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Comparison of Early Vs Late Initiation of Trophic Feeding in Preterm Neonates

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ABSTRACT

Objective: To compare early versus late initiation of trophic feeding with respect to neonatal outcomes. **Methods:** A randomized controlled trial was conducted in the Neonatal Intensive Care Unit of Allied Hospital, Faisalabad, over six months. Sixty preterm neonates (1000–1500 g) were randomized into early trophic feeding (within 48 h of birth, n=30) and late trophic feeding (after 72 h of birth, n=30) groups. Primary outcomes assessed were the time required to regain birth weight, the duration of parenteral nutrition, and the overall length of hospitalization. **Results:** Baseline characteristics were comparable between groups. Infants in the early feeding group regained birth weight significantly sooner (13.6 ± 3.1 vs. 19.8 ± 4.9 days, p<0.001), required shorter parenteral nutrition (9.2 ± 1.7 vs. 14.6 ± 2.4 days, p<0.001), and had reduced hospital stay (12.6 ± 2.8 vs. 21.6 ± 4.2 days, p<0.001). No increase in necrotizing enterocolitis or sepsis was observed. **Conclusion:** Early trophic feeding is safe and effective in preterm neonates, improving weight regain and reducing hospital stay without added risk of complications. Implementation of early feeding protocols should be considered to optimize neonatal outcomes.

INTRODUCTION

A birth is considered preterm if it occurs before the completion of 37 weeks of gestation, corresponding to fewer than 259 days from the onset of the last menstrual period of pregnant women, is considered preterm.[1–2] In 2010, the global prevalence was 11.1%, declining slightly to 10.6% in 2014. However, these figures mask wide regional disparities, with approximately 60% of preterm deliveries reported from South Asia and Sub-Saharan Africa.[3–4]

Ensuring optimal nutrition plays a pivotal role in lowering both mortality and chronic morbidities, including extra-uterine growth restriction and adverse neurodevelopmental consequences in preterm infants.[5–6] It supports weight gain comparable to that of full-term neonates at equivalent postmenstrual ages, reduces postnatal growth failure and gastrointestinal risks such as enterocolitis, and enhances long-term developmental outcomes. Trophic feeding (TF) is widely considered the method of choice for addressing these nutritional challenges in preterm infants.[7]

Defined as the initiation of very small quantities of enteral feeds within the first few days of life, trophic feeding (TF) represents a strategy to condition the immature gut of preterm neonates.[8] Known interchangeably as minimal enteral nutrition (MEN), gut priming, or hypo-caloric feeding, it involves providing insignificant nutritional volumes (1–2 ml/kg/dose or 10–15 ml/kg/day). While these amounts do not meet the infant's full nutritional requirements, they stimulate gastrointestinal maturation and provide limited nutrients, ideally through colostrum. Importantly, TF is designed to support intestinal development rather than overall growth, and serves as a means to decrease dependency on parenteral nutrition and the complications that accompany it.[9]

According to a study comparing early (<48 h) and late (>72 h) trophic feeding in preterm neonates, no significant

differences were found in baseline maternal or neonatal profiles.[10] Nevertheless, the early feeding group demonstrated superior outcomes: earlier regain of birth weight (13.75 ± 5.21 vs. 20.53 ± 6.31 days, P<0.001), reduced parenteral nutrition dependency (9.26 ± 4.57 vs. 14.11 ± 6.42 days, P<0.001), and shorter hospitalization (12.14 ± 8.61 vs. 21.11 ± 1.16 days, P<0.001). Both groups had similar rates of late-onset sepsis (P=0.73), with one confirmed case of NEC reported in each.

The present study set out to compare early and late initiation of trophic feeding in preterm neonates. If early trophic feeding is shown to be advantageous, it may be endorsed in the future as a preferred feeding strategy to facilitate quicker weight recovery, reduce hospitalization, and ensure better early growth outcomes.

METHODOLOGY

This study was designed as a randomized controlled trial conducted in the Neonatal Intensive Care Unit (NICU) of Allied Hospital, Faisalabad from 31st January 2025 and 31 May 2025 following the approval of the synopsis by the institutional ethical review committee.

Regarding sample size estimation, we applied a 5% level of significance and 80% power of the test. Based on published data showing mean duration of hospitalization in early trophic feeding (9.26 ± 4.57 days) and late trophic feeding groups (14.11 ± 6.41 days), a total sample of 60 neonates was determined, with 30 participants allocated to each group. Patient enrollment was carried out using a non-probability consecutive sampling method.

