

Rapid Versus Gradual Advancement of Enteral Feeding in Preterm Low Birth Weight Neonates: A Randomized Controlled Trial

Dr. Most. Airin Afroz^{1*}, Prof. Dr. Monir Hossain², Dr. Sadia Alam³, Dr. Suraya Akter⁴, Dr. Naziah Rahman Chowdhury Tania⁵, Dr. Mukta Thakur⁶

¹Registrar, Department of Cardiology, National Institute of Traumatology & Orthopedic Rehabilitation (NITOR), Dhaka, Bangladesh.

²Professor, Department of Neonatal Medicine & Neonatal Intensive Care Unit, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh.

³Registrar, Department of Paediatrics, Gonoshasthaya Samaj Vittik Medical College, Dhaka, Bangladesh.

⁴Specialist, Department of Paediatrics, Square Hospital Limited, Dhaka, Bangladesh.

⁵Consultant, Department of Paediatrics, Directorate General of Health Services (DGHS), Dhaka, Bangladesh

⁶Junior Consultant, Department of Paediatrics, Directorate General of Health Services (DGHS), Dhaka, Bangladesh

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***Corresponding Author:** *Dr. Most. Airin Afroz, Registrar, Department of Cardiology, National Institute of Traumatology & Orthopedic Rehabilitation (NITOR), Dhaka, Bangladesh.*

Abstract

Background: Preterm birth is a major global health concern, causing complications and long-term developmental challenges. Early nutritional intervention improves the growth, development, and health outcomes of premature newborns. The aim of this study was to evaluate impact of rapid enteral feeding advancement on morbidities and mortality among preterm neonates

Methods: This was a randomized controlled trial conducted in the Neonatal Unit of Bangladesh Shishu Hospital & Institute among 88 neonates who were randomly assigned in a 1:1 ratio by random allocation software version 2 to receive either rapid enteral feeding advancement group (group A) or gradual enteral feeding advancement group (group B). In both groups, neonates received 5-10 ml enteral nutrition/kg/d on feeding day 1.

Results: The median time to achieve full feed was significantly shorter in the rapid group (7.0 vs. 8.5 days, p=0.004), and the duration of parenteral nutrition was also significantly lower (5.0 vs. 7.5 days, p=0.001). Hospital stay was shorter in the rapid group (7.0 vs. 10.0 days, p=0.002). Feed intolerance was more frequent in the rapid group (29.5% vs. 15.9%), though not statistically significant. No significant differences were observed in mortality (p=0.616) or discharge weight (p=0.740) between groups. The findings support rapid feeding as a safe and efficient approach in stable preterm neonates.

Conclusion: Rapid enteral feeding advancement enhances early achievement of full enteral feed, reduces the use of parenteral nutrition, and reduces duration of hospital stay in low birth weight preterm neonates compared to gradual advanced enteral nutrition.

Keywords: *Preterm neonates, low birth weight, enteral feeding, rapid advancement, gradual advancement, randomized controlled trial, feed intolerance, parenteral nutrition.*

1. INTRODUCTION

Preterm birth, defined as delivery before 37 weeks of gestation, has a considerable worldwide health impact and is acknowledged as a leading cause of newborn mortality [1]. Every year, 20.5 million (14.6%) newborns are born with low birth weight, with 48% in South Asia [2]. Preterm

birth has been associated to a variety of short- and long-term complications in babies, including breathing, hearing, and feeding issues [1].

Oral feeding and swallowing problems in preterm newborns are typical medical issues in neonatal intensive care units (NICUs) and families of premature babies. Preterm infants are more likely to experience oral feeding difficulties due to delayed oral motor skill development and poor suck-swallow-breathe coordination.

Furthermore, sucking and swallowing difficulties in preterm newborns reduces food availability, which may have an impact on their growth, development, and neurological function [3].

Better somatic growth and neurodevelopmental outcomes have been linked to increased energy and macronutrient consumption during the first four weeks of life. The nonnutritive aspects of breast milk, such as its ability to prevent nosocomial infections, are thought to be more important for improving lung outcomes than its macronutrient composition [4].

