Abstract:

Prematurity is one of the major causes of neonatal death in developing countries like Bangladesh. Appropriate protocol for nutritional support of the preterm infants is essential to achieve a postnatal growth rate similar to that of a normal fetus. Objective of the study was to assess the effects of the existing nutritional support protocol of Bangabandhu Sheikh Mujib Medical University (BSMMU) in the early postnatal growth velocity of the preterm infants. This quasi-experimental study was conducted in the Department of Neonatology, BSMMU, Bangladesh from January to December 2015. All admitted infants aged < 48 hours and born < 32 weeks of gestational age were included in this study. Infants were provided with nutritional support as per the BSMMU feeding guideline. The subsequent growth of the children was followed up routinely to measure the growth velocity. Of the 38 infants of our study, the mean calorie intake was 66.71 Kcal/kg/day. Overall mean growth velocity of weight, length and occipitofrontal circumference (OFC) up to discharge were 8.97 g/kg/day, 0.85 cm/week, and 0.41 cm/week respectively. Very low birth weight (VLBW) infants got significantly more calories compared to low birth weight (LBW) infants (p = 0.009). Mean growth velocity in weight of LBW infants were 8.18 g/kg/day and VLBW were 9.95 g/kg/day (p = 0.233). At birth, only 2.6% of infants had weight < 10th centile, but at discharge, it was 52.6%. Early postnatal nutritional supplementation was not adequate, and postnatal growth failure remains very high in the hospital admitted preterm infants.

Key words: Growth velocity, Preterm infant, Nutritional protocol, Growth failure.

Introduction:

In developing countries like Bangladesh, prematurity, and low birth weight births had been a major concern because of its high rate of subsequent neonatal mortality. However, the survival rate of premature infants improved significantly due to meticulous care through the Neonatal Intensive Care Unit (NICU) in the last few decades. Bangladesh has already achieved Millennium Development Goal targets in reducing the mortality rate of under 5 (five) children mainly by reducing the incidence of neonatal death. Nevertheless, the neonatal mortality rate is still 17 per 1000 live births, which contributes to almost 55% of under-five mortality. The most common causes of neonatal deaths are birth asphyxia (43%), infections (29.3%), and prematurity (22.2%). Despite socio-economic progress and improvement of overall health status, a high prevalence of low birth weight delivery is still a major concern.

Preterm infants are born with inadequate stores of all the major nutrients, including protein, energy, minerals, and vitamins. On the other hand, premature babies are born before the transplacental transfer of maternal immunoglobulin is completed and before the developmental maturity of lymphocyte function. As a result, infants with LBW or intrauterine growth retardation (IUGR) or who were small for gestational age (SGA) have a lower percentage of T or B lymphocytes than newborn infants with normal birth weight. So, an infant born prematurely with inadequate stores of all major nutrients as well as physiological immunodeficiency is at a nutritional and immunological disadvantage compared to a well-grown infant born at term. This vulnerable nutritional status leaves preterm infants at increased risk of necrotizing enterocolitis and sepsis.
Among the survived babies, a large proportion of them show subsequent growth restriction (weight < 10th centile for postmenstrual age), and it usually persists into early childhood. Also, suboptimal nutritional intake in the early days leads to a poor neurodevelopmental outcome of the infants.

So, proper nutritional management of the preterm infants during the first few days is essential to reduce the morbidity and mortality of the children. The goal of nutritional support in preterm infants is to achieve a postnatal growth rate similar to that of a normal fetus at the same postconceptual age. Term infants need 100-120 Kcal/kg/day to induce weight gain at a rate of 15-30 g/day. On the other hand, the preterm infant needs more calories (110-140 Kcal/kg/day) as they have limited ability to metabolize nutrients that we offer and face more caloric loss in the stool due to difficulty in absorbing fat.

Ideally, total parenteral nutrition (TPN) is needed to maintain calorie requirements during the early few days for virtually all the very low birth weight infants. But in Bangladesh, total parenteral nutrition is still not commonly practiced. Due to the limitation of TPN use in Bangladesh, adequate nutritional requirement of the preterm and low birth weight infants in NICU is compromised.

BSMMU follows a standardized protocol for the early nutritional management of the preterm infants and this study was carried out to assess the effects of this nutritional protocol in the early postnatal growth velocity of the preterm infants.

