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Glycemic Status and its Effect in Neonatal Sepsis in a Tertiary Care Hospital

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Abstract

Introduction: *Neonatal sepsis can alter the glucose level and both hypoglycemia and hyperglycemia may occur. A high or low blood glucose level may have a significant effect on the outcomes in patients of neonatal sepsis.*

Objective: *To see the glycemic status and its effect on outcome of neonatal sepsis.*

Methods: *This prospective observational study was done in the department of paediatrics, Sylhet MAG Osmani Medical College Hospital, Sylhet from July 2013 to December 2013. Clinically suspected neonatal sepsis cases were enrolled in the study. Venous blood was collected before giving any intravenous fluid or antibiotics for blood sugar, full blood counts, CRP levels and blood culture and send to labouratory within half hour of collection. All patients included in this study were treated accordingly and followed up strictly. Blood glucose level and mortality of neonates having hypoglycemia and hyperglycemia were analyzed among CRP and culture positive patients. 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.*

Results: *A total of 62 patients clinically diagnosed as neonatal sepsis were studied. Fifty two (83.9%) patients were found CRP positive and 21(33.9%) patients were blood culture positive. Glycemic status was analyzed among CRP and culture positive patients. Majority (71.2%) patients were found normoglycemic, 13.5% were found hypoglycemic and 15.3% were found hyperglycemic in this study. Fifty one (82.2%) patients were cured and 9(17.8%) were died. Mortality was high in hypoglycaemic patients (42.8%) compare with normoglycaemic patients (10.8%), but the difference was not statistically significant ($p>0.05$) between two groups whereas mortality was also high in hyperglycaemic patients (50%) compare with normoglycaemic patients (10.8%) and the difference was statistically significant ($p<0.05$) between two groups.*

Conclusion: *Alteration of glycemic status occurred in septic newborn. Mortality is higher among the septic newborn with hyperglycemia.*

Key words: *Glycemic status, Neonatal sepsis, Outcome.*

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Introduction

Despite advances in maternal and neonatal care, infection remain a frequent and important cause of neonatal and infant mortality and morbidity.[1] Neonatal mortality is associated with about 41% of all death among under-five children.[2] Glucose is a very important substrate of metabolism especially in the brain.[3] Hypoglycemia is defined as a blood glucose less than 40 mg/dl.[4] Many different neonatal groups are at a risk of developing low blood glucose concentration for

example pre-term baby, large for gestational age, infant of diabetic mother, intrauterine growth restriction (IUGR), sepsis, shock, asphyxia, hypothermia, respiratory distress syndrome (RDS).[5] Sepsis has been known to be the cause of 9.6% cases of neonatal hypoglycemia.[6] A neonate having sepsis develops reluctance to feed and this can lead to hypoglycemia. Similarly increased metabolic demand and hypothermia caused by sepsis can bring down the glucose level.[7] 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.[5] 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. Hyperosmolar state can also cause water to move from intracellular compartment to extracellular compartment. The resultant contraction of intracellular volume of the brain may cause intracranial haemorrhage.[5]

In neonatal sepsis several neuroendocrine and inflammatory mediators are released which causes hyperglycemia. In septicaemia there is an increased production of stress hormone like glucagon, growth hormone, catecholamines, and glucocorticoids. These hormonal changes (also known as the counter-regulatory response) and an increase in pro-inflammatory cytokines, i.e- interleukin (IL-1, IL-6), and tumor necrosis factor (TNF)- alpha, are important factors leading to hyperglycemia.[8]

A high or low blood glucose level may have a significant effect on the outcomes in patients of neonatal sepsis. A recent study in Pakistan found that those patients of neonatal sepsis with altered glucose level had higher mortality.[7] 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 during July 2013 to December 2013 in the Department of Paediatrics, Sylhet MAG Osmani Medical College Hospital, Sylhet. 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 labour 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.

Term neonate having birth weight ≥ 2000 gm and ≤ 4000 gm with clinically suspected neonatal sepsis presented with one or more of the clinical features of neonatal sepsis: According to the **"**National Neonatal Health Strategy and Guideline for Bangladesh 2009" were included in this study**.** Clinical features of neonatal sepsis are **:** 1) Not feeding well 2) Convulsions 3) Fast breathing (>60 breath/min on second count) 4) Severe chest indrawing 5) Low body temperature (less than 35.5ºC or 95.9ºF) 6) Fever (more than 37.5ºC or 99.5ºF) 7) Movement only when stimulated or no movement at all. 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 or antibiotics for blood sugar, full blood counts, CRP levels and blood culture. Sample was send to labouratory with in half hour of collection. CRP levels > 6mg/L considered as positive and d"6mg/L considered as negative. For this study glucose levels were divided into three groups i.e. < 45 mg/dl, 45-145mg/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.

Data were processed manually and analyzed with the help of SPSS (Statistical package for social sciences)

Version 16.0. 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 was considered statistically significant and p<0.01 was considered highly significant but p >0.05 taken as non-significant.

Informed written consent was taken from each patient's guardians. This study was approved by ethical committee of Sylhet MAG Osmani Medical College, Sylhet.

