

Effect of Rapid Enteral Feeding Advancement on Sepsis and NEC in Preterm Neonates

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Abstract

Original Research Article

Background: Preterm neonates face high risks of sepsis and necrotizing enterocolitis (NEC), which contribute to neonatal morbidity and mortality. Optimal enteral feeding advancement remains debated, especially in resource-limited settings where cautious feeding is practiced to prevent complications. However, extended parenteral nutrition may increase sepsis risk. This study evaluates the effect of rapid versus gradual enteral feeding advancement on sepsis and NEC incidence in preterm neonates. **Methods:** A randomized controlled trial was conducted at the Department of Neonatology, Bangladesh Shishu Hospital & Institute, from July 2022 to June 2024. A total of 88 hemodynamically stable preterm neonates (gestational age 30–<37 weeks; birth weight 1000–<2500 g) were randomly allocated to either a rapid (Group A) or gradual (Group B) enteral feeding advancement protocol. Data on clinical outcomes, including sepsis and NEC, were collected using structured tools and analyzed with SPSS v26. Chi-square and Mann-Whitney U tests were used, with $p < 0.05$ considered statistically significant. **Results:** Sepsis occurred in 13.6% of Group A and 27.3% of Group B neonates ($p = 0.113$). NEC was observed in 4.5% and 6.8% of neonates in Groups A and B, respectively ($p = 0.999$). No significant differences were observed between groups. **Conclusion:** Rapid enteral feeding advancement appears to be a safe and feasible strategy for preterm neonates, with a trend toward reduced sepsis.

Keywords: Preterm neonates, enteral feeding, sepsis, NEC, feeding advancement.

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INTRODUCTION

Preterm birth, defined as delivery before 37 completed weeks of gestation, remains one of the key global public health challenges that causes a significant share of neonatal morbidity and mortality. Approximately 11% of pregnancies worldwide display this condition, with a considerably higher prevalence in low- and middle-income countries, as the latest data indicate [1]. Weanling infants carry an increased risk for complications, including sepsis and necrotizing enterocolitis (NEC), which translates to prolonged hospital stay, lifelong neurodevelopmental disabilities, and poorer rates of survival [2].

Enteral feeding optimization results in substantial progress in the clinical health of preterm

infants. Progression of enteral feeds is an essential component of neonatal nutrition programmes because it leads to full enteral nutrition and reduces the risk of complications of parenteral nutrition, such as infections and liver disease. Although providers agree as to the need for cautious advancement, the debate about just how quickly to increase feeds is far from resolved and will differ from setting to setting. The fear of feeding intolerance, NEC, and sepsis has caused many neonatal units, especially those in low-resource settings, to enact conservative feeding strategies [4].

However, in some cases, it is conceived that delaying codevelopment of enteral feeding decreases the risk of NEC. At the same time, this actually increases the risk of late-onset sepsis, which stretches the use of

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central venous catheters and parenteral nutrition [5]. Recent studies suggest that speeding up the advancement of feed does not heighten the risk of NEC and may reduce the incidence of sepsis and other hospital-acquired disorders by having infants receive full feeds earlier [6,7].

Increasing the feeds from 15–20 mL/kg/day to 30–40 was identified by the 2017 Cochrane review. However, it was related to earlier achievement of full feeds and earlier discharge from the hospital [8]. Nonetheless, in situations of flawed assets, evidence is still weak because of such aspects as the lack of human milk, staff issues, and varied feeding procedures that all contribute to influencing results [9].

South Asian NICUs, which are associated with high preterm birth rates and limited neonatal care capacity, seldom report specific neonatal outcome data. Understanding how the various feeding protocols affect necrotizing enterocolitis (NEC) and sepsis in South Asian neonates is essential in optimizing care. It should lead to better outcomes amongst the affected group [10].

This study seeks to address this gap by evaluating the effect of varying rates of advancement regarding enteral feeding on sepsis occurrence and NEC of pre-term infants at Dhaka Shishu Hospital NICU. This work aims to provide insights into the practical NICU environment with its scarce resources, intent on improving clinical protocols and encouraging safe, earlier enteral feeding procedures for similar environments.

Objective

The objective of this study was to evaluate the effect of rapid versus gradual enteral feeding advancement on the incidence of sepsis and necrotizing enterocolitis (NEC) in preterm neonates.

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).

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

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.

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 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.

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.

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.