**Materials and Methods:**

This quasi-experimental study was conducted in the NICU of the Department of Neonatology, BSMMU, Bangladesh, over one year (from January to December 2015). All admitted premature neonates (gestation ≤ 32 weeks) aged < 48 hours were selected as the study population with informed written consent from the parent or caregiver. Infants who expired before discharge or left against medical advice and infants diagnosed with major congenital or chromosomal abnormalities were excluded.

A total of 38 eligible infants who fulfilled the criteria were included. A detailed history was taken and gestational age was calculated either by the total duration of pregnancy in weeks from the first date of the last menstrual period (LMP) to birth of the baby or by ultrasound (USG) or by New Ballard Scoring after birth. Mean of three consecutive measurements of weight in grams, length, and head circumference in centimeters were recorded. The nutritional support was provided as per the BSMMU feeding guide line.

As parenteral fluid, 5% dextrose in aqua was given at 60-80 mL/kg/day on the first day of life if the birth weight was < 1000 g, and 10% dextrose in aqua was given if the birth weight was ≥ 1000 g. Daily increment of fluid was 20 mL/kg/day. After 24 hours of postnatal age, it was changed to dextrose in quarter strength normal saline along with amino acid. The initial dose of amino acid was 0.5-1 g/kg/day and gradually increased up to 3.5 g/kg/day and the rate of advancement was 0.5-1 g/kg/day. When infants achieved enteral feeds > 70% of the total requirement, parenteral amino acid was stopped.

The initial feeding method in infants < 28 weeks of gestational age was parenteral. If hemodynamically stable after 24 hours of postnatal age, breast milk as trophic feeds at 10 mL/kg/day was started by orogastric tube. Infants of 28 to 32 weeks of gestational age and who were hemodynamically stable, initial feeding method was parenteral along with trophic feeds by nasogastric or orogastric tube. In both cases, parenteral fluid volume was reduced gradually and enteral feeding was increased at 20 mL/kg/day. Parenteral fluid was stopped when full enteral feeds were achieved.

Sources of carbohydrate were breast milk and parenteral dextrose. Protein was given in the form of breast milk and intravenous supplementation. Intravenous protein was provided in the form of amino acid by a 5% composite amino acid solution with D-sorbitol (Proliv™, Orion Infusion Ltd. Bangladesh). The study population got fat only from breast milk.

All infants were examined twice daily and closely monitored up to discharge. Feeds were discontinued temporarily if the patient developed any of the following conditions: (a) feed intolerance, (b) significant apnea, (c) convulsion, (d) requirement of mechanical ventilation, and/or (e) requirement of vasopressors. During such condition, infants were managed according to the institutional guidelines.

Time to reach full feeding was calculated by the difference between the age at the start of feed and the age of getting 150 mL/kg/day of feed. Calories consumed by infants were calculated using Atwater factors as 4 Kcal/g for carbohydrates, 4 Kcal/g for proteins, and 9 Kcal/g for fat. The calorie value from direct breast feeding was not recorded as it was non-observed data.

We calculated growth velocity in weight from the interval between days 7 and discharge as the impact of nutritional support is usually not seen until at least day 7. Growth velocity in length and OFC were calculated as Growth velocity (Length or OFC) = [(Length or OFC in cm at given time - length or OFC in cm at birth or Day 14/ duration in weeks of two points)].
Mean and standard deviation were calculated for continuous variables and proportion was calculated for categorical variables. Comparisons for continuous variables were made by independent sample t-test. For comparisons of categorical data, chi-square test was used. The level of significance was set at $p<0.05$. For statistical analysis, we used IBM SPSS version 20 (SPSS Chicago, IL).

Prior ethical clearance was taken from the institutional review board (IRB) of BSMMU.

**Results:**

A total of 38 infants were included in this study. The mean gestational age of the infants was 30.79 weeks. Mean birth weight was 1479.61 g and mean birth OFC and birth length were 28.05 cm and 39.72 cm respectively (Table I).

Among the study population, 55.3% were low birth weight (LBW) infants and 44.7% were very low birth weight (VLBW) infants. (Fig-1)

The mean growth velocity of weight from postnatal age day 14 to CGA 34 weeks was 11.49 g/kg/day and it was higher in comparison to the first 14 days of postnatal age. For length and OFC, mean growth velocity up to discharge was 0.85 cm/week 0.41 cm/week respectively (Table III).

