermia among neonates presented to neonatal intensive care unit. J Nepal Paediatr Soc 2013;33:166-71.
- Zayeri F, Kazemnejad A, Ganjali M, G. Babaei G, Nayeri F. Incidence and risk factors of neonatal hypothermia at referral hospitals in Tehran, Islamic Republic of Iran. Eastern Medit Health J 2007;13:1308-18.
- 15. Haque KN. Definitions of bloodstream infection in the newborn. *Pediatr Crit Care Med* 2005;**6**:45-49.
- 16. Watson G, Caldwell C, Kennea N. Neonatal early onset sepsis: A reflection on the NICE guidance. *Infant* 2016;**12**:133-35.
- World Health Organization. Thermal protection of the newborn: A practical guide. Geneva: World Health Organization;1997. Report No.WHO/RHT/ MSM/97.2
- 18. Getabelew A, Aman M, Fantaye E, Yeheyis T. Prevalence of neonatal sepsis and associated factors among neonates in neonatal intensive care unit at selected governmental hospitals in Shashemene Town, Oromia Regional State, Ethiopia, 2017. Hindawi International Journal of Pediatrics 2018;doi.org/10.1155/2018/7801272.
- Hossain MM, Afroza S, Shirin M, Chowdhury NA, Saha SK. Bacterial aetiology of neonatal sepsis in a tertiary care hospital in Bangladesh. *Bang J Child Health* 2004;28:81-85.
- 20. Zakariya BP, Bhat V, Harish BN, Arun Babu TA, Joseph NM. Neonatal sepsis in a tertiary care

- hospital in South India: Bacteriological profile and antibiotic sensitivity pattern.  $Indian\ J$   $Pediatr\ 2011; 78:413-17.$
- Kaistha N, Mehta M, Singla N, Garg R, Chander J. Neonatal septicemia isolates and resistance patterns in a tertiary care hospital of North India. J Infect Dev Ctries 2009;4:55-57
- 22. Shitaye D, Asrat D, Woldeamanuel Y, Worku B. Risk factors and etiology of neonatal sepsis in Tikur Anbessa University Hospital, Ethiopia. *Ethiop Med J* 2010;48:11-21.
- 23. Demissie BW, Abera BB, Chichiabellu TY, Astawesegn FH. Neonatal hypothermia and associated factors among neonates admitted to neonatal intensive care unit of public hospitals in Addis Ababa, Ethiopia. *BMC Pediatrics* 2018;18:263.
- 24. Wilson E, Maier RF, Norman M, Misselwitz B, Howell EA, Zeitlin J, et al. Admission Hypothermia in Very Preterm Infants and Neonatal Mortality and Morbidity. *J Pediatr* 2016;175:61-67.
- Zayeri F, Kazemnejad A, Ganjali M, Babaei G, Khanafshar N, Nayeri F. Hypothermia in Iranian newborns. Incidence, risk factors and related complications. Saudi Med J 2005;26:1367-71.
- Mullany LC, Katz J, Khatry SK, Leclerq SC, Darmstadt GL, Tielsch JM. Neonatal hypothermia and associated risk factors among newborns of southern Nepal. *BMC Med* 2010;8:43.
- 27. Bergström A, Byaruhanga R, Okong P. The impact of newborn bathing on the prevalence of neonatal hypothermia in Uganda: A randomized, controlled trial. *Acta Paediatr* 2005;**94**:1462-67.
- 28. Hofer N, Müller W, Resch B. Neonates presenting with temperature symptoms: Role in the diagnosis of early onset sepsis. *Pediatrics International* 2012:**54**:486-90.
- Ahmad MS, Ali N, Mehboob N, Mehmood R, Ahmad M, Wahid A. Temperature on admission among cases of neonatal sepsis and its association with mortality. J Pak Med Assoc 2016: 66:1303-06.
- 30. Ogunlesi TA, Ogunfowora OB. Predictors of mortality in neonatal septicemia in an under resourced setting. J Natl Med Assoc 2010;**102**:915-21.