Current preterm neonatal guidelines encourage high nutritional intakes to reduce extrauterine growth restriction (EUGR) and the potential long-term implications of malnutrition. When physiological intestinal insufficiency limits the use of enteral nutrition (EN) in the first postnatal week, parenteral nutrition (PN) is required to address nutritional needs in this vulnerable population. However, the tolerance of severely ill patients to PN is still debatable [5]. Various side effects and consequences associated with PN, including parenteral nutrition associated liver disease (PNALD), intravenous glucose and lipid intolerance, and catheter-related infections. As a result, enteral nutrition (EN) needs to be initiated as soon as feasible and rapidly increased. Moreover, there are well defined benefits of own mother's milk colostrum and this important feeding step should not be missed [6].

There are significant differences in the standardised protocols for the best feeding regimen and there are broad variations in the introduction and progress of enteral feeds for preterm newborns. Concerns regarding intestinal intolerance and a possible increased threat of focal intestinal perforation (FIP) and necrotizing enterocolitis (NEC) are further issues raised by the fast progression of feeding volumes. Conversely, cautious feeding practices raise the danger of late-onset sepsis by delaying the beginning of full enteral feeding and prolonging exposure to parenteral nourishment [4]. Early nutritional support is receiving more attention in an effort to reduce the nutritional deficits that develop during the earliest stages of sickness and gastrointestinal immaturity [7].

The practice of early enteral feeding involves giving a modest amount of milk typically less than 24 milliliters per kilogram per day to promote the release of gastrointestinal hormones and gastrointestinal motility. It is believed that enteral feeding enhances eating tolerance and gastrointestinal tract maturation by changing the microbial colonization of the gastrointestinal tract in favor of beneficial microflora. A possible reduction in the length of parenteral nutrition and the danger of morbidities such as late-onset sepsis, metabolic, and liver problems is another advantage of more rapid and progressive feeding [8].

The objective of this study was to evaluate impact of rapid enteral feeding advancement on morbidities and mortality among preterm neonates.

2. METHODOLOGY & MATERIALS

This study was designed as a randomized controlled trial conducted in the Department of Neonatology at Bangladesh Shishu Hospital & Institute (BSH & I), Dhaka, over two years, from July 2022 to June 2024. The study population comprised all low-birth-weight preterm neonates admitted during the study period who met the eligibility criteria. A total of 88 neonates were included and randomized equally into two groups: Group A (rapid feeding advancement) and Group B (gradual feeding advancement).

2.1. Sample Selection

Inclusion Criteria

- Hemodynamically stable preterm neonates
- Birth weight between 1000g and <2500g
- Gestational age between 30 weeks and <37 weeks

Exclusion Criteria

- Required resuscitation beyond initial steps
- Critically ill neonates
- Major congenital anomalies
- Requiring breathing support with a head box
- Requiring vasopressor support at the time of randomization
- Refusal to provide informed consent

2.2. Data Collection Procedure

Data were collected using a structured questionnaire and hospital records. Parental interviews and direct observation were used to gather demographic and clinical information, including age, sex, birth history, and maternal history when available. Since all neonates were outborn, maternal documentation was sometimes incomplete. Postnatal events, feeding details, and clinical signs were recorded daily. Tools used included medical records, laboratory reports (CBC, CRP, S. procalcitonin, blood culture), and abdominal radiography when NEC was suspected.

2.3. Study Procedure

Eligible neonates were randomized into two groups using computerized randomization (Random Allocation Software version 2). Feeding was initiated within 72 hours of age and 24 hours of hospital admission. All neonates received intermittent bolus gavage feeding every three hours.

Group A (Rapid advancement): Started with 5–10 mL/kg/day on day 1, then advanced by 20–30 mL/kg/day if tolerated, until full feeds (140–160 mL/kg/day) were achieved.

Group B (Gradual advancement): Also began with 5–10 mL/kg/day on day 1, then advanced by 10–15 mL/kg/day, continuing to full feeds.