Table II shows that the mean postnatal age to achieved full enteral feed was 17.29 days. The mean duration of hospital stay was 25.58 days and mean duration of parenteral nutrition was 16.95 days. On the other hand, mean calorie intake during the first 14 days of postnatal age was 56.45 Kcal/kg/day and from admission to discharge, it was 66.71 Kcal/kg/day.

Table IV shows the comparison between LBW and VLBW infants. We found that LBW infants achieved full enteral feed earlier (15.16 ± 5.85 days) than VLBW (19.06 ± 6.22 days) infants but there was no statistical significance ($p = 0.079$). Mean duration of hospital stays for VLBW infants (31.22 days) was longer than LBW infants (21.00 days) which was statistically
significant ($p = 0.005$). Mean duration of parenteral nutrition for LBW infants was 15.55 days but longer duration (18.11 days) was required for VLBW infants. VLBW infants got more calories ($71.28 \pm 9.75$ Kcal/kg/day) in comparison to LBW infants ($63.01 \pm 8.24$ Kcal/kg/day) and it was statistically significant ($P = 0.009$). Growth velocity in weight up to discharge of LBW infants was $8.18 \pm 5.31$ g/kg/day and for VLBW, it was $9.95 \pm 3.65$ g/kg/day and it was not statistically significant. We also did not find any statistical significance for growth velocity in OFC and length at discharge between LBW and VLBW.

**Table IV: Comparison between LBW and VLBW infants**

| Variable                                         | LBW Mean ± SD | VLBW Mean ± SD | $P$ value |
|--------------------------------------------------|---------------|----------------|-----------|
| Postnatal age at initiation of enteral feed (days) | 2.86 ± 1.20   | 3.39 ± 1.24    | 0.28      |
| Postnatal age at initiation of amino acid (days)  | 3.05 ± 0.99   | 3.50 ± 1.21    | 0.241     |
| Postnatal age to achieve full enteral feed (days) | 15.16 ± 5.85  | 19.06 ± 6.22   | 0.079     |
| Postnatal age to regain birth weight (days)       | 17.82 ± 8.64  | 18.00 ± 6.87   | 0.787     |
| Duration of hospital stay (days)                  | 21.00 ± 10.28 | 31.22 ± 9.20   | 0.005     |
| Calorie intake for postnatal age D14 to CGA 34 weeks (Kcal/kg/day)* | 59.56 ± 11.48 | 80.03 ± 17.58 | 0.004     |
| Calorie intake for admission to discharge (Kcal/kg/day)* | 63.01 ± 8.24 | 71.28 ± 9.75 | 0.009     |
| Growth velocity in weight up to discharge (g/kg/day) | 8.18 ± 5.31  | 9.95 ± 3.65    | 0.233     |
| Growth velocity in OFC up to discharge (cm/week)  | 0.40 ± 0.14   | 0.41 ± 0.08    | 0.081     |
| Growth velocity in length up to discharge (cm/week) | 0.76 ± 0.28  | 0.96 ± 0.32    | 0.051     |

*Calorie value from direct breastfeeding was not measured.

Mean calorie intake of enrolled preterm infants during the first 7 days, 14 days, corrected gestational age 34 weeks, and up to discharge were 44.47, 56.44, 61.71 and 66.71 Kcal/kg/day respectively (Table II). Figure 2 shows that the mean length of enrolled preterm infants was 41.17 cm at postnatal age of day 14, 42.27 cm at corrected gestational age 34 weeks, and 43.51 cm at discharge. Mean OFC was 29.06 cm at postnatal age of day 14, 29.06 cm at corrected gestational age 34 weeks and 30.13 cm at discharge. Furthermore, mean weight was 1344 g at postnatal age of day 7, 1398g at day 14, 1495g at corrected gestational age 34 weeks and 1549 g at discharge.

![Figure 2: Mean length, OFC, and weight of the enrolled infants at different points.](image)

Table V shows that at discharge, weight of 52.6% infants were <10th centile whereas at birth, it was only 2.6%. In OFC at birth, only 7.9% infants were below 10th centile, but at discharge it was 50%.

