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Association of Neonatal Sepsis with Hypoglycemia and Hypothermia in Preterm Infant

Dr. Farhana Rahman[1*], Dr. Fauzia Nahid[2], Dr. Dilruba Sharmin[3], Dr. Mahmuda Begum[4]

[1]Associate Professor, Department of Paediatrics, Bashundhara Ad-din Medical College and Hospital, Dhaka, Bangladesh

[2]Assistant Professor, Department of Paediatrics, Green Life Medical College, Dhaka, Bangladesh

[3]Consultant Pediatrician, Ad-din Barrister Rafique-ul-Haque Hospital, Jurain, Postogola, Dhaka, Bangladesh

[4]Assistant Professor, Department of Paediatrics, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh

***Corresponding Author**

Dr. Farhana Rahman,

Associate Professor, Department of Paediatrics, Bashundhara Ad-din Medical College and Hospital, Dhaka, Bangladesh

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ABSTRACT

Background*:* Despite advances in neonatal care, early recognition of sepsis and its associated metabolic disturbances remains challenging, particularly in vulnerable preterm neonates. Therefore, the purpose of this study was to investigate the association between neonatal sepsis and the occurrence of hypoglycemia and hypothermia in preterm newborns. ***Aim of the study:*** The aim of the study was to investigate the association between neonatal sepsis and the occurrence of hypoglycemia and hypothermia in preterm neonates.

Methods*:* This observational, comparative study was conducted in the Department of Paediatrics and Neonatal at Bashundhara Ad-din Medical College and Hospital, along with other private hospitals in Dhaka, Bangladesh, from June 2023 to May 2024. A total of 200 preterm neonates were included to investigate the association between neonatal sepsis, hypoglycemia, and hypothermia. Neonatal sepsis was diagnosed based on clinical signs and laboratory confirmation. Hypoglycemia was defined as blood glucose levels <45 mg/dL, and hypothermia was defined as a body temperature <36.5°C. Data were analyzed using SPSS version 25.0, with statistical significance set at $p<0.05$.

Results*:* Preterm neonates with neonatal sepsis had significantly lower gestational age (34.1 weeks) and birth weight (2050 grams) compared to non-septic neonates (35.3 weeks, 2170 grams). Neonatal sepsis remained predominant, accounting for 62.5% of cases. Sepsis was strongly associated with hypoglycemia (44.4% vs. 17.2%) and hypothermia (52.8% vs. 21.9%) among preterm neonates.

Conclusion*:* This study demonstrates a significant association between neonatal sepsis and the increased occurrence of hypoglycemia and hypothermia in preterm newborns.

Keywords: *Neonatal Sepsis, Hypoglycemia, Hypothermia, Preterm Neonates, Neonatal Sepsis*

1. INTRODUCTION

Neonatal sepsis refers to the presence of bacterial growth in the blood or cerebrospinal fluid and remains a major cause of morbidity and mortality in newborns [1–3]. It predominantly affects preterm and low birth weight neonates, with mortality rates ranging from 11% to 16%, and cognitive impairments observed in 12% of survivors [4,5]. The occurrence of neonatal sepsis (EONS) declines as gestational age advances, with a reported incidence of 10.96 per 1000 live births among preterm neonates [6]. EONS is typically caused by vertical transmission of bacteria during delivery [7,8] and is associated with various perinatal risk factors, including maternal group B streptococcal colonization, premature or prolonged rupture of membranes, cesarean delivery, and chorioamnionitis [9]. Despite improvements in neonatal care, early detection of EONS remains challenging, emphasizing the need for better diagnostic methods to reduce treatment delays and improve outcomes [10].

Hypoglycemia is a prevalent metabolic concern in neonatal care [11], particularly among preterm and low birth weight neonates [12,13]. Its prolonged effects on brain development, including both temporary and permanent structural abnormalities, have been documented in both preterm and full-term neonates. However, the definition of hypoglycemia remains inconsistent, as clinical thresholds for blood glucose levels vary widely across studies. Many clinicians consider hypoglycemia to be a plasma glucose level of ≤40 to 45 mg/dL, but this lack of standardization has led to conflicting findings

regarding its long-term neurodevelopmental impact [14,15]. Similarly, neonatal hypothermia, particularly in high-risk preterm neonates, is another common issue. Defined as a body temperature below 36.0°C at SCABU/NICU admission, hypothermia is associated with increased mortality and morbidity, including sepsis, intraventricular hemorrhage, bronchopulmonary dysplasia, necrotizing enterocolitis, and retinopathy of prematurity [16–18]. Research indicates that hypothermia during the neonatal period is linked to higher rates of SCABU/NICU admissions, respiratory support requirements, and longer hospital stays [19].