The included cases were preterm neonates of both genders, admitted to the NICU, with a birth weight ranging from 1000 to 1500 grams whereas those with major congenital anomalies, severe asphyxia, referral from other hospitals, those already started on direct breast milk or alternative feeding prior to admission, and infants with pre-diagnosed stage II/III necrotizing enterocolitis were excluded from the trial.

Eligible neonates were enrolled after written informed consent was obtained from their parents. Baseline demographic and clinical information, including gravidity, gestational age, mode of delivery, cause of preterm labor, surfactant administration, birth weight, and first and fifth minute Apgar scores, were recorded in a predesigned proforma. Random allocation into two groups was performed by the lottery method. Group A was assigned to early trophic feeding, commenced within 48 hours of birth, whereas Group B was assigned to late trophic feeding, initiated after 72 hours.

Bolus feeding was employed as the standard method. A radio-opaque feeding tube (2 × 47 mm) was inserted by the attending nurse and retained between feeds, with replacement on a daily basis. Feeds consisted of 1–2 cc/kg of expressed human milk where available, or preterm infant formula (Fre-Nan, Nestlé; prepared as two scoops of formula for every 60 ml of boiled water) when breast milk supply was insufficient. Feeds were administered every 4–6 hours via gravity using a syringe placed above the infant.

Body weight of each neonate was measured daily at the same time using a digital baby scale. Outcomes were assessed in terms of duration of hospitalization, time to regain birth weight, and duration of parenteral nutrition. Parenteral nutrition was started within the first 72 hours after birth and continued until discontinued as per clinical stability.

The statistical analysis was performed in SPSS version 25. Quantitative variables, including gestational age, birth weight, Apgar scores, number of days to regain birth weight, length of hospital stay, and parenteral nutrition requirement, were described using mean and standard deviation. Frequencies and percentages were calculated for qualitative variables including gender, gravidity, mode of delivery, cause of preterm delivery, and surfactant administration. The Independent Samples t-test was applied to compare mean outcomes between groups. Effect modifiers such as gestational age, gravidity, mode of delivery, cause of preterm labor, gender, and surfactant administration were controlled through stratification. Post-stratification Independent Samples t-test was applied, with p-value <0.05 considered statistically significant.

RESULTS

This table compares the demographic and baseline clinical features between infants randomized to early trophic feeding (TF) and late TF groups. The groups were well matched in terms of birth weight and gestational age (p >0.05). The distribution of gender (male/female) and mode of delivery (normal vaginal vs. cesarean section) was also balanced, with p-values >0.05. (Table 1)

Table 1

Baseline characteristics of preterm neonates (N=60)

Variables		Early TF (n=30)	Late TF (n=30)	p-value
Gestational age(weeks), mean ± SD		31.00 ± 2.15	32.03 ± 2.16	0.068
Birth weight (g), mean ± SD		1309 ± 108.9	1270.5 ± 104.0	0.167
Gender	Male	14 (46.7%)	15 (50.0%)	0.796
	Females	16 (53.3%)	15 (50.0%)	
Mode of delivery	Normal Vaginal Delivery	14 (46.7%)	14 (46.7%)	1.000
	Cesarean Section	16 (53.3%)	16 (53.3%)	

This table presents the main outcomes. Infants in the early TF group regained their birth weight significantly earlier (mean 13.6 vs. 19.8 days, p<0.001), required a shorter duration of parenteral nutrition (9.2 vs. 14.6 days, p<0.001), and had a shorter hospital stay (12.6 vs. 21.6 days, p<0.001) compared to the late TF group. The mean differences with 95% confidence intervals highlight the magnitude of benefit associated with early initiation of trophic feeding.(Table 2)

Table 2

Primary outcomes by feeding group

Outcome	Early TF (n=30)	Late TF (n=30)	Mean difference (95% CI)	p-value
Time to regain birth weight (days)	13.65 ± 3.07	19.76 ± 4.85	−6.11 (−8.21 to −4.01)	<0.001
Duration of parenteral nutrition (days)	9.25 ± 1.72	14.59 ± 2.35	−5.34 (−6.41 to −4.28)	<0.001
Duration of hospitalization (days)	12.64 ± 2.81	21.61 ± 4.24	—	<0.001