Results

A total of 62 patients clinically diagnosed as neonatal sepsis were studied. The mean age was found 10.1±8.5 days with range from 1 to 28 days and more than half (51.6%) patients belonged to age ≤7 days. More than two third (67.7%) patients were male and 32.3% were female. 52(83.9%) patients were found CRP positive and 10(16.1%) were negative CRP . 33.9% patients were blood culture positive and 41(66.1%) patients were culture negative (Table -I). Glycemic status was analyzed among CRP positive and culture positive patients.

Table - I

Distribution of the study patients by blood culture (n=62)

Blood for Culture	Number of patients	Percentage
Positive	21	33.9
Negative	41	66.1

Majority (71.2%) of CRP positive patients were found normoglycemic, 13.5% were found hypoglycemic and only 15.3% were found hyperglycemic (Table-II). Among 21 culture positive patients 12(57.2%) were normoglycaemic, 4(19%) were hypoglycemic and 5(23.8%) were hyperglycemic (Table-III). It was observed that 51(82.2%) patients were cured and 11(17.8%) were died. Among the 11 expired patients all were CRP positive and 9 patient were also culture positive. Out of expired 11 patients, 4 patients were hyperglycemic, 3 were hypoglycemia and 4 were normoglycemic. Fifty percentage (50%) of hyperglycemic and 42.8% of hypoglycemic patients were died where as only 10.8% of normoglycemic patients were died (Table-IV).

Table-II

Glycemic status of the CRP positive patients (n=52)

Glucose level (mg/dl)	No. of patients	Percentage
<45 (Hypoglycemia)	7	13.5
45-145 (Normoglycemia)	37	71.2
>145 (Hyperglycemia)	8	15.3

Table-III

Glycemic status of the culture positive patients (n=21)

Glucose level (mg/dl)	No. of patients	Percentage
<45 (Hypoglycemia)	4	19.0
45-145 (Normoglycemia)	12	57.2
>145 (Hyperglycemia)	5	23.8

Table -IV

Glycemic status among the expired patient (n=11)

Glucose level (mg/dl)	No. of patients	Died No(%)
<45 (Hypoglycemia)	7	3(42.8)
45-145 (Normoglycemia)	37	4(10.8)
>145 (Hyperglycemia)	8	4(50.0)
Total	52	11

Mortality was high in hypoglycaemic patient (42.8%) in comparison with normoglycaemic patient (10.8%) and the difference was not statistically significant (p>0.05) between two groups (Table-V). Mortality was also high in hyperglycaemic patient (50%) in comparison with normoglycaemic patient (10.8%) and the difference was statistically significant (p<0.05) between two groups (Table VI).

Table-V

Association of hypoglycemia with mortality (n=44)

Glucose status	Total	Mortality		P
	no	Total	%	value
Normoglycemia	37	4	10.8%	0.095^{ns}
Hypoglycemia	7	3	42.8%	

ns= not significant

P value reached from chi-square test

Table-VI

Association of hyperglycemia with mortality (n=45)

Glucose status	Total	Mortality		P
	no	Total	%	value
Normoglycemia	37	4	10.8%	0.044[s]
Hyperglycemia	8	4	50.0%	

s= significant

P value reached from chi-square test

Discussion

This observational study was carried out with an aim to determine the glycemic status in neonatal sepsis and to evaluate the association of hypoglycemia and hyperglycemia with mortality in patient of neonatal sepsis.

In this study it was observed that majority (71.2%) of the patients were normoglycemic (45-145 mg/dl) followed by 13.5% hypoglycemic (<45 mg/dl) and 15.3% hyperglycemic (>145 mg/dl). Ahmad and Khalid[7] 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[9] 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.

During the past few years many studies have been conducted to ascertain importance and consequences of hyperglycemia and hypoglycemia in both paediatric and adult patients. Several studies have shown that hyperglycemia is associated with adverse outcomes in the paediatric age group. Different reasons for this association have been proposed e.g. enhanced apoptosis, increased production of cytokine, hypercoagulation, acute dyslipidemia, endothelial dysfunction etc. A study by Wintergerst et al[10] has shown that hyperglycemia, hypoglycemia and glucose variability are associated with increased mortality rates and increased length of stay in PICU.

In this present study It was observed that mortality was high in hypoglycaemic patient (42.8%) compared with normoglycaemic patient (10.8%), but the difference was not statistically significant (p>0.05). Ahmad and Khalid[7] found 32% mortality in hypoglycemic patient which is consistent with the finding of present study.

It was also observed in this current study that mortality was also high in hyperglycaemic patient (50.0%) compared with normoglycaemic patient (10.8%), which is statistically significant (p<0.05). Lugt et al[11] found that 27 out of 66 infants with hyperglycemia (41.0%) died. Similar finding also observed by Ahmad and Khalid[7] which are comparable with the present study.

Patients of neonatal sepsis with high blood glucose levels are at increased risk of death, and should be treated as high risk patients. Patients of neonatal sepsis should be detected early and should receive early treatment, before hyperglycemia set in.

Conclusion

Alteration of glycemic status occurred in septic newborn. Mortality is higher among the septic newborn with hyperglycemia.

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