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EFFECT OF GLYCEMIC STATUS IN NEONATAL SEPSIS-A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Introduction: Neonatal hypoglycemia is a common and readily treatable risk factor for neurologic impairment in children. Although associations between prolonged symptomatic neonatal hypoglycemia and brain injury are well established, the effect of milder hypoglycemia on neurologic development is uncertain. **Objective:** To determine the glycemic status among patients with neonatal sepsis and to evaluate their association with the mortality. **Methods:** It was a prospective observational study conducted at Department of Pediatrics, Rajshahi Medical College Hospital, Rajshahi, Bangladesh from July 2021 to June 2022. Total 52 patients clinically diagnosed as neonatal sepsis were studied, a detailed history and thorough physical examination was done in each patient on admission. History included age of newborn, sex, gestational age, h/o prolonged rupture of membrane (PROM), intrapartum fever or fever 3 days before delivery, per vaginal foul smelling discharge, prolonged labor and features of sepsis. Physical examination included respiratory rate, heart rate, temperature, chest indrawing, grunting, cyanosis, convulsion, breath sound, added sound, weight, jaundice, bleeding manifestation, status of fontanelles, umbilicus and capillary refill time. Blood glucose level and mortality of neonates having hypoglycemia and hyperglycemia were analyzed. **Results:** Out of 52 patients clinically diagnosed as neonatal sepsis were

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studied. The mean age was found 10.2 ± 8.4 days with range from 1 to 28 days and more than half (51.6%) patients belonged to age ≤ 7 days. More than two third (68.7%) patients were male and 31.3% were female. 42(80.77%) patients were found CRP positive and 10(19.23%) were negative CRP. 34.62% patients were blood culture positive and 65.38% patients were culture negative. Majority (71.43%) of CRP positive patients were found normoglycemic, 11.90% were found hypoglycemic and only 16.67% were found hyperglycemic. Among 18 culture positive patients 11(61.11%) were normoglycaemic, 3(16.67%) were hypoglycemic and 4(22.22%) were hyperglycemic. 57.1% of hyperglycemic and 40% of hypoglycemic patients were died whereas only 13.3% of normoglycemic patients were died. Out of 10 expired patients, 2 patients Hypoglycemia, 4 patients Normoglycemia and 4 patients Hyperglycemia. Mortality was high in Hypoglycemia patient (40.0%) in comparison with normoglycaemic patient (13.33%) and the difference was not statistically significant ($p > 0.05$) between two groups. Mortality was also high in hyperglycaemic patient (57.14%) in comparison with normoglycaemic patient (13.33%) and the difference was statistically significant ($p < 0.05$) between two groups. **Conclusion:** Alteration of glycemic status occurred in septic newborn. Our study showed mortality is higher among the septic newborn with hyperglycemia. The incidence of hypoglycemia was high as compared to hyperglycemia. Neonatal hypoglycemia and hyperglycemia was a significant factor in the overall mortality in neonatal sepsis.

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INTRODUCTION

Neonatal hypoglycemia is a common and readily treatable risk factor for neurologic impairment in children. Although associations between prolonged symptomatic neonatal hypoglycemia and brain injury are well established, [1] the effect of milder hypoglycemia on neurologic development is uncertain [2]. Consequently, large numbers of newborns are screened and treated for low blood glucose concentrations, which involves heel-stick blood tests, substantial costs, and the possibility of iatrogenic harm. Under current guidelines, [3] up to 30% of neonates are considered to be at risk for hypoglycemia, 15% receive a diagnosis of hypoglycemia, and approximately 10% require admission to a neonatal intensive care unit, [4] costing an estimated \$2.1 billion annually in the United States alone [5]. Severe and prolonged

neonatal hypoglycemia is associated with a risk of long term neurodevelopmental sequelae like microcephaly, epilepsy, visual impairment and long-term disability. Persistent hypoglycemia leads to irreversible cellular dysfunction, organ failure and eventually death. Hyperglycemia is defined as a plasma glucose level more than 145mg/dl [6]. Neonatal hyperglycemia can occur in conditions like - parenteral glucose, very low birth baby, lipid infusion, sepsis, mechanical ventilation, hypoxia, surgical procedures, neonatal diabetes etc. Major clinical problem associated with hyperglycemia are hyperosmolarity and osmotic diuresis that leads to alteration of cerebral autoregulation. In neonatal sepsis several neuroendocrine and inflammatory mediators are released which causes hyperglycemia. In septicemia there is an increased production of stress hormone like

glucagon, growth hormone, catecholamine's, and glucocorticoids. Associated formula feeding and possible separation of mother and baby reduce breast-feeding rates, [7] with potentially adverse effects on broader infant health and development. In addition, pain-induced stress in neonates, such as repeated heel sticks, may itself impair brain development [8]. Thus, to determine appropriate glycemic thresholds for treatment, there have been repeated calls for studies of the effect of neonatal hypoglycemia on long-term development [3,9]. The present study was designed to determine the glycemic status among patients with neonatal sepsis and to evaluate their association with the mortality.

