Temperature on admission among cases of neonatal sepsis and its association with mortality

Mirza Sultan Ahmad, Naila Ali, Nazia Mehboob, Ramlah Mehmood, Mubashra Ahmad, Abdul Wahid

Abstract
Objective: To ascertain the prevalence of hyperthermia and different categories of hypothermia among the cases of probable and culture-proven neonatal sepsis, and to evaluate association of mortality rate with axillary temperature at admission.

Methods: This analytical study was conducted at Fazl-e-Omar Hospital, Rabwah, Pakistan, from January to December 2013, and comprised all cases of culture-proven and probable neonatal sepsis admitted in the neonatal intensive-care unit of the hospital. Using World Health Organisation classification, cases were categorised according to their temperature on admission, and outcome was recorded. SPSS 20 was used for data analysis.

Results: Of the 374 patients, 47 (12.6%) died. Besides, 217 (58%) cases had normal temperature, 49 (13.1%) had hyperthermia, 50 (13.4%) had mild hypothermia, and 58 (15.5%) had moderate hypothermia. Mortality rate was high among cases with mild and moderate hypothermia i.e. 15 (32.6%) and 15 (33%), compared with the mortality rate in cases with normal temperature i.e. 12 (6.1%). Mortality rate among cases with hyperthermia was 5 (11.6%). In early onset cases, 33 (16.2%) had mild and 45 (22.1%) had moderate hypothermia. In late onset cases, 37 (21.8%) had hyperthermia.

Conclusion: Most cases with neonatal sepsis had normal temperature. Mild and moderate hypothermia were found to be associated with higher mortality rate.

Keywords: Newborn, Hypothermia, Sepsis. (JPMA 66: 1303; 2016)

Introduction
Neonatal mortality rate is decreasing at a slower rate compared with under-5 mortality. As a result, the proportion of neonatal deaths among total childhood mortality is increasing, and they now account for more than 40% of under-5 mortality.¹-³ This makes it clear that the study of factors aggravating mortality rate in neonatal population cannot be overstressed. Sepsis and other infections are important causes of death in this age group and collectively they account for approximately one-third of the global burden of neonatal deaths.⁴

Patients of neonatal sepsis can present with normal, raised or low temperature. Neonatal hypothermia is one of the important factors contributing to neonatal morbidity and mortality. The World Health Organisation (WHO) has classified neonatal hypothermia in three categories i.e. mild, moderate and severe hypothermia.⁵ Many studies have evaluated the incidence and outcome of point of admission hypothermia among neonates suffering from different diseases. But according to our research, no study so far had evaluated the association between temperature and mortality rate exclusively among the cases of probable and culture-proven neonatal sepsis. Our hypothesis was that among cases of neonatal sepsis, hypothermia is associated with increased mortality and increasing severity of hypothermia can increase the mortality rate among such cases. To check this hypothesis, we compared mortality rate in different groups according to axillary temperature. This study was planned to determine whether there was any association between axillary temperature and mortality rate among cases of neonatal sepsis.

Patients and Methods
This analytical study was conducted at Fazl-e-Omar Hospital, Rabwah, Pakistan, from January to December 2013, and comprised all cases of culture-proven and probable neonatal sepsis admitted in the neonatal intensive-care unit (NICU) of the hospital. Neonatal sepsis was defined as the case of a neonate presenting with clinical signs and symptoms of neonatal sepsis with isolation of pathogen from blood, cerebrospinal fluid (CSF) or urine. Probable neonatal sepsis was defined as the case with clinical signs and symptoms of sepsis, without growth of any pathogen from blood, CSF or urine, but with one or more of these criteria: 1) the presence of leukocyte count above 30,000/cu mm, or leukocyte count below 5,000/cu mm, or C-reactive protein (CRP) >6ug/ml; 2) existence of predisposing
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factors i.e. maternal fever or foul-smelling liquor or prolonged rupture of membranes (>18 hours) or presence of gastric polymorphic leukocytes (5 or more leukocytes/high power field). All patients from birth to thirty days of age were included. Those cases of neonatal sepsis with onset of disease at ≤ 72 hours of life were categorised as early onset sepsis, and the cases with onset of the disease at > 72 hours of life were categorised as late onset sepsis. Patients with congenital heart diseases, congenital anomalies, hypoxic ischaemic encephalopathy, metabolic disorders, and respiratory distress syndromes were excluded. Blood samples of all the patients were obtained for Full Blood Count (FBC) (Merck Madonic CA 620 analyser), CRP levels, (CRP latex reagent kit of Spinreact and Merck) and blood cultures, at the time of admission. Urine samples of all the patients were obtained at the time of admission and sent for routine examination and culture. Patients were assessed for signs of meningeal irritation. Lumbar puncture was performed in cases where signs of meningeal irritation were found. CSF of these cases was sent for microscopic examination, checking of protein and glucose levels, gram staining and cultures. Stomach aspirate of those patients who were admitted in the first 24 hours of life were sent for microscopic examination.