Emerging evidence suggests a complex relationship between neonatal sepsis and metabolic disturbances, such as hypoglycemia. The mechanisms behind sepsis-induced hypoglycemia include elevated metabolic rates, depleted glycogen stores, increased peripheral glucose utilization, and metabolic effects mediated by bacterial endotoxins [20,21]. Neonatal sepsis can also cause severe hemodynamic instability, presenting as cold shock, due to reduced cardiac output and increased vascular resistance, or warm shock, characterized by increased cardiac output and vascular dilation [22]. These circulatory changes further worsen neonatal morbidity. Additionally, both hypothermia and sepsis are inversely related to major neonatal complications like intraventricular hemorrhage and late-onset sepsis. Considering the interconnected nature of these factors, it is essential to explore the combined impact of hypoglycemia, hypothermia, and sepsis to better understand their roles in neonatal outcomes and enhance management strategies for affected neonates.

Despite improvements in neonatal care, promptly identifying neonatal sepsis and related metabolic disturbances remains difficult, especially among preterm neonates who are naturally at higher risk. Although hypoglycemia and hypothermia are frequently observed in this group, their connection to neonatal sepsis has not been thoroughly explored, and existing data are often inconclusive. Gaining clearer insight into these relationships is crucial for enabling earlier interventions and optimizing neonatal outcomes. Therefore, the purpose of this study was to investigate the association between neonatal sepsis and the occurrence of hypoglycemia and hypothermia in preterm neonates.

Objective

- The aim of the study was to investigate the association between neonatal sepsis and the occurrence of hypoglycemia and hypothermia in preterm neonates.

2. METHODOLOGY & MATERIALS

This observational, comparative study was conducted in the Department of Paediatrics and Neonatal at Bashundhara Ad-din Medical College and Hospital and other private hospitals in Dhaka, Bangladesh, between June 2023 and May 2024. A total of 200 preterm neonates were included in the study, selected based on specific inclusion criteria to investigate the association between neonatal sepsis and the occurrence of hypoglycemia and hypothermia in preterm neonates.

Inclusion Criteria

- Preterm neonates with a gestational age <36 weeks
- Birth weight < 2200 grams
- Neonates diagnosed with neonatal sepsis (Sepsis Group) or without sepsis (Non-Sepsis Group)

Exclusion Criteria

- Full-term neonates
- Neonates with major congenital anomalies
- Neonates with RDS or congenital heart disease

Informed consent was acquired from the parents of all included neonates. Baseline characteristics, including gestational age, birth weight, sex, and Apgar scores at 1 and 5 minutes, were recorded for all preterm neonates. Sepsis was diagnosed based on clinical signs and laboratory confirmation of infection. Hypoglycemia was defined as blood glucose levels <45 mg/dL, and hypothermia was defined as a body temperature <36.5°C. Data were analyzed using SPSS version 25.0, with continuous variables presented as mean ± standard deviation (SD) and categorical variables as frequencies and percentages. The difference between the groups was assessed using the Student's t-test for continuous variables and the chi-square test for categorical variables, with a p-value of <0.05 considered statistically significant.

3. RESULTS

Table 1: Baseline Characteristics of Preterm Neonates in the Sepsis and Non-Sepsis Groups

Variable	Sepsis Group (n=72)	Non-Sepsis Group (n=128)	P-value
Gestational Age (weeks)	34.1 (0.6)	35.3 (0.5)	0.001
Birth Weight (grams)	2050 (120)	2170 (110)	0.001
Male	38 (52.8%)	64 (50.0%)	0.720
Apgar Score at 1 Minute	4 (1.5)	6 (1.2)	0.002
Apgar Score at 5 Minutes	7 (1.0)	8 (0.8)	0.004

The mean gestational age was significantly lower in the sepsis group (34.1 ± 0.6 weeks) compared to the non-sepsis group (35.3 ± 0.5 weeks) (p = 0.001). Similarly, the mean birth weight was lower in the sepsis group (2050 ± 120 grams) than in the non-sepsis group (2170 ± 110 grams) (p = 0.001). The proportion of male neonates was comparable between the two groups, with 52.8% in the sepsis group and 50.0% in the non-sepsis group (p = 0.720). The mean Apgar score at 1 minute was significantly lower in the sepsis group (4.0 ± 1.5) than in the non-sepsis group (6.0 ± 1.2) (p = 0.002), and at 5 minutes, the score remained lower in the sepsis group (7.0 ± 1.0) compared to the non-sepsis group (8.0 ± 0.8) (p = 0.004).

Table 2: Association Between Sepsis and Hypoglycemia in Preterm Neonates (n=200)

Hypoglycemia Status	Sepsis Group (n = 72)	Non-Sepsis Group (n = 128)	p-value
Hypoglycemia	32 (44.4%)	22 (17.2%)	<0.001
No Hypoglycemia	40 (55.6%)	106 (82.8%)	

Table 2 presents the association between neonatal sepsis and hypoglycemia among preterm neonates. In the Sepsis Group (n = 72), 44.4% (32 neonates) were diagnosed with hypoglycemia, compared to 17.2% (22 neonates) in the Non-Sepsis Group (n = 128). The difference between the two groups is statistically significant with a p-value of <0.001, suggesting a strong association between neonatal sepsis and the occurrence of hypoglycemia in preterm neonates.

