DS (Child) H J 2019; 35(2) : 105-110

ORIGINAL ARTICLE

Role of Macronutrient in Better Survival of Critically Sick Neonates Admitted in Neonatal Intensive Care Unit (NICU)

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Abstract

Background*: Neonates are considered more susceptible to macronutrient deficits. During critical illness, sick children cannot normally be fed by mouth, and as a result a pronounced macronutrient deficit often develops after a few days. This macronutrient deficit has been associated with weakness, infections and increased risk of mortality.Therefore, macronutrient as energy source is an important key concern to care and for overall to achieve better survival.*

Objective*: The present study is intended to evaluate the role of macronutrient such as blood glucose, serum calcium, hemoglobin as iron status, serum albumin, in critically sick neonates admitted in NICU and their outcome.*

Methods*: This observational prospective study was carried out at NICU of Dhaka Shishu (Children) Hospital from January 2014 to July 2014. Total 121 neonates were enrolled and analyzed their essential macronutrient profile e.g, blood glucose, serum calcium, hemoglobin, serum albumin and other relevant investigation as complete blood count with film, CRP, blood culture and chest X ray as a part of management as well as to predict their survival.*

Results*: Macronutrient of critically sick neonates play important role to predict their better survival. Perinatal asphyxia and sepsis were major diagnosed pathological conditions of these neonates. In sepsis lower value of serum albumin were statistically significant. Lower value of glucose, calcium, hemoglobin and albumin were also statistically significant in Non-survivors than Survivors.*

Conclusion: *During critical illness in neonates, emphasis should be paid on of adequate macronutrient as energy source. This is necessary for better optimization survival of critically sick neonates.*

Keywords*: Macronutrient, survival, critically sick neonates.*

Introduction

Neonates can acutely decompensate from a variety of causes. However, they have a limited repertoire of responses to stress and their presenting signs are nonspecific. Therefore prompt evaluation, initial stabilization with proper management of critically ill neonates present a special challenge for pediatrician to encounter the compromised condition. Critical

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Received: 08 September 2019; **Accepted**: 15 October 2019

illness in newborn, major devastating health problems with survival in Bangladesh like other developing countries.

Critical illness is accompanied by a hypermetabolic state related to stress response inducing catabolic state with activation of various catabolic hormones[1] characteristic of the critically ill newborn infant.[2] Their activation are critical short-term adaptations to promote survival[2] allows the body to quickly catabolize macronutrient from their stores, in order to cover the immediate high energy demands.[3] This situation results in elevated energy expenditure and thereby increased energy requirements.[4] Therefore, on any critical situation energy source is the valuable need.Poor energy reservoir or less intake increased incidence of complications as infections, even organ failure and increased risk of mortality.[5,6] During critical illness should provide essential macronutrient as glucose, calcium, hemoglobin, albumin- important impact on the patient's positive clinical outcome.[7]

Neonates are considered more susceptible to macronutrient deficits.[8] Critically ill neonates cannot normally be fed by mouth, as a result a pronounced macronutrient deficit often develops after a few days. This macronutrient deficiency has been associated with infections, weakness, and delayed recovery.[9-12] Hypoglycemia can occur in stress situation of any critical ill newborn due to an inability to perform adequate gluconeogenesis. Glucose serves as the major source of energy for living cells in the form of ATP. Most tissues of the body can live without O_2 for several minutes even as long as 30 minutes. During this time as anaerobic metabolism, the tissue cells obtain their energy through breaking down glucose and glycogen at the expense of consuming tremendous amounts. However, it does keep the tissues alive.[13] Undernormal conditions most brain energy is supplied by glucose.The neonatal brain is highly dependent on glucose as an energy source to support its high metabolic rate.[14] Hypoglycaemic neonates may have used their glycogen stores during perinatal asphyxia.[15] So in asphyxia at the molecular level as a failure of energy supply sufficient to cause cellular damage.[16] The body makes metabolic adaptations to increase the chance of survival. The adaptations produce additional fuel, primarily in the form of glucose from glycogen, de-aminated amino acids and triglycerides. Peripheral insulin resistance is prominent presumably as a mechanism to shunt glucose to organs necessary for survival such as the brain and the heart. The response is similar in critically ill children.[17] Regular ward monitoring of blood glucose with dipsticks or tapes is standard practice.[15]