Feed intolerance was monitored daily. Feeding was paused if intolerance developed and resumed once resolved. Sepsis was diagnosed based on clinical signs and laboratory parameters, classified as clinical or culture-proven. NEC was **3. RESULTS** diagnosed using clinical signs and confirmed by abdominal radiography, and classified per modified Bell's staging. Neonates were discharged once stable and on full enteral feeds.

2.4. Ethical Considerations

Ethical approval for the study was obtained from the Ethical Review Committee of BSH & I. Informed written consent was taken from all parents or legal guardians after explaining the study's purpose, procedures, risks, and benefits. Participation was voluntary, and confidentiality and autonomy were ensured throughout the study.

2.5. Statistical Analysis

Data were coded, entered, and analyzed using SPSS version 26.0. Descriptive statistics were presented as frequency and percentage for categorical variables and median with interquartile range (IQR) for continuous variables due to non-normal distribution. Chi-square test and Fisher's exact test were used for categorical variables, while the Mann-Whitney U test was used for continuous variables. A p-value <0.05 was considered statistically significant.

Baseline characteristics	Group A (n=44)	Group B (n=44)	p value
Age at admission (in hours)			
Within 12	20 (45.5%)	16 (36.4%)	0.486
More than 12 to 24	18 (40.9%)	18 (40.9%)	
More than 24 to 48	6 (13.6%)	10 (22.7%)	
Median [IQR]	16.0 [9.0,24.0]	23.0 [12.0,24.0]	0.120
Gender			
Male	22 (50.0%)	18 (40.9%)	0.392
Female	22 (50.0%)	26 (59.1%)	
Gestational age (in weeks)			
30-31	10 (22.7%)	7 (15.9%)	0.423
32-33	17 (38.6%)	23 (52.3%)	
34-35	17 (38.6%)	14 (31.8%)	
Median [IQR]	33.0 [32.0,34.0]	32.5 [32.0,34.0]	0.772
Birth weight (in grams)			
<1500	27 (61.4%)	31 (70.5%)	0.368
≥1500	17 (38.6%)	13 (29.5%)	
Median [IQR]	1400.0[1200.0,1600.0]	1356.5[1230.5,1500.0]	0.300
Antenatal steroid			
Yes	7 (15.9%)	5 (11.4%)	0.534
No	37 (84.1%)	39 (88.6%)	
Mode of delivery			
NVD	30 (68.2%)	29 (65.9%)	0.821
LUCS	14 (31.8%)	15 (34.1%)	

Table I. Baseline characteristics of the respondents (n=88)

Group A= Rapid enteral feeding advancement group, group B= gradual enteral feeding advancement group, categorical variables were presented in frequency with percentage, continuous variables were presented in median with interquartile range (IQR), statistical analysis was done by Chi-

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square test & Mann Whitney U test, p value <0.05 was considered statistically significant.

Table I shows the baseline characteristics of the respondents. The median age of the neonates in group A and B were 16.0 [9.0, 24.0] and 23.0 [12.0, 24.0] hours respectively. In group A, 22 (50.0%) were male while in group B, 18 (40.9%) were male. The median gestational age of the neonates in group A and B were 33.0 [32.0, 34.0] and 32.5 [32.0, 34.0]

weeks respectively while the median birth weight of the neonates in group A and B were 1400.0 [1200.0, 1600.0] and 1356.5 [1230.5, 1500.0] grams respectively. In group A, 30 (68.2%) while in group B, 29 (65.9%) neonates were born by normal vaginal delivery. There were no significant difference between the groups regarding age at admission, gender, gestational age, birth weight, antenatal corticosteroid and mode of delivery as p>0.05.



Figure 1. *Distribution of neonates by feed intolerance (n=88)*

Figure 1 showed that, in group A, 13 (29.5%) neonates had feed intolerance while in group B, 7 (15.9%) neonates had feed intolerance. Though

in group B, feed intolerance is less but no statistically significant difference was found between the groups as p=0.127.

