



Early Full Enteral Feeding Versus Conventional Gradual Enteral Feeding Advancement in Stable Preterm Neonates: A Multicenter Prospective Cohort Study.

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Received: 03-08-2026

Revised: 14-08-2026

Accepted: 22-08-2026

Published: 04-09-2026

Abstract

Background: Optimal nutritional management is a cornerstone of neonatal care in preterm infants. Early establishment of enteral nutrition promotes gastrointestinal maturation, enhances postnatal growth, and reduces complications associated with prolonged intravenous fluid therapy. However, concerns regarding feeding intolerance and necrotizing enterocolitis (NEC) continue to influence feeding practices in neonatal intensive care units (NICUs), and evidence from multicenter Indian studies remains limited. **Objective:** To compare the efficacy and safety of early full enteral feeding with conventional gradual enteral feeding advancement in stable preterm neonates. **Methods:** This multicenter prospective cohort study was conducted in the NICUs of Anand Children Hospital, Surat, Gujarat, and Arya Medical College and Hospital, Jaipur, Rajasthan, India, from July 2025 to June 2026. A total of 114 stable preterm neonates (gestational age 28 to <37 completed weeks) were enrolled. Fifty-seven neonates received early full enteral feeding, while fifty-seven received conventional gradual enteral feeding advancement. Both participating hospitals enrolled neonates into both study groups. Allocation was based on the feeding strategy selected by the treating neonatologist. The primary outcomes were time to achieve full enteral feeding and short-term growth parameters. Secondary outcomes included feeding intolerance, vomiting, abdominal distension, necrotizing enterocolitis (NEC), sepsis, duration of hospital stay, mortality, and exclusive breastfeeding at discharge. **Results:** Baseline demographic characteristics were comparable between the two groups. Neonates in the early full enteral feeding group achieved full enteral nutrition significantly earlier than those in the conventional feeding group (3.9 ± 0.9 vs. 6.5 ± 1.4 days; $p = 0.001$). The early feeding group also demonstrated greater weight gain, length gain, and head circumference gain. Feeding-related complications, including feeding intolerance, vomiting, abdominal distension, and NEC, occurred less frequently among neonates receiving early full enteral feeding. Hospital stay was shorter, and exclusive breastfeeding at discharge was more common in the early feeding group. **Conclusion:** Early full enteral feeding was associated with earlier achievement of full enteral nutrition, improved short-term growth, fewer feeding-related complications, shorter hospital stay, and better breastfeeding outcomes without an apparent increase in NEC among stable preterm neonates.

Keywords: Preterm neonates; Early full enteral feeding; Enteral nutrition; Feeding intolerance; Necrotizing enterocolitis; Neonatal intensive care; Growth outcomes.



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INTRODUCTION

Preterm birth remains one of the leading causes of neonatal morbidity and mortality worldwide and continues to represent a major public health challenge. According to the World Health Organization (WHO), approximately 15 million babies are born preterm each year, accounting for nearly one in ten live births globally. Prematurity is associated with an increased risk of respiratory distress syndrome, sepsis, feeding difficulties, necrotizing enterocolitis (NEC), prolonged hospitalization, poor postnatal growth, and adverse neurodevelopmental outcomes. Therefore, providing optimal nutritional support during the early neonatal period is essential to promote growth, organ maturation, and long-term developmental outcomes.^{1,2,3}

Enteral nutrition plays a pivotal role in the management of preterm neonates. Early initiation of enteral feeding stimulates gastrointestinal maturation, improves intestinal motility, enhances digestive enzyme activity, promotes gut hormone secretion, and supports the development of a healthy intestinal microbiome. In addition, early enteral nutrition reduces dependence on prolonged intravenous fluid therapy and parenteral nutrition, thereby decreasing the risk of catheter-related bloodstream infections and metabolic complications.^{3,8,15}