Axillary temperature was recorded by using mercury thermometer. Before the checking of the temperature it was ensured that axilla was dry, and the thermometer was put in the axilla and the arm was pressed against the side of chest and that the bulb was in contact with the skin. Thermometer was kept in this position for 3 minutes. Hypothermia was defined according to WHO criterion, i.e. body temperature below the normal range (36.5°C to 37.5°C). Hypothermia was sub-classified into three grades: mild (36.0°C to 36.5°C), moderate (32.0°C to 35.9°C) [5], and severe (<32.0°C) hypothermia. Temperature above 37.5°C was categorised as hyperthermia.

Name, date of admission, age, diagnosis, temperature, category of temperature, white blood cell (WBC) count, platelet count, granulocyte count, CRP levels, blood culture reports, urine routine reports and culture reports, and if applicable stomach aspirate and CSF reports, and the outcome were recorded on a data form.

All the participants received appropriate antibiotics. Double entry of the data was done by doctors in charge and the statistician involved in this study. SPSS 20 was used for data analysis.

Chi-square test was used to determine association between categorical variables. P<0.05 was considered significant. The normality for continuous variables was determined using Shapiro-Wilk test.

Appropriate sample size was calculated by using WHO sample size calculator. The sample size as calculated at the prevalence of 32%, 6 level of confidence 95% and required precision of 5%. Approval was obtained from the institutional ethics committee.

Results

Of the 374 patients, 170(45.5%) were diagnosed as cases of probable sepsis and 204(54.5%) as those of cultural proven sepsis. Early onset sepsis was present in 204(54.5%) cases and late onset sepsis in 170(45.5%). Moreover, 284(75.9%) patients were discharged, 43(11.5%) left against medical advice, and 47(12.6%) died. The median axillary temperature was 36.66°C (inter-quartile range [IQR]: 0.77). Minimum and maximum axillary temperatures were 34.4°C and 40°C respectively. Besides, 217(58%) cases had normal temperature, 49(13.1%) had hyperthermia, 50(13.4%) had mild hypothermia and 58(15.5%) had moderate hypothermia. There was no case of severe hypothermia.

In early onset cases, hyperthermia was found in 12(5.8%) cases, 114(55.9%) had normal temperature, whereas 33(16.2%) had mild and 45(22.1%) had moderate hypothermia. In late onset cases, 37(21.8%) had hyperthermia, 103(60.6%) had normal temperature, while 17(10.0%) had mild and 13(7.6%) had moderate hypothermia (p=0.0001) (Table-1).

Of the 43(11.5%) hypothermia, 197(52.67%) normal temperature, 46(12.3%) mild hypothermia and 45(12.03%) moderate hypothermia cases assessed for mortality rate, 5(11.6%), 12(6.1%), 15(32.6%) and 15(33%) died (p<0.0001). Patients who left against medical advice

<table>
<thead>
<tr>
<th>Timing of Onset of Sepsis</th>
<th>Hyperthermia</th>
<th>Normal</th>
<th>Mild Hypothermia</th>
<th>Moderate Hypothermia</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early onset</td>
<td>12 (5.8%)</td>
<td>114(55.9)</td>
<td>33(16.2%)</td>
<td>45 (22.1%)</td>
<td>204</td>
</tr>
<tr>
<td>Late onset</td>
<td>37(21.8%)</td>
<td>103(60.6)</td>
<td>17(10.0%)</td>
<td>13(7.6%)</td>
<td>170</td>
</tr>
<tr>
<td>Total</td>
<td>49</td>
<td>217</td>
<td>50</td>
<td>58</td>
<td>374</td>
</tr>
</tbody>
</table>

P<0.0001.
were not included in this comparison. (Table-2).