MATERIALS AND METHODS

It was a prospective observational study conducted at Department of Pediatrics, Rajshahi Medical College Hospital, Rajshahi, Bangladesh from July 2021 to June 2022. Total of 52 patients clinically diagnosed as neonatal sepsis were studied. A detailed history and thorough physical examination was done in each patient on admission. History included age of newborn, sex, gestational age, h/o prolonged rupture of membrane (PROM), intrapartum fever or fever 3 days before delivery, per vaginal foul smelling discharge, prolonged labor and features of sepsis. Physical examination included respiratory rate, heart rate, temperature, chest indrawing, grunting, cyanosis, convulsion, breath sound, added sound, weight, jaundice, bleeding manifestation, status of fontanelles, umbilicus and capillary refill time. Patients with infants of diabetic mother, perinatal asphyxia, meconium aspiration syndrome, Congenital anomalies were excluded. Those cases who received intravenous glucose or antibiotics before admission were also excluded from this study. Blood glucose level and mortality of neonates having hypoglycemia and hyperglycemia were analyzed.

Venous blood was collected before giving any intravenous fluid, dextrose or antibiotics and blood sugar, complete blood counts, CRP levels and blood culture were send to laboratory within half hour of collection. Lumbar puncture was done in those patients who showed signs and symptoms of meningitis to obtain cerebrospinal fluid for microscopic examination, protein, glucose levels and culture. CRP levels > 6 mg/L considered as positive and less than 6 mg/L considered as negative. For this study glucose levels were divided into three groups i.e. < 45 mg/dl, 45-145 mg/ dl, and > 145 mg/dl. All patients included in this study were treated accordingly and followed up strictly. The outcome and relevant data from history, physical examination and investigations were recorded in predesigned questionnaire.

Sepsis screening criteria:

- Absolute Neutrophil Count (ANC): < 1800/cu mm.
- Total Leukocyte Count (TLC): < 5000/cu mm or > 20,000/ cu mm.
- CRP: > 6 mg/dL.
- Platelets < 150000 /cu mm.

Data were processed manually and analyzed with the help of SPSS (Statistical package for social sciences) Version 19.0. Quantitative data were expressed as mean and standard deviation. Qualitative data were expressed as frequency and percentage and comparison carried by Chi-square (χ^2) test. A probability (p) value of 0.05 taken as non-significant.

RESULTS

Out of 52 patients clinically diagnosed as neonatal sepsis were studied. The mean age was found 10.2 ± 8.4 days with range from 1 to 28 days and more than half (51.6%) patients belonged to age ≤ 7 days. More than two third (68.7%) patients were male and 31.3% were female. 42(80.77%) patients were found CRP positive and 10(19.23%) were negative CRP. 34.62% patients were blood culture positive

and 65.38% patients were culture negative (Table-1, Fig-1).

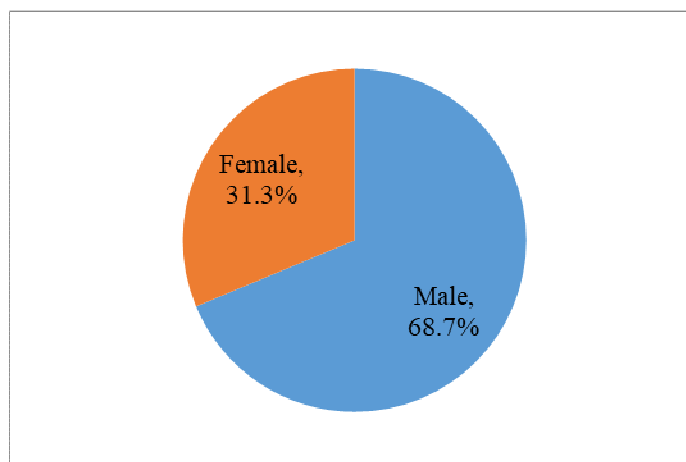


Fig-1: Sex distribution of the patients.

Table-1: Distribution of the study patients by blood culture (n=52)

Blood for Culture	Number of patients	Percentage
Positive	18	34.62
Negative	34	65.38

Table-2: Glycemic status of the CRP positive patients (n=42)

Glucose level (mg/dl)	Number of patients	Percentage
<45 (Hypoglycemia)	5	11.90
45-145 (Normoglycemia)	30	71.43
>145 (Hyperglycemia)	7	16.67

Majority (71.43%) of CRP positive patients were found normoglycemic, 11.90% were found hypoglycemic and only 16.67% were found hyperglycemic (Table-2).

Table-3: Glycemic status of the culture positive patients (n=18)

Glucose level (mg/dl)	Number of patients	Percentage
<45 (Hypoglycemia)	3	16.67
45-145 (Normoglycemia)	11	61.11
>145 (Hyperglycemia)	4	22.22

Among 18 culture positive patients 11(61.11%) were normoglycaemic, 3(16.67%) were hypoglycemic and 4(22.22%) were hyperglycemic (Table-3).