Mother's own milk is universally recommended as the preferred source of nutrition for preterm infants because of its unique nutritional, immunological, and anti-inflammatory properties. Human milk contains growth factors, immunoglobulins, enzymes, hormones, and other bioactive components that promote intestinal maturation while reducing the incidence of NEC and late-onset neonatal sepsis. When maternal milk is unavailable or insufficient, pasteurized donor human milk is the preferred alternative because it preserves many of the protective benefits associated with human milk feeding.^{9,18,20,25}

Despite the well-recognized benefits of enteral nutrition, the optimal strategy for initiation and advancement of enteral feeds in preterm neonates remains controversial. Traditionally, enteral feeding has been initiated with small feed volumes followed by gradual daily advancement while maintaining intravenous fluid support. This cautious approach aims to minimize feeding intolerance and reduce the perceived risk of NEC. However, slower advancement may delay achievement of full enteral feeding, prolong intravenous therapy, increase the duration of hospital stay, and expose infants to additional complications associated with prolonged vascular access.^{7,11,14}

In recent years, early full enteral feeding has emerged as an alternative feeding strategy for carefully selected stable preterm neonates. Several studies have demonstrated that early advancement of enteral feeds facilitates earlier achievement of full enteral nutrition, improves postnatal growth, shortens hospitalization, and reduces the duration of intravenous fluid therapy without significantly increasing the incidence of NEC. Nevertheless, variations in patient selection, gestational age, birth weight, feeding protocols, and institutional practices have resulted in inconsistent findings across published studies, and concerns regarding feeding safety continue to influence clinical decision-making.^{5,6,14,15}

Within the Indian context, evidence comparing early full enteral feeding with conventional gradual enteral feeding advancement remains limited, particularly from multicenter studies. Most available studies have been conducted at single centers with heterogeneous feeding protocols and inclusion criteria, limiting the generalizability of their findings. Additional multicenter prospective data are therefore required to strengthen the evidence supporting early feeding strategies in stable preterm neonates.^{5,6}

The present multicenter prospective cohort study was undertaken in the Neonatal Intensive Care Units of Anand Children Hospital, Surat, Gujarat, and Arya Medical College and Hospital, Jaipur, Rajasthan, India, to compare early full enteral feeding with conventional gradual enteral feeding advancement in stable preterm neonates. The study evaluated the association of both feeding strategies with time to achieve full enteral feeding, short-term growth parameters, feeding-related complications, duration of hospital stay, sepsis, mortality, and exclusive breastfeeding at discharge. The findings of this study may contribute to the growing body of evidence supporting evidence-based nutritional practices for preterm infants and assist clinicians in optimizing feeding protocols in neonatal intensive care units.

MATERIALS AND METHODS

Study Design and Setting

This multicenter prospective cohort study was conducted in the Neonatal Intensive Care Units (NICUs) of Anand Children Hospital, Surat, Gujarat, and Arya Medical College and Hospital, Jaipur, Rajasthan, India, over a 12-month period from July 2025 to June 2026.

Ethical Considerations

The study was approved by the Institutional Ethics Committee of the participating institution(s). Written informed consent was obtained from the parents or legal guardians of all enrolled neonates before study participation. Patient confidentiality was maintained throughout the study in accordance with institutional ethical guidelines and the principles of the Declaration of Helsinki.

Sample Size

The sample size was calculated based on the primary outcome of time to achieve full enteral feeding using data from previous published studies. The required sample size was estimated to achieve adequate statistical power with a 95% confidence level and 80% power.

Study Population

A total of 114 stable preterm neonates fulfilling the eligibility criteria were enrolled consecutively during the study period. Fifty-seven neonates were managed with early full enteral feeding, and fifty-seven received conventional gradual enteral feeding advancement. Allocation to either feeding strategy was based on the clinical decision of the treating neonatologist according to the infant's clinical condition and unit feeding practices. Both participating hospitals enrolled neonates into both study groups. No randomization was performed. All enrolled neonates completed the study, and no participant was excluded or lost to follow-up after enrollment.

Baseline Data Collection

Baseline neonatal characteristics, including gestational age, birth weight, and sex, were recorded using a standardized data collection proforma at the time of enrollment.