### Discussion

Studies, conducted both in hospitals and community, show that hypothermia is a common neonatal problem. Various community-based studies have shown that the prevalence of hypothermia varies from 11% to 92.3% among neonates in different countries.6,7 Similarly different hospital-based studies showed that hypothermia was present in 32% to 85% of cases admitted with different diseases.8,9  

The above mentioned studies included patients with different diagnoses. Parameters of our study included only cases of neonatal sepsis. Hyperthermia was relatively less common i.e. 13.1%. As mentioned above, different studies show widely different prevalence rates of neonatal hypothermia. The reason for this can be that different factors like age, weight, gestational age, feeding, place of birth, early bathing, Appearance, Pulse, Grimace, Activity, Respiration (APGAR) scores, season, ambient temperature, and maternal temperature can alter the prevalence of hypothermia in neonates.10-18

Hypothermia is associated with increased risk of mortality and morbidity in neonates and children suffering from different diseases.19-25 A study by Mathur NB et al. evaluated WHO classification of hypothermia as a predictor of fatality. This study showed that mortality was 39.3% in mildly hypothermic babies, 51.6% in moderately hypothermic babies and 80% in severely hypothermic babies. Besides, that study included neonates suffering from different diseases.22 In contrast, our study showed that though the patients with hypothermia had higher mortality rate as compared to patients with normal temperature, there was no significant difference between mortality rates of babies suffering from mild and moderate hypothermia.

As hypothermia is a common neonatal problem and is associated with increased mortality,19-25 it is essential to know its clinical manifestations and complications. Health workers should be well versed with the management of neonates suffering from low temperatures. Infants suffering from hypothermia may become irritable but more often are lethargic with reduced movements, and feeding is reduced and may vomit after feeding. They will feel cold when touched, often described as clammy or with a feel like cold dough. The skin may actually become bright red, because the oxygen bound to haemoglobin fails to dissociate, which may make them look healthier while they are hypoxic. Both the respiratory rate and the heart rate decreases as body temperature falls. In critical cases scleraema can appear. If hypothermia continues, it can result in metabolic acidosis. Hypoglycaemia occurs more commonly in those infants with hypothermia as compared with neonates with normal temperature. Hypothermia is associated with dysfunction of different organs, including acute renal failure and may lead to coagulopathy.16,22-24

Treatment should focus on gradual warming. The infant’s oxygen saturation should be monitored and supplemental oxygen should be given whenever required. Moreover, blood glucose levels and arterial blood gasses should be monitored and treated as indicated. Oral feeding is recommended to be stopped and intravenous fluids are given until the patient’s temperature is close to normal.10,16

Keeping in view the serious consequences of hypothermia, it is necessary to prevent this complication. Temperature management is one of the most important components of management in neonatal intensive care units (ICUs) and delivery rooms. The greatest risk of hypothermia occurs in the initial few minutes after birth when the heat losses caused by evaporation, convection, or radiation can be very high. Without precautions, the body temperature can rapidly drop by 2°C to 3°C in just a few minutes. Despite WHO recommendations that the delivery site should be warmed to 25°C, the temperature of many well-equipped hospital delivery and operation rooms is still managed for the comfort of the adults, and thus is kept several degrees lower than the recommended level. The use of heating devices, such as a radiant warmer or additional heat lamps, is helpful, especially in reducing conductive heat loss, but do little to diminish heat loss by other routes.16-18 Healthy term newborns should be quickly dried after birth. They should then be placed in a place that can readily and effectively be kept warm. This can include a pre-heated radiant warmer, or incubator, but an even better choice following vaginal birth is to quickly place the neonate on his or her mother’s chest and cover them both with a light blanket. Skin-to-skin contact will warm the infant quickly,9 and provide a
neutral thermal environment, and will promote bonding and early breast feeding. This is effective in premature newborns as well.\textsuperscript{22,24}

**Conclusion**
Most cases of culture-proven and probable neonatal sepsis had normal axillary temperature. Hypothermia was found to be more common as compared with hyperthermia. Both mild and moderate hypothermia were found associated with mortality. Early onset neonatal sepsis was associated with hypothermia.

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**References**