Table II. Comparison of neonates by time to achieve full feed and duration of parenteral nutrition (n=87)

Criteria (in days)	Group A (n=43) Median [IQR]	Group B (n=44) Median [IQR]	p value
Time to achieve full feed	7.0 [6.0,10.0]	8.5 [7.0,10.0]	0.004
Duration of parenteral nutrition	5.0 [5.0,9.0]	7.5 [6.2,9.0]	0.001

Group A= Rapid enteral feeding advancement group, group B= gradual enteral feeding advancement group, data were presented in median with interquartile range (IQR), statistical analysis was done by Mann Whitney U test, p value < 0.05was considered statistically significant.

Table II showed that, the median time to achieve full feed of the neonates in group A and B were 7.0 [6.0, **Table III.** *Comparison of neonates by mortality* (*n*=88)

10.0] and 8.5 [7.0, 10.0] days respectively. The time to achieve full feed was significantly shorter in group A than group B (p=0.004). The median duration of parenteral nutrition of the neonates in group A and B were 5.0 [5.0, 9.0] and 7.5 [6.2, 9.0] days respectively. The duration of parenteral nutrition was also significantly lower in group A than group B (p=0.001).

Mortality	Group A	Group B	p value
	(n=44)	(n=44)	
Present	1 (2.3%)	3 (6.8%)	0.616
Absent	43 (97.7%)	41 (93.2%)	

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Group A= Rapid enteral feeding advancement group, group B= gradual enteral feeding advancement group, categorical variables were presented in frequency with percentage, statistical analysis was done by Fisher Exact test Table III Showed that, in group A, 1 (2.3%) neonates died while in group B, 3 (6.8%) neonates died. Though in Group B, mortality is high but here were no significant difference between the groups regarding mortality as p=0.616.



Figure 2. *Distribution of neonates by duration of parenteral nutrition (n=87)*

Figure 2 showed that, in group A, the duration of parenteral nutrition was 1-2 days in 9 (20.9%) neonates, 3-4 days in 5 (11.6%) neonates and 5-6 days in 13 (30.2%) while in group B, duration of parenteral nutrition was 7 to 8 days in 18

(40.9%) neonates, 9- 10 days in 10 (22.7%) neonates and >10 days in 4 (9.1%) neonates & statistically significant difference was found between the groups.

Table IV. Comparison of neonates by hospital stay and weight at discharge (n=84)

Criteria	Group A Median [IQR] (n=43)	Group B Median [IQR] (n=41)	p value
Hospital stay (in days)	7.0 [7.0, 11.0]	10.0 [8.5, 11.0]	0.002
Weight at discharge (in gram)	1300.0[1100.0, 1450.0]	1230.0[1110.0, 1400.0]	0.740

Group A= Rapid enteral feeding advancement group, group B= gradual enteral feeding advancement group, data were presented in median with interquartile range (IQR), statistical analysis was done by Mann Whitney U test, p value < 0.05was considered statistically significant

Table IV showed that, in group A, the median duration of hospitalization was 7.0 [7.0, 11.0] days and in group B, it was 10.0 [8.5, 11.0] days. Duration of hospitalization was significantly higher in group B than group A as p=0.002. There were no significant difference between the groups regarding weight at discharge as p=0.740.

4. **DISCUSSION**

This randomized controlled trial was conducted among 88 LBW preterm neonates to evaluate

impact of rapid enteral feeding advancement on mortality and morbidities. Neonates were randomly assigned in a 1:1 allocation ratio to receive either rapid enteral feeding advancement group or gradual enteral feeding advancement group. This study found that the time to achieve full feed, duration of parenteral nutrition and duration of hospitalization were significantly shorter in rapid enteral feeding advancement group than gradual enteral feeding advancement group. There was no significant difference between the groups regarding feed intolerance, occurrence of sepsis, necrotizing enterocolitis and mortality rate.