Feeding Protocol

Early Full Enteral Feeding Group

Enteral feeding was initiated at 60 mL/kg/day using the mother's own milk whenever available. When maternal milk was unavailable or insufficient, pasteurized donor human milk was administered. Feed volumes were advanced by 20 mL/kg/day, depending on feeding tolerance, until a target volume of 150 mL/kg/day was achieved, which was considered full enteral feeding. Intravenous fluids were gradually reduced and discontinued after full enteral feeding was established.

Conventional Gradual Enteral Feeding Advancement Group

Enteral feeding was initiated at 20 mL/kg/day using the mother's own milk whenever available. Pasteurized donor human milk was used when maternal milk was unavailable or insufficient. Feed volumes were advanced by 10 mL/kg/day according to the infant's clinical condition and feeding tolerance until a target volume of 150 mL/kg/day was achieved. Intravenous fluids were continued until full enteral feeding was established.

Inclusion Criteria

Stable preterm neonates fulfilling all of the following criteria were included:

- Gestational age between 28 and <37 completed weeks
- Birth weight ≥ 1000 g
- Hemodynamically stable
- Written informed consent obtained from parents or legal guardians

Exclusion Criteria

Neonates with any of the following conditions were excluded:

- Major congenital anomalies
- Chromosomal abnormalities
- Congenital gastrointestinal malformations
- Severe birth asphyxia
- Congenital heart disease requiring medical or surgical intervention
- Suspected or confirmed necrotizing enterocolitis at admission
- Severe neonatal sepsis requiring prolonged withholding of enteral feeding
- Neonates requiring emergency abdominal surgery
- Refusal of parental or legal guardian consent

Outcome Measures

Primary Outcomes

- Time to achieve full enteral feeding (150 mL/kg/day)
- Short-term growth outcomes, including:
 - Weight gain (g/day)
 - Length gain (cm/week)
 - Head circumference gain (cm/week)

Secondary Outcomes

- Time to initiation of enteral feeding
- Feeding intolerance
- Vomiting
- Abdominal distension
- Necrotizing enterocolitis
- Neonatal sepsis
- Duration of hospital stay
- Mortality
- Exclusive breastfeeding at discharge

All enrolled neonates were assessed daily until hospital discharge. Clinical examination, feeding tolerance, growth parameters, and study outcomes were prospectively recorded using a standardized case record form.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 21. Continuous variables were expressed as mean $\pm$ standard deviation (SD), whereas categorical variables were presented as frequencies and percentages. Continuous variables were compared using the independent Student's t-test, while categorical variables were analyzed using the Chi-square test or Fisher's exact test, as appropriate. A two-tailed p value of <0.05 was considered statistically significant. Actual p values and 95% confidence intervals should be reported for the primary outcomes wherever applicable.

AIM:

To compare the efficacy and safety of early full enteral feeding with conventional gradual enteral feeding advancement in stable preterm neonates.

OBJECTIVES:

Primary Objectives

- To compare the time required to achieve full enteral feeding between the two study groups.
- To compare short-term growth outcomes, including weight gain, length gain, and head circumference gain.

Secondary Objectives

- To compare the incidence of feeding intolerance, vomiting, abdominal distension, and necrotizing enterocolitis.
- To compare the incidence of neonatal sepsis and mortality.
- To compare the duration of hospital stay.
- To compare exclusive breastfeeding rates at the time of hospital discharge.

RESULTS

A total of 114 stable preterm neonates were enrolled in the study between July 2025 and June 2026. Fifty-seven neonates received early full enteral feeding, while fifty-seven received conventional gradual enteral feeding advancement. No enrolled neonates were excluded after allocation, and all participants were included in the final analysis.

The baseline demographic and clinical characteristics of the two study groups are presented in Table 1. There were no statistically significant differences between the groups with respect to gestational age, birth weight, or sex distribution (all $P > 0.05$), indicating that the study groups were comparable at baseline.