**Table V: Percentile category of enrolled infants**

| Variable   | At birth (<10th centile) | At discharge (<10th centile) |
|------------|--------------------------|------------------------------|
| Number     | Percentage               | Number                       | Percentage   |
| Weight     | 1                        | 2.6%                         | 20           | 52.6%         |
| Length     | 2                        | 5.2%                         | 4             | 10.5%         |
| OFC        | 3                        | 7.9%                         | 19            | 50%           |

**Discussion:**

Baseline characteristics were more or less the same as those reported by Collins et al., which was a similar study. We found that the mean birth weight of the study infants was 1479.61g, which was slightly higher than that of Collins et al., where they found the mean birth weight was 1333g. However, mean gestational age (30.79 weeks) of the infants in our study was slightly
higher than the mean gestational age (29.3 weeks) of the study population of Collins et al. which might explain the higher birth weight of the infants in our study22.

Mean postnatal age at initiation of enteral feeding in our study was 3.05 days whereas in studies done by Fenton et al22 and Martin et al22 it was started from day1. In the NICU of BSMMU, parenteral fat infusion is not practiced, so our study infants did not get any parenteral fat. For this reason, we had a notable reduction in daily calorie intake from the recommended level. In our study, mean calorie intake up to discharge was 66.71Kcal/kg/day whereas in Collins et al. it was 119.10Kcal/kg/day22. However, we did not calculate calories that the infants got from direct breast feeding. May be low-calorie intake was one of the causes of low growth velocity in weight (>15 g/kg/day and 15.7g/kg/day respectively)12,22.

While we compared the LBW and VLBW infants, we found that postnatal age at achieving full enteral feeds between LBW and VLBW was not statistically significant (p = 0.079) but duration of hospital stay was significantly higher for the VLBW infants compared to LBW infants (p = 0.005). We also found that the mean calorie intake of VLBW infants from admission to discharge was higher (71.28 Kcal/kg/day) than LBW infants (63.01 Kcal/kg/day) and it was statistically significant (p = 0.009).

In our study, it took almost 3 days for the initiation of amino acid, but in studies by Collins et al22 and Martin et al22 it was started from day1. In the NICU of BSMMU, parenteral fat infusion is not practiced, so our study infants did not get any parenteral fat. For this reason, we had a notable reduction in daily calorie intake from the recommended level. In our study, mean calorie intake up to discharge was 66.71Kcal/kg/day whereas in Collins et al. it was 119.10Kcal/kg/day22. However, we did not calculate calories that the infants got from direct breast feeding. May be low-calorie intake was one of the causes of low growth velocity in weight (>15 g/kg/day and 15.7g/kg/day respectively)12,22.

Although most of the studies showed growth velocity only by weight parameter, we also have seen growth velocity by length and OFC. Recommended preterm growth velocity in length is 0.5-0.8 cm/week and OFC is 0.8-1.0 cm/week. Premature infants exhibit catch-up growth in head circumference that may exceed the normal growth rate. However, in this study growth velocity of OFC was 0.41 cm/week which was less than recommendation and growth velocity in length up to discharge was 0.85 cm/week which was at the lower end of the normal recommended range.

At discharge, 52.6% infants had weight <10th centile. It indicates that more than 50% infants in our study suffered postnatal growth failure. In contrast, 32% infants had growth failure in the study done by Collins et al22. We also found that half of the infants of our study had OFC <10th centile at discharge. However, most of the infants were above 10th centile in regards to their length at discharge.

All these findings point out that the growth velocity of our study population with the existing nutritional protocol is not optimal for achieving the recommended growth of the preterm infants. Further interventions such as total parenteral nutrition might be necessary to catch up with the recommended growth velocity.

Limitations:

Our study was conducted in a single centre and had small sample size. As a result, our findings may not reflect the whole population. Additionally, calorie value from direct breast feeding was not measured.

Conclusion:

Mean calorie intake and growth velocity of the preterm infants were much lower than the recommendation. Early postnatal nutritional supplementation was not adequate with the existing nutritional protocol and postnatal growth failure remains very high. Total parenteral nutrition may yield maximum energy gain and the preterm infants may achieve recommended growth velocity. However, large sample size and multicenter studies are recommended to find out further information regarding the population.

Conflict of interest: None

References:

1. Liu L, Johnson HL, Cousens S, Perin J, Scott S, Lawn JE, et al. Global, regional, and national causes of child mortality: An updated systematic analysis for 2010 with time trends since 2000. Lancet 2012; 379(9832):2151-61.