The median age of the neonates in group A and B were 16.0 and 23.0 hours respectively while

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the median gestational age of the neonates in group A and B were 33.0 and 32.5 weeks respectively. The median birth weight of the neonates in group A and B were 1400.0 grams and 1356.5 grams respectively. There were no significant difference between the groups regarding age at admission, gender, gestational age, birth weight, antenatal corticosteroid and mode of delivery which indicated the ideal random allocation of neonates without biasness.

In group A, 29.5% neonates had feed intolerance while in group B, 15.9% neonates had feed intolerance which showed no significant difference. In India, Jajoo et al., also found no difference between early total enteral nutrition intervention group and control group [9]. This was also supported by Behnke et al. [4]. However, study of Nangia et al., observed that total episodes of feed intolerance were significantly lower (15.9%) in early group when compared to conventional group (30.2%) [10].

The median time to achieve full feed was significantly shorter in group A (7 days) than group B (10 days). Similar result was presented by Modi et al., who also found that the median time to achieve full feed was significantly shorter in aggressive feeding group (7 days) than conventional group (10 days) [11]. Jajoo et al., found that the median time to achieve full feed was significantly shorter in early feeding group (6 days) than gradual advancement group (10 days) [9]. In the study of Behnke et al., the median time to achieve full feed was significantly shorter in early feeding group (7 days) than gradual advancement group (11 days) [4]. In the study of Nangia et al., the mean time to achieve full feed was significantly shorter in early feeding group (6.5 days) than gradual advancement group (10.1 days) [10]. However, in the study of Salas et al., the median time to achieve full feed was longer than these studies (early feeding group: 17 days; delayed feeding group: 19 days) [12]. This might be due to the inclusion of extremely preterm infants in their study.

In group A, parenteral nutrition was discontinued within 1 to 2 days in one fifth neonates and near about one third neonates within 5-6 days. On the other hand, in group B, parenteral nutrition was discontinued within 7-8 days in 40.9% neonates, within 9- 10 days in 22.7% neonates. Moreover, the median duration of parenteral nutrition was significantly lower in group A (5 days) than group B (7.5 days). Salas et al., also found significantly lower duration of parenteral nutrition in early feeding group compared to delayed group [12].

Duration of hospitalization was significantly longer in group B (10 days) than group A (7.0 days). As the duration of parenteral nutrition is significantly longer in group B (10 days) than group A, the longer duration of hospitalization was understandable. This finding was well supported by other studies [13, 14, 15]. However, Modi et al., found no difference in duration of hospitalization between the groups. Early discharge from hospital has a direct effect on the hospital cost. In a lowermiddle-income country like Bangladesh, this would be a great support for the families [11].

There were no significant difference between the groups regarding weight at discharge which was in accordance with the study Jajoo et al., and Modi et al., [9, 11]. Brinkis et al., found that early progressive enteral feeding with human milk is well tolerated in very LBW newborns [6]. Target enteral nutrient intake can be achieved early, boosting in-hospital development. Many studies and meta-analyses suggest that slowly advancing the volume of enteral feeding probably does not reduce the risk of NEC or death before discharge in very preterm or very LBW infants [16, 17]. A number of other studies have shown that early enteral feeding in preterm infants can promote postnatal gastrointestinal functional maturity, reduce mucosal atrophy, improve feeding tolerance, expedite the initiation of whole intestinal feeding, shorten the parenteral nutrition time, and shorten the hospital stay without increasing the incidence of NEC [8, 18, 19].

5. LIMITATIONS OF THE STUDY

In this study recruiting outborn babies, all neonates' antenatal details were not available, so some of the critical risk factors for sepsis and NEC might have been missed.

6. **RECOMMENDATIONS**

Rapid enteral feeding advancement could be initiated in LBW preterm neonates. A multicenter study with large sample is also recommended.

7. CONCLUSION

Rapid enteral feeding advancement enhances early achievement of full enteral feed, reduces the use of parenteral nutrition, and reduces duration of hospital stay in low birth weight preterm neonates compared to gradual advanced enteral nutrition.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

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