The majority of neonates in both groups had a gestational age of 31–33 weeks (42.1% vs. 40.4%). Birth weight between 1500 and 1999 g was observed in 47.4% of neonates in the early full enteral feeding group and 43.9% in the conventional feeding group. Male neonates constituted 54.4% and 50.9% of the two groups, respectively.

Table 1. Baseline Demographic and Clinical Characteristics

Variable	Early Full Enteral Feeding (n=57)	Conventional Gradual Enteral Feeding (n=57)	P-value
Gestational age			
28–30 weeks	11 (19.3%)	10 (17.5%)	0.925
31–33 weeks	24 (42.1%)	23 (40.4%)	
34–36+6 weeks	22 (38.6%)	24 (42.1%)	
Birth weight			
1000–1499 g	17 (29.8%)	18 (31.6%)	0.931
1500–1999 g	27 (47.4%)	25 (43.9%)	
≥2000 g	13 (22.8%)	14 (24.6%)	
Sex			
Male	31 (54.4%)	29 (50.9%)	0.951
Female	26 (45.6%)	28 (49.1%)	

Interpretation: Baseline demographic characteristics, including gestational age, birth weight, and sex distribution, were comparable between the two study groups, indicating that the groups were well matched before initiation of the feeding protocols.

The comparison of feeding outcomes is presented in Table 2. Neonates receiving early full enteral feeding achieved full enteral nutrition significantly earlier than those managed with conventional gradual enteral feeding advancement. The mean time to achieve full enteral feeding was 3.9 ± 0.9 days in the early feeding group compared with 6.5 ± 1.4 days in the conventional feeding group.

The time to initiation of enteral feeding was also shorter in the early feeding group (3.6 ± 1.2 hours) than in the conventional feeding group (4.0 ± 1.3 hours).

Table 2. Comparison of Feeding Outcomes

Outcome	Early Full Enteral Feeding (n=57)	Conventional Gradual Enteral Feeding (n=57)	P-value
Time to first feed (hours)	3.6 ± 1.2	4.0 ± 1.3	0.091
Time to achieve full enteral feeding (days)	3.9 ± 0.9	6.5 ± 1.4	0.0001*

Interpretation: Early full enteral feeding resulted in earlier establishment of full enteral nutrition compared with conventional gradual feed advancement.

Short-term growth outcomes are summarized in Table 3. Neonates in the early full enteral feeding group demonstrated superior growth compared with those receiving conventional gradual enteral feeding.

The mean daily weight gain was 19.8 ± 3.4 g/day in the early feeding group compared with 16.9 ± 3.1 g/day in the conventional feeding group. Similarly, greater weekly length gain (0.92 ± 0.18 cm/week vs. 0.79 ± 0.17 cm/week) and head circumference gain (0.76 ± 0.12 cm/week vs. 0.68 ± 0.11 cm/week) were observed in the early feeding group.

Table 3. Short-Term Growth Outcomes

Outcome	Early Full Enteral Feeding	Conventional Gradual Enteral Feeding	P-value
Weight gain (g/day)	19.8 ± 3.4	16.9 ± 3.1	0.0001*
Length gain (cm/week)	0.92 ± 0.18	0.79 ± 0.17	0.0001*
Head circumference gain (cm/week)	0.76 ± 0.12	0.68 ± 0.11	0.0001*

Interpretation: Early full enteral feeding was associated with improved short-term growth, reflected by greater weight gain, length gain, and head circumference growth.

The duration of hospital stay is shown in Table 4. Neonates receiving early full enteral feeding had a shorter mean hospital stay (12.6 ± 2.9 days) compared with those receiving conventional gradual enteral feeding advancement (16.1 ± 3.5 days).

Table 4. Duration of Hospital Stay

Outcome	Early Full Enteral Feeding	Conventional Gradual Enteral Feeding	P-value
Hospital stay (days)	12.6 ± 2.9	16.1 ± 3.5	0.0001*

Interpretation: Earlier achievement of full enteral nutrition was associated with a reduction in the duration of hospitalization.

Feeding-related complications are summarized in Table 5. The incidence of feeding intolerance, vomiting, abdominal distension, and necrotizing enterocolitis (NEC) was lower in the early full enteral feeding group than in the conventional feeding group.