Calcium is another major need for living cells, an important second messenger in the body helps carrying out muscle function and acts as cofactor for several enzymatic activities. Hypocalcemia is common in critically sick neonates due to defective hydroxylation of 25-hydroxycholecalciferol as in intrapartum hypoxia or physiological immaturity. Experienced clinicians will recognize slight jitteriness as a good guide to this condition.[18] Maintaining homeostasis and normal serum concentrations of calcium is important because hypocalcemia can affect optimal respiratory and cardiac function. Transient neonatal hypocalcemia often is exacerbated by acute respiratory disease and, when severe, can cause tetany and cardiac arrhythmias.[19] Therefore, correct measurement of serum calcium level is more important and proper remedy as supplement to better survival of critically ill neonates[19]. Hypoglycemia and hypocalcemia are common nutritional problems and have direct consequences in neonatal period. Prompt identification and treatment to prevent worse outcome.

Protein status is also negatively influenced by illness in neonates. Protein breakdown is an essential part of stress physiology because de-aminated amino acids are recycled through the liver as carbon sources for gluconeogenesis, particularly when the glycogen stores of the neonate have been utilized.[14] Protein catabolism occurs during neonatal sepsis,[20] presumably driven by pro-inflammatory cytokines.[21] Hypoalbuminemia is frequent among critically ill neonates with sepsis.[22] Lower albumin status leads to low oncotic pressure, which can result in or exacerbate edema might be associated with a poorer prognosis of newborn.[19] Hypoalbuminemia also affect on calcium concentration.[23] Therefore, protein specially albumin is more than essential for optimal life survival.

Although it may be important to maintain normal hemoglobin concentrations in neonates who have acute respiratory disease to optimize oxygen

delivery. Most infants are born with sufficient iron stores to maintain them through the period of acute disease, rapid decrease in hemoglobin(due to blood drawing) are treated by transfusion, not by infusion of parenteral iron.[19]

Timely recognition, a high index of needed and a through understanding of common macronutrient as energy source are necessary to ensure their adequate provision as well as reduce mortality of critically ill neonates. This study was carried out in neonates with various ailments admitted in NICU at a tertiary care hospital, Dhaka Shishu Hospital, Dhaka, Bangladesh.

Materials and Methods

This observational prospective study was conducted at NICU, Dhaka Shishu (Children) Hospital during the period of January 2014 to July 2014. For each neonate, a detailed history from mother or other care-giver was recorded in a preset questionnaire.

Total 161 neonates admitted during this period. Out of them, 40 were excluded from this study due to congenital anomalies(medical or surgical), jaundiced due to blood group incompatibilities or received LAMA (Left against medical advice). Before enrollment, parent of each neonate was given a detail explanation about nature and purpose of the study.

Total 121 neonates were analyzed for essential macronutrients parameter, e.g., blood glucose, serum calcium, hemoglobin, albumin as well as other baseline investigations for proper management. Blood glucose was done using glucometer and values were estimated by glucose oxidase method. Serum calcium was measured by calorimetric test method.

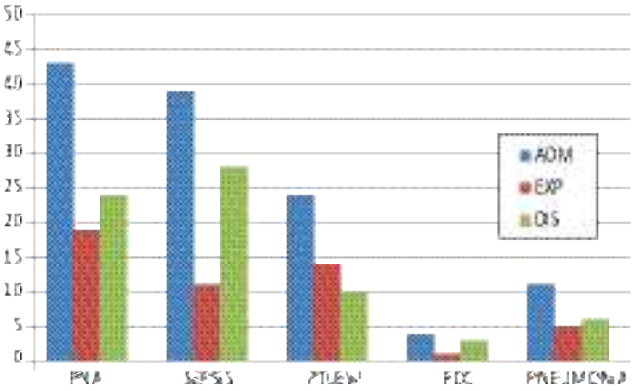
Each case was thoroughly examined and follow-up regularly. Definite neonatal septicemia was diagnosed by positive blood culture and probable septicemia was diagnosed by a scoring system[24] or positive CRP.