Table 3: Association Between Sepsis and Hypothermia in Preterm Neonates (n=200)

Hypothermia Status	Sepsis Group (n = 72)	Non-Sepsis Group (n = 128)	p-value
Hypothermia	38 (52.8%)	28 (21.9%)	<0.001
No Hypothermia	34 (47.2%)	100 (78.1%)	

Table 3 shows the distribution of hypothermia among preterm neonates with and without sepsis. Among the sepsis group (n=72), 38 neonates (52.8%) experienced hypothermia, compared to 28 neonates (21.9%) in the non-sepsis group (n=128). The difference was statistically significant (p<0.001), indicating a strong association between hypothermia and neonatal sepsis in preterm neonates.

4. DISCUSSION

This study highlights the association between neonatal sepsis and the occurrence of hypoglycemia and hypothermia among preterm neonates admitted to hospitals in Dhaka, Bangladesh. Neonatal sepsis remains a significant cause of morbidity and mortality in preterm populations, often presenting with subtle metabolic disturbances that can complicate clinical management. The findings underscore the critical link between infection and metabolic instability, with lower gestational age, lower birth weight, and compromised Apgar scores emerging as important contributing factors. The strong association between sepsis, hypoglycemia, and hypothermia emphasizes the need for vigilant monitoring and early intervention to improve outcomes in vulnerable preterm neonates.

In the present study, preterm neonates with neonatal sepsis had significantly lower gestational age, lower birth weight, and lower Apgar scores compared to non-septic neonates, while the distribution of sex was comparable between the two groups. These findings are consistent with the results of Jatsho et al.[23], who also reported that neonates with sepsis tended to have lower gestational age, reduced birth weight, and lower Apgar scores at 5 minutes, although no significant difference was

observed regarding sex distribution. Similarly, Al-Wassia et al.[24] demonstrated that lower gestational age and birth weight were strongly associated with the development of neonatal sepsis, supporting the trends observed in the current study. Additionally, the study by Li et al.[25] corroborated these findings, highlighting that younger gestational age, lower birth weight, and male sex were common among neonates who developed sepsis, although in our cohort the sex distribution was not statistically different between groups. These parallels reinforce that in preterm neonates, physiological immaturity and poor Apgar performance may predispose to both sepsis and its related complications, such as hypoglycemia and hypothermia, which remain key concerns in neonatal care.

In this study, hypoglycemia was observed in 44.4% of the sepsis group compared to 17.2% of the non-sepsis group, demonstrating a statistically significant association ($p < 0.001$). These findings are consistent with the results reported by Kumar et al.[26], who identified hypoglycemia as a significant risk factor for neonatal sepsis in preterm neonates. The higher incidence of hypoglycemia among septic preterm neonates highlights the metabolic vulnerability associated with sepsis in this population. This observation underscores the importance of routine glucose monitoring and prompt management of hypoglycemia as part of the comprehensive care strategy for preterm neonates at risk of sepsis.

In this study, hypothermia was significantly more frequent in the sepsis group compared to the non-sepsis group (52.8% vs. 21.9%, $p<0.001$), indicating a strong association between hypothermia and neonatal sepsis in preterm neonates. These findings are consistent with the results reported by Yu et al.[27], who, through a multicenter study across 28 NICUs in China, demonstrated that admission hypothermia was significantly associated with adverse neonatal outcomes, including an increased risk of sepsis in very low-birth weight neonates. Similarly, Hogeveen et al.[28] highlighted that hypothermia in very preterm neonates is linked to higher rates of mortality and morbidity, underscoring the critical role of maintaining normothermia to prevent complications such as sepsis. The results of the present study reinforce the importance of vigilant thermal regulation in the early management of preterm neonates to mitigate the risk of sepsis.

Limitations of the study

This study had some limitations:

- The sample was not randomly selected.
- The study's limited geographic scope may introduce sample bias, potentially affecting the broader applicability of the findings.

5. CONCLUSION

In conclusion, this study highlights a significant association between neonatal sepsis and the occurrence of hypoglycemia and hypothermia in preterm neonates. Neonates with sepsis were found to have lower gestational age, low birth weight, and Apgar scores compared to non-septic neonates. Additionally, neonatal sepsis was strongly correlated with increased incidences of both hypoglycemia and hypothermia, emphasizing the need for early identification and management of these conditions in preterm neonates. These findings underscore the importance of close monitoring and prompt intervention to improve outcomes for preterm neonates at risk of sepsis and its complications.

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