Feeding intolerance occurred in 10.5% of neonates receiving early full enteral feeding compared with 24.6% of those receiving conventional gradual feeding advancement. NEC occurred in 1.8% and 5.3% of neonates, respectively.

Table 5. Feeding-Related Complications

Complication	Early Full Enteral Feeding n (%)	Conventional Gradual Enteral Feeding n (%)	P-value
Feeding intolerance	6 (10.5%)	14 (24.6%)	1.000
Vomiting	3 (5.3%)	7 (12.3%)	
Abdominal distension	4 (7.0%)	10 (17.5%)	
Necrotizing enterocolitis	1 (1.8%)	3 (5.3%)	

Interpretation: Early full enteral feeding was associated with fewer feeding-related complications and did not appear to increase the incidence of necrotizing enterocolitis in the study population.

Clinical outcomes are presented in Table 6. The incidence of neonatal sepsis and mortality was lower among neonates receiving early full enteral feeding than among those managed with conventional gradual enteral feeding advancement. Sepsis occurred in 8.8% of neonates in the early feeding group compared with 14.0% in the conventional feeding group. Mortality was observed in 1.8% and 3.5% of neonates, respectively. Exclusive breastfeeding at hospital discharge was achieved in 89.5% of neonates in the early feeding group compared with 78.9% in the conventional feeding group.

Table 6. Clinical Outcomes

Outcome	Early Full Enteral Feeding n (%)	Conventional Gradual Enteral Feeding n (%)	P-value
Sepsis	5 (8.8%)	8 (14.0%)	0.505
Mortality	1 (1.8%)	2 (3.5%)	
Exclusive breastfeeding at discharge	51 (89.5%)	45 (78.9%)	

Interpretation: Early full enteral feeding was associated with favourable clinical outcomes, including lower rates of sepsis and mortality and a higher rate of exclusive breastfeeding at discharge.

DISCUSSION

Optimal nutritional management is fundamental to improving survival and promoting adequate growth in preterm neonates. Early enteral nutrition facilitates gastrointestinal maturation, reduces dependence on intravenous fluids, and may decrease complications associated with prolonged hospitalization.^{2,3,15} The present multicenter prospective cohort study compared early full enteral feeding with conventional gradual enteral feeding advancement in stable preterm neonates and demonstrated that early full enteral feeding was associated with earlier achievement of full enteral nutrition, improved short-term growth, shorter hospital stay, fewer feeding-related complications, and more favorable clinical outcomes.

The baseline demographic and clinical characteristics of the two study groups were comparable with respect to gestational age, birth weight, and sex distribution, suggesting that the observed differences in outcomes were unlikely to be explained by baseline differences between the groups. Comparable baseline characteristics have also been reported by Nangia et al.⁵ and Baloda et al.⁶

One of the principal findings of the present study was the significantly earlier achievement of full enteral feeding in the early feeding group. Neonates receiving early full enteral feeding achieved full feeds in 3.9 ± 0.9 days, compared with 6.5 ± 1.4 days in the conventional feeding group. Earlier attainment of full enteral nutrition reduces exposure to intravenous fluids and vascular access, thereby potentially decreasing catheter-related complications and facilitating earlier nutritional rehabilitation. Similar findings were reported by Nangia et al., who demonstrated significantly earlier achievement of full enteral nutrition in stable very-low-birth-weight infants receiving early total enteral feeding.⁵ Baloda et al. also observed that early full enteral feeding enabled faster establishment of full feeds without increasing adverse gastrointestinal outcomes.⁶

The present study also demonstrated improved short-term growth among neonates receiving early full enteral feeding. Infants in the early feeding group showed greater daily weight gain, weekly length gain, and weekly head circumference growth than those receiving conventional gradual feed advancement. Adequate early nutritional intake is essential for preventing extrauterine growth restriction in preterm infants, and earlier establishment of full enteral nutrition likely contributed to the improved growth observed in this study. Similar observations have been reported by Nangia et al.⁵ and Villar et al.¹⁰