Table-4: Glycemic status among the expired patient (n=10)

Glucose level (mg/dl)	Number of patients	Died No (%)
<45 (Hypoglycemia)	5	2(40.0)
45-145 (Normoglycemia)	30	4(13.33)
>145 (Hyperglycemia)	7	4(57.14)

57.14% of hyperglycemic and 40% of hypoglycemic patients were died whereas only 13.33% of normoglycemic patients were died. Out of 10 patients, 2 patients Hypoglycemia, 4 patients Normoglycemia and 4 patients Hyperglycemia (Table-4).

Table-5: Association of hypoglycemia with mortality (n=35)

Glucose status	Total	Mortality		p-value
		N	%	
Normoglycemia	30	4	13.33	0.095 ^{ns}
Hypoglycemia	5	2	40.0	

Mortality was high in Hypoglycemia patient (40.0%) in comparison with normoglycaemic patient (13.33%) and the difference was not statistically significant ($p>0.05$) between two groups (Table-5).

Table-6: Association of hyperglycemia with mortality (n=37)

Glucose status	Total	Mortality		p-value
		N	%	
Normoglycemia	30	4	13.33	0.044 ^s
Hyperglycemia	7	4	57.14	

Mortality was also high in hyperglycaemic patient (57.14%) in comparison with normoglycaemic patient (13.33%) and the difference was statistically significant ($p<0.05$) between two groups (Table-6).

DISCUSSION

This observational study was carried out with an aim to determine the glycaemic status in neonatal sepsis and to evaluate the association of hypoglycemia and hyperglycemia with mortality in patient of neonatal sepsis. Out of 52 patients clinically diagnosed as neonatal sepsis were studied. The mean age was found 10.2 ± 8.4 days with range from 1 to 28 days and more than half (51.6%) patients belonged to age ≤ 7 days. In this study it was observed that majority (71.43%) of the patients were normoglycemic (45-145 mg/dl) followed by 11.90% hypoglycemic (<45 mg/dl) and 16.67% hyperglycemic (>145 mg/dl). Ahmad and Khalid [10] study showed the glucose levels were below 40 mg/dl in 9.9%, between 40 mg/dl to 100 mg/dl in 64.1%, between 101 mg/dl to 200 mg/dl in 18.9% and above 200 mg/dl in 6.9% patients. In another study Begum et al [11] observed hyperglycemia in 4.62% of their study patients. A neonate having sepsis develops

reluctance to take feed and this can lead to hypoglycemia. Similarly increased metabolic demand and hypothermia caused by sepsis can bring down the glucose level. Different reasons for this association have been proposed e.g. enhanced apoptosis, increased production of cytokine, hypercoagulation, acute dyslipidemia, endothelial dysfunction etc. During the past few years many studies have been conducted to ascertain importance and consequences of hyperglycemia and hypoglycemia in both pediatric and adult patients. Several studies have shown that hyperglycemia is associated with adverse outcomes in the pediatric age group. A study by Wintergerst et al [12] has shown that hyperglycemia, hypoglycemia and glucose variability are associated with increased mortality rates and increased length of stay in PICU. A neonate having sepsis develops reluctance to take feed and this can lead to hypoglycemia. Similarly increased metabolic demand and hypothermia caused by sepsis can bring down the glucose level. Different reasons for this association have been proposed e.g. enhanced apoptosis, increased production of cytokine, hyper coagulation, acute dyslipidaemia, endothelial dysfunction

etc. During the past few years many studies have been conducted to ascertain importance and consequences of hyperglycemia and hypoglycemia in both pediatric and adult patients. Several studies have shown that hyperglycemia is associated with adverse outcomes in the pediatric age group. Among 18 culture positive patients 11(61.11%) were normoglycaemic, 3(16.67%) were hypoglycemic and 4(22.22%) were hyperglycemic. Ahmad and Khalid [10] found 32% mortality in hypoglycemic patient which was consistent with the finding of present study. It was observed that, 57.14% of hyperglycemic and 40% of hypoglycemic patients were died whereas only 13.33% of normoglycemic patients were died. Out of 10 patients, 2 patients Hypoglycemia, 4 patients Normoglycemia and 4 patients Hyperglycemia. Lugt, et al. found that 27 out of 66 infants with hyperglycemia (41.0%) died [12]. Similar finding also observed by Ahmad & Khalid which are comparable with the present study. Patients of neonatal sepsis with high blood glucose levels were at increased risk of death, and should be treated as high risk patients [7]. Limitation of this study is we measure blood sugar level from peripheral blood samples. Venous blood samples can provide more accurate information on blood sugar levels in the body. Blood sugar levels was taken when neonate diagnosed with sepsis so that it cannot detect episodes of changes in blood sugar levels earlier.

CONCLUSION

Alteration of glycaemic status occurred in septic newborn. Our study showed mortality is higher among the septic newborn with hyperglycemia. The incidence of hypoglycemia was high as compared to hyperglycemia. Neonatal hypoglycemia and hyperglycemia was a significant factor in the overall mortality in neonatal sepsis.

Conflict of Interest: None.

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