RESULTS

Table 1: Baseline characteristics of the respondents (n=88)

Characteristics	Group A (n=44)	Group B (n=44)	p-value
Gestational age (weeks) Median [IQR]	33.0 [32.0–34.0]	32.5 [32.0–34.0]	0.772
Birth weight (g), Median [IQR]	1400 [1200–1600]	1356.5 [1230–1500]	0.3
Male sex, n (%)	22 (50.0%)	18 (40.9%)	0.392
Antenatal steroids, n (%)	7 (15.9%)	5 (11.4%)	0.534
Cesarean delivery, n (%)	14 (31.8%)	15 (34.1%)	0.821

Table 1 presents the baseline characteristics of the preterm neonates enrolled in the study, with 44 neonates in each group (Group A and Group B). Median gestational age was 33.0 weeks in Group A and 32.5 weeks in Group B ($p = 0.772$). Median birth weight was 1400 g in Group A and 1356.5 g in Group B ($p = 0.300$).

Male infants comprised 50.0% of Group A and 40.9% of Group B ($p = 0.392$). Antenatal steroid use and cesarean delivery rates were also similar between groups ($p = 0.534$ and $p = 0.821$, respectively). No significant differences were observed in any baseline variable.

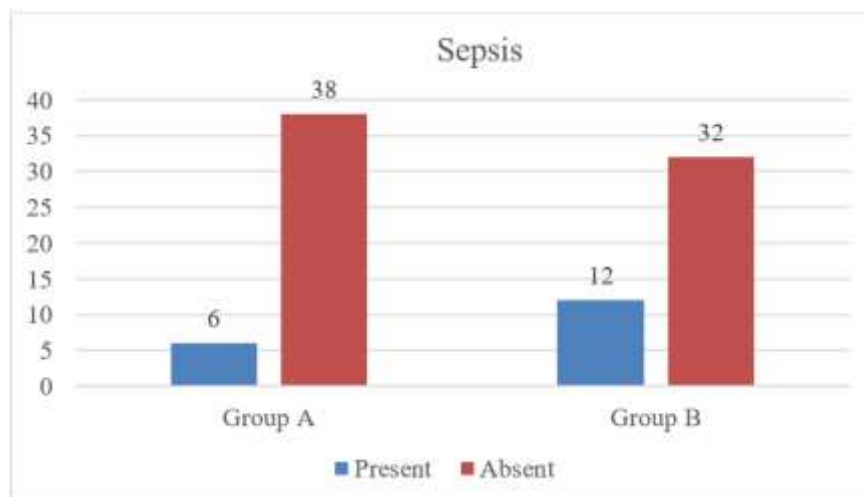


Figure 1: Distribution of neonates by sepsis (n=88)

Figure 1 shows that, in group A, 6 (13.6%) neonates had developed sepsis, while in group B, 12 (27.3%) neonates developed sepsis. Though sepsis was

found less in group A than group B, no statistically significant difference was found between the groups regarding the occurrence of sepsis, as $p=0.113$.

Table 2: Comparison of neonates by type of sepsis (n=18)

Type of sepsis	Group A (n=6)	Group B (n=12)	p value
Clinical	4 (66.7%)	5 (41.7%)	0.62
Culture proven	2 (33.3%)	7 (58.3%)	

Table 2 shows that, in group A, 6 infants developed sepsis, where 4 had clinical sepsis and 2 had culture-positive sepsis (*Klebsiella pneumoniae*). In group B, 12 infants developed sepsis, where 5 had clinical sepsis and 7 had culture-positive sepsis. Among

the 7 patients with culture-positive sepsis, 3 had *Klebsiella pneumoniae*, 2 had *Acinetobacter*, and 1 had *E. coli*. There was no significant difference between the groups regarding the type of sepsis, as $p=0.620$.

Table 3: Comparison of neonates by NEC (n=88)

NEC	Group A (n=44)	Group B (n=44)	p value
Present	2 (4.5%)	3 (6.8%)	0.999

Absent	42 (95.5%)	41 (93.2%)	
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Table 3 showed that, in group A, 2 (4.5%) neonates had developed necrotizing enterocolitis (NEC) while in group B, 3 (6.8%) neonates developed NEC. There was no significant difference between the groups regarding NEC, as $p=0.999$.

DISCUSSION

This study evaluated whether early or slow advancement of enteral feeds could decrease the incidence of sepsis and necrotizing enterocolitis in preterm neonates. The data indicated that rapid feed advancement was associated with a numerically reduced rate of both sepsis and NEC, though numerically observed differences did not reach the level of statistical significance. Our results reflect the latest research indicating that feeding protocols for preterm babies could be relatively restrictive.

Sepsis remains a significant threat to preterm neonatal care and significantly affects neonatal morbidity and mortality (Shane *et al.*) [11]. We found that 13.6% of neonates who had rapid feeding advancement needed sepsis treatment, while 27.3% of neonates in the group of gradual feeding advancement needed sepsis treatment. However, the trend identified ($p = 0.113$) suggests a potentially clinically meaningful benefit with rapid go or advance, especially when assessed in large clinical trials. Concurrence with our findings, Jajoo *et al.*, reported that early total enteral nutrition was associated with a non-significant trend toward lower sepsis rates [6].