Hospital stay was shorter in the early full enteral feeding group than in the conventional feeding group. Earlier achievement of nutritional stability, together with improved feeding tolerance and growth, may have facilitated earlier discharge. A reduced duration of hospitalization has important clinical and economic implications by decreasing healthcare utilization, minimizing the risk of hospital-acquired infections, and reducing the emotional and financial burden on families. Comparable findings have been reported by Nangia et al.⁵ and Terefe et al.⁴

An important concern regarding early enteral feeding is the potential risk of feeding intolerance and necrotizing enterocolitis (NEC). In the present study, feeding intolerance, vomiting, abdominal distension, and NEC occurred less frequently in the early feeding group than in the conventional feeding group. These findings suggest that early full enteral feeding, when implemented in carefully selected hemodynamically stable preterm neonates under close clinical monitoring, does not appear to increase gastrointestinal morbidity. Similar findings have been reported by Baloda et al.⁶ Caple et al.⁷ also demonstrated that more rapid advancement of enteral feeds did not significantly increase the incidence of NEC in appropriately selected preterm infants.

Clinical outcomes also favored the early full enteral feeding group. Lower rates of neonatal sepsis and mortality and a higher proportion of exclusive breastfeeding at discharge were observed compared with the conventional feeding group. Earlier discontinuation of intravenous therapy may reduce the risk of bloodstream infection, while successful establishment of enteral feeding may support continued breastfeeding. These findings are consistent with previous reports by Nangia et al.⁵ and Baloda et al.⁶

The findings of the present study are in agreement with current recommendations supporting early establishment of enteral nutrition in clinically stable preterm infants whenever feasible. Contemporary nutritional guidelines recommend minimizing unnecessary delays in enteral feeding while maintaining careful clinical surveillance for feeding intolerance and gastrointestinal complications.^{15,16,17}

Strengths of the Study

The strengths of this study include its prospective multicenter design involving two tertiary-level NICUs, inclusion of comparable study groups, standardized assessment of feeding protocols, and evaluation of multiple clinically relevant outcomes, including growth parameters, feeding tolerance, complications, duration of hospital stay, mortality, and exclusive breastfeeding at discharge.

Limitations of the Study

The present study has several limitations. First, allocation to feeding groups was based on the clinical decision of the treating neonatologist rather than randomization, which may have introduced selection bias and residual confounding. Second, the study included a relatively modest sample size from two centers, which may limit the generalizability of the findings. Third, maternal variables and certain potential confounding factors were not evaluated. Finally, long-term growth, neurodevelopmental outcomes, and post-discharge follow-up were not assessed. Larger multicenter randomized controlled trials with longer follow-up are warranted to further validate these findings.

CONCLUSION

The present multicenter prospective cohort study suggests that early full enteral feeding is a safe and effective nutritional strategy for carefully selected stable preterm neonates. Compared with conventional gradual enteral feeding advancement, early full enteral feeding was associated with earlier achievement of full enteral nutrition, improved short-term growth outcomes, including greater weight gain, length gain, and head circumference growth, and a shorter duration of hospital stay. In addition, neonates receiving early full enteral feeding experienced lower rates of feeding intolerance, vomiting, abdominal distension, necrotizing enterocolitis, sepsis, and mortality, together with a higher proportion of exclusive breastfeeding at hospital discharge. These findings indicate that early full enteral feeding may improve both nutritional and short-term clinical outcomes without increasing feeding-related complications in stable preterm neonates.

Although the findings are encouraging, the non-randomized study design and relatively modest sample size warrant cautious interpretation. Further large, multicenter randomized controlled trials with long-term follow-up are required to confirm these findings and evaluate the impact of early full enteral feeding on long-term growth, neurodevelopmental outcomes, and overall neonatal health.

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Citation: Tailor DR, Sodha S. Early full enteral feeding versus conventional gradual enteral feeding advancement in stable preterm neonates: a multicenter prospective cohort study. *Int. J. Med.*, 2026;**8**(9):189-196.

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