2. Kyser KL, Morriss FH, Bell EF, Klein JM, Dagle JM. Improving survival of extremely preterm infants born between 22 and 25 weeks of gestation. Obstet Gynecol. 2012; 119(4):795-800.

3. Directorate General of Health Services Bangladesh. Health Bulletin 2018 [Internet]. [Date accessed: 2020 Jan 17]. Available from: https://dghs.gov.bd/images/docs/Publicaations/HB%202018%20final.pdf

4. Halim A, Dewez JE, Biswas A, Rahman F, White S, Van Den Broek N. When, where, and why are babies dying? Neonatal death surveillance and review in Bangladesh. PLoS One 2016; 11(8):1-14.

5. Rahman MS, Howlader T, Masud MS, Rahman ML. Association of low-birth weight with malnutrition in children under five years in Bangladesh: Do mother's education, socio-economic status, and birth interval matter? PLoS One 2016; 11(6):1-14.

6. Nasreen HE, Kabir ZN, Forsell Y, Edhborg M. Low birth weight in offspring of women with depressive and anxiety symptoms during pregnancy: Results from a population based study in Bangladesh. BMC Public Health 2010; 10:1-8.
7. Embleton ND. Optimal protein and energy intakes in preterm infants. Early Hum Dev. 2007; 83(12):831-7.

8. Finch CW. Review of trace mineral requirements for preterm infants: What are the current recommendations for clinical practice? Nutrition in Clinical Practice. 2015; 30:44-58.

9. Rennie JM, Roberton NRC. Rennie and Roberton's textbook of neonatology. 5th ed. Churchill Livingstone; 2012.

10. Raqib R, Alam DS, Sarker P, Ahmad SM, Ara G, Yunus M, et al. Low birth weight is associated with altered immune function in rural Bangladeshi children: A birth cohort study. Am J Clin Nutr. 2007; 85(3):845-52.

11. Lucas A, Cole TJ. Breast milk and neonatal necrotising enterocolitis. Lancet 1990; 336(8730-8731):1519-23.

12. Martin CR, Brown YF, Ehrenkranz RA, O'Shea TM, Allred EN, Belfort MB, et al. Nutritional practices and growth velocity in the first month of life in extremely premature infants. Pediatrics 2009; 124(2):649-57.

13. Clark RH, Thomas P, Peabody J. Extrauterine growth restriction remains a serious problem in prematurely born neonates. Pediatrics 2003; 111(5):986-90.

14. Hay WW. Aggressive Nutrition of the Preterm Infant. CurrPediatr Rep. 2013; 1(4):229-39.

15. Rao R, Georgieff MK. Iron Therapy for Preterm Infants. Clinics in Perinatology 2009; 36:27-42.

16. Lucas A, Morley R, Cole TJ. Randomised trial of early diet in preterm babies and later intelligence quotient. Br Med J. 1998; 317(71):1481-7.

17. Velaphi S. Nutritional requirements and parenteral nutrition in preterm infants. South African Journal of Clinical Nutrition. 2011(24): 27-31.

18. Ehrenkranz RA, Younes N, Lemons JA, Fanaroff AA, Donovan EF, Wright LL, et al. Longitudinal growth of hospitalized very low birth weight infants. Pediatrics 1999; 104(2):280-9.

19. Tan MJ, Cooke RW. Improving head growth in very preterm infants - A randomised controlled trial I: Neonatal outcomes. Arch Dis Child Fetal Neonatal Ed. 2008; 93(5):337-41.

20. Ballard JL, Khoury JC, Wedig K, Wang L, Eilers-Walsman BL, Lipp R. New Ballard Score, expanded to include extremely premature infants. J Pediatr. 1991; 119(3):417-23.

21. Merrill AL, Watt BK. Energy Values of Food: Basis and Derivation. Agricultural Handbook No. 74. 1973.

22. Collins CT, Chua MC, Rajadurai VS, McPhee AJ, Miller LN, Gibson RA, et al. Higher protein and energy intake is associated with increased weight gain in pre-term infants. J Paediatr Child Health. 2010; 46(3):96-102.

23. Fenton TR, McMillan DD, Sauve RS. Nutrition and growth analysis of very low birth weight infants. Pediatrics 1990; 86(3):378-83.