Normal range of blood glucose (2.75-4.4mmol/L),[25] Serum calcium (2.25-2.65mmol/L),[26] Hemoglobin (14-20 gm/dl with an average value of 17gm/dl)[27] and Serum albumin (25-43gm/2)[23] were considered.

For further follow-up nutritional parameter and relevant investigations were done as required. Unpaired t-test was used to test significance difference of macronutrient status of critically ill neonates and also significance difference among survivors and non-survivors.

Results

The study was carried out on the basis of neonates suffering from a wide variety of disease pattern admitted NICU care and their mortality (Fig1). The selection was unbiased and generalized.



ADM=Admission, EXP=Expired, DIS=Discharge

Fig 1 *Disease pattern of enrolled neonates and their outcome*

This study was carried out over a period of six months. The median age of neonates was 7 days. Preponderance of males in this age group. Among 121, eighty four (84%) neonates were male and thirty seven (37%) were female, 2.27:1.

Non-survivors had significantly lower glucose, calcium level (at admission/initial) than Survivors (Table I). Among major diagnosed pathological diseases of critically sick neonates, neonatal sepsis had significantly lower value of serum albumin (Table II). Even non-survivors had significantly lower not only glucose, calcium level also hemoglobin and albumin than survivors (at discharge/death) (Table III).

Table I

Baseline Macronutrient profile (Mean ±SD) in Survivors and Non-Survivors (admission/initial)

	Survivors (n=71) Mean±SD	Non-Survivors (n=50) Mean±SD	p value
B. Glucose	3.61±2.25	3.22±0.07	**0.020^{s}**
S. Calcium	2.06±0.17	2.03± 0.15	**0.020^{s}**
Hemoglobin	17.61±4.42	15.50±6.33	0.055^{ns}
S. Albumin	23.04±0.24	25.92±4.11	0.060^{ns}

p value reached from unpaired t-test

Table II
Macronutrient profile (Mean ± SD) in major diagnosed pathological condition Perinatal Asphyxia (PNA) & Sepsis of critically ill neonates (admission/initial)

	PNA(n=43) Mean±SD	Sepsis(n=39) Mean±SD	p value
B. Glucose(mmol/L)	2.18±0.39	3.08±0.15	0.109[ns]
S. Calcium(mmol/L)	2.03±0.24	2.07±0.15	0.346[ns]
Hemoglobin(gm/dl)	16.85±3.46	13.97±5.59	0.070[ns]
S. Albumin(gm/L)	26.14±4.75	22.20±4.12	0.040[s]

p value reached from unpaired t-test

Table III
Macronutrient profile (Mean ±SD) in Survivors and Non-Survivors (discharge/death)

	Survivors (n=71) Mean±SD	Non-Survivors (n=50) Mean±SD	p value
B. Glucose	7.14±6.06	6.15±3.24	0.013[s]
S. Calcium	2.06±0.20	2.09± 0.18	0.048[s]
Hemoglobin	15.44±5.06	14.33±6.88	0.022[s]
S. Albumin	24.46±1.61	23.7±0.14	0.034[s]