There are several possible explanations for this trend. The gradual feeding group reports an increased use of parenteral nutrition with extended central line placement, which leads to amplified bloodstream infections (El Manouni El Hassani *et al.*) [3]. Early change to full enteral nutrition may reduce the period of intravenous treatment, with the aim of affecting the trend seen. As did Hay, early initiation of enteral nutrition contributes to gut maturation and gut mucosal barrier improvement, which would possibly decrease the risk of bacterial translocation and infection [12].

According to our study, 4.5% of neonates in the rapid feeding group developed NEC, with 6.8% appearing in the gradual group ($p = 0.99$). As with earlier works including those conducted by Salas *et al.* [10], our findings show that a rapid feeding rate does not considerably increase the incidence of NEC in preterm infants. In line with our findings, the systematic review by Young *et al.* found insufficient evidence in favor of a decreased NEC for a slower feeding progression [13]. On the other side of the spectrum, the long-standing idea that fast feeding increases the chances of NEC exists due to older studies with small samples and non-standard feeding regulations (Oddie *et al.*) [14].

The randomized controlled design of our study ensures that variables such as gestational age, birth weight, and antenatal problems were similarly distributed. An equal distribution of baseline variables minimizes the risk of confounding and the quality of our outcomes. Our balanced baseline features are in agreement with those in Nangia *et al.*, where no significant differences in NEC and feeding intolerance were observed between rapid and gradual feed advancement [8].

However, caution is still advised. The need for individualized care as a point of emphasis is paramount in our study of the safe use of rapid feed advancement in stable preterm infants. Gut maturity varies substantially among preterm infants (Indrio *et al.*), and the clinician must pay close attention to feeding intolerance regardless of the feeding strategy chosen [15]. Our results show that events of feed intolerance led to temporary modifications of feeding, emphasizing the necessity for pragmatic clinical schemes.

From a nutritional perspective, early enteral feeding has significant advantages. Optimizing feeding forward results in earlier arrival at the full feeds, reduces the need for the central venous access, and allows early initiation of exclusive breastfeeding or expressed breast milk feed (Boscarino *et al.*) [16]. In addition, early enteral nutrition initiates and preserves gut trophism, avoids villous atrophy, and improves the maturation of enzymes (Harding *et al.*) [17]. According to Puntis, early enteral nutrition increases gastrointestinal motility and hormonal responses, hence improved nutrient absorption and weight gain [18].

Our microbiological analysis revealed that *Klebsiella pneumoniae*, *Acinetobacter*, and *E. coli* were most common in cases where culture-confirmed sepsis. According to Odabasi and Bulbul, this microbial profile represents regional late-onset sepsis patterns of South Asia [19]. Studies have reported preterm infants with NICU sepsis multiple times to have a high burden of *Klebsiella* spp, such as by Pammi *et al.*, who correlated this to gut dysbiosis and immaturity [9].

Paralleling Modi *et al.*, we noted that aggressive early feeding of neonates ranging in weight between 750–1250 grams was not associated with higher NEC chances and led to greater weight gain and shorter hospitalizations [20]. Although our research did not follow hospital length of stay or weight growth, the observed tendency towards lower sepsis incidence provides an argument for speedy stabilization and possible early discharge, emphasizing this aspect.

This study is in consensus with accumulating research that high-escalation feeding of enteral nutrition

in stable preterm infants does not increase the risk of NEC or sepsis. It may thus contribute to sepsis prevention because of decreased dependence on parenteral nutrition. Further extensive multicenter clinical trials are needed to validate these findings and establish consistent feeding guidelines that can be implemented across a variety of health-care settings.

Limitations and Recommendations

Study limitations include a small sample size, which may have reduced power to detect significant differences in rare outcomes like NEC. The study did not stratify infants by gestational age or account for exclusive breastfeeding versus formula feeding, factors that may influence sepsis and NEC risk. Future research should include multicenter designs, larger cohorts, and subgroup analyses to assess feeding strategies across preterm populations. Clinical protocols in resource-limited settings should cautiously adopt rapid feed advancement in stable neonates with close monitoring.

CONCLUSION

This study demonstrated that rapid enteral feeding advancement in stable preterm neonates did not significantly increase sepsis or NEC compared to gradual feeding. Though not statistically significant, reduced sepsis in the rapid group suggests clinical benefits.

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Ethical approval

The study was approved by the Institutional Ethics Committee.

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