p value reached from unpaired t-test

Discussion

The study was carried out in critically ill neonates. Detection of essential macronutrient as energy source is an important key concern in admitted sick neonates are discussed as follows to predict their survival. Macronutrient, e.g., blood glucose, serum calcium, hemoglobin as iron status, serum albumin play important role in that aspect. The focus of neonatal macronutrient has become increasingly evident that nutrition during the first few weeks of life while the infant is struggling for survival is crucial.[28] Faisy et al. demonstrated that negative energy balance is an independent determinant of intensive care unit (ICU) mortality in very sick patients.[5] In this study similar to that, non-survivor had significantly lower macronutrient parameter (glucose, calcium, hemoglobin, albumin) than survivors. Martin et al.[29] observed that patient who received proper nutrition had better clinical outcome. These findings are in agreement with the results from the work of van Schijndelet al.[30] who conducted a prospective observational cohort study. They assessed the effects of achieving optimal nutrition in ICU patients. In another study by Singer et al[31] who conducted a review and analysis of literature related to nutrition in the ICU. Targeting the energy goal, optimal energy supply in critically ill patients. The metabolic changes from the stress response have an impact on the macronutrient requirements of critically ill patients.[1,3] Several clinical studies in neonates who had sepsis or any critical illness have demonstrated increased levels of both TNF alpha and IL6, cytokines known to be involved in the stress response and multisystem organ failure syndrome. Energy requirements in these neonates were elevated in proportion to the degree of illness. The septic neonates required more energy delivery during the acute phase of their illness than similarly ill non-septic neonates.[19] In our study, there was lower mean value of albumin and hemoglobin in septic neonates (Table II).

Glucose is a ready source of energy in the form of ATP, and neonates are particularly dependent on glucose as an energy source.[19] ATP is confined to living cells. As the energy currency of cells ATP depletion sufficient to cause irreversible or partially reversible cellular damage, which also accelerates damage by hypoglycemia.[16] The body makes metabolic adaptations to increase the chance of survival by use of additional fuel, primarily glucose to shunt to organs for survival such as the brain and the heart. The response is similar in critically ill children.[17] In our study glucose level was significantly lower in non-survivors than survivors (Table I, Table III) (both admission and death/ discharge).

Calcium balance are difficult to maintain in critically sick neonate.[32] Hypocalcemia can affect optimal respiratory and cardiac function.Transient neonatal hypocalcemia often is exacerbated by acute respiratory disease and, when severe, can cause tetany and cardiac arrhythmias.[19] So more hazardous may be happened in hypocalcemia of critically sick neonates.

Hypoglycemia and hypocalcemia are common in critically ill neonate, significant concern among neonatal and pediatric critical care specialists.[33,20] In our study both level were significantly lower in non-survivors than survivors (Table I, Table III) (both admission and death/discharge).So initial

prevention of both by accurate measuring techniques and monitoring potentially improve survival of critically ill neonates.

The divalent metals iron also at risk during neonatal illness. Certain subgroups of neonates are born with low iron stores.[34,35] It is likely that inflammation or stress situation significantly alters iron absorption and trafficking in the sick newborn.[36] Additional hemoglobin should be synthesize or required. Otherwise, the consequence of hemoglobin deficit becomes worst outcome.[37] In our study, similar to that as non-survivors had lower value of hemoglobin than survivors.

Hypoalbuminemia was frequent among critically ill neonates with sepsis.[11] Sepsis alters protein requirements more acutely by its effect on cytokine-mediated muscle catabolism. This condition causes a dramatic increase in muscle catabolism, most likely to provide a ready source of amino acids in the liver for acute phase reactant synthesis. Sepsis causes the most profound changes in negative nitrogen balance among in septic neonates in which the degree negative nitrogen balance is related directly to the degree of the severity of physiologic instability. There are concomitant increases in cytokine and acute phase reactant protein concentration. The same study demonstrated that critically ill infants remained in negative nitrogen balance for as long as 10 days after the sepsis began. The concern is that this duration of negative nitrogen balance would lead to worst outcome as morbidity (predisposition to further episodes of sepsis) and mortality.[19] Therefore, lower albumin levels might be associated with a poorer prognosis of newborn[23] similar in our study (Table III).

Conclusion

In this brief overview, the main message is that during critical illness in neonates, emphasis should be placed on the provision of adequate macronutrient source. This is necessary for better optimization survival of critically ill neonates.

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