Stratified analyses demonstrated that early trophic feeding consistently reduced time to regain birth weight, duration of parenteral nutrition, and hospital stay across

most subgroups. The benefits were significant in both males and females, and were evident irrespective of mode of delivery (normal vaginal or cesarean). When stratified by cause of preterm birth, significant improvements were observed in infants born due to PIH, APH, and PROM. In cases of multiple pregnancy, early TF shortened parenteral nutrition and hospital stay though the difference in regaining birth weight was not significant. For the small unexplained subgroup, trends favored early TF but statistical significance was limited by small sample size. (Table 3)

Table 3

Stratified outcomes by gender, mode of delivery, and cause of preterm

Variables		Outcome	Early TF (mean ± SD)	Late TF (mean ± SD)	p-value
Gender	Male	Time to regain BW (days)	14.25 ± 3.07	21.47 ± 3.60	<0.001
		Parenteral nutrition (days)	9.46 ± 1.97	13.99 ± 1.66	<0.001
		Hospital stay (days)	12.82 ± 3.42	19.87 ± 3.26	<0.001
	Female	Time to regain BW (days)	13.12 ± 3.07	18.05 ± 5.44	0.004
		Parenteral nutrition (days)	9.06 ± 1.51	15.19 ± 2.82	<0.001
		Hospital stay (days)	12.48 ± 2.25	23.35 ± 4.48	<0.001
Mode of Delivery	Normal vaginal	Time to regain BW (days)	12.90 ± 2.02	19.91 ± 4.80	<0.001
		Parenteral nutrition (days)	9.41 ± 1.67	14.96 ± 2.71	<0.001
		Hospital stay (days)	12.44 ± 2.44	21.59 ± 3.05	<0.001
	Cesarean	Time to regain BW (days)	14.30 ± 3.70	19.63 ± 5.05	0.002
		Parenteral nutrition (days)	9.11 ± 1.81	14.26 ± 2.03	<0.001
		Hospital stay (days)	12.81 ± 3.17	21.63 ± 5.16	<0.001
Cause of Preterm	PIH	Time to regain BW (days)	14.36 ± 2.83	21.93 ± 5.26	0.003
		Parenteral nutrition (days)	8.40 ± 0.94	15.49 ± 2.47	<0.001
		Hospital stay (days)	12.65 ± 2.68	22.54 ± 1.98	<0.001
	APH	Time to regain BW (days)	13.72 ± 3.60	20.60 ± 3.23	0.021
		Parenteral nutrition (days)	10.18 ± 1.43	14.83 ± 2.77	0.013
		Hospital stay (days)	11.46 ± 2.12	21.50 ± 3.21	0.001
	PROM	Time to regain BW (days)	11.56 ± 2.19	18.96 ± 3.86	<0.001
		Parenteral nutrition (days)	8.91 ± 1.31	13.79 ± 2.14	<0.001
		Hospital stay (days)	11.39 ± 2.07	22.34 ± 6.53	<0.001
	Multiple pregnancy	Time to regain BW (days)	14.66 ± 3.36	18.76 ± 6.64	0.148
		Parenteral nutrition (days)	9.48 ± 2.37	14.31 ± 2.33	0.002
		Hospital stay (days)	14.25 ± 3.44	19.36 ± 4.33	0.024
	Unexplained	Time to regain BW (days)	16.10 (n=1)	17.33 ± 3.12(n=3)	0.765
		Parenteral nutrition (days)	12.20 (n=1)	14.67 ± 2.99	0.549
		Hospital stay (days)	15.50 (n=1)	22.60 ± 0.95	0.023

DISCUSSION

The findings of this randomized controlled trial demonstrate that early initiation of trophic feeding in preterm neonates resulted in significantly shorter time to regain birth weight, reduced duration of parenteral nutrition, and decreased length of hospitalization compared to late initiation. These results reinforce the importance of timely nutritional support in preterm infants and are consistent with the growing international evidence favoring early feeding strategies.

Globally, preterm birth is a major contributor to neonatal morbidity and mortality, with more than one in ten live births affected and the highest burden reported in South Asia and Sub-Saharan Africa [11]. Optimal nutrition during the neonatal period has been highlighted as a fundamental strategy to reduce mortality, prevent growth restriction, and improve neurodevelopmental outcomes [12]. In this context, our findings support the role of early trophic feeding as a safe and effective intervention to accelerate recovery and minimize complications associated with delayed enteral nutrition.

Evidence from other low-resource settings echoes these observations. Tewoldie et al. demonstrated that earlier initiation of enteral feeding in Ethiopian preterm infants facilitated faster achievement of full feeds, although determinants such as gestational age and clinical stability influenced the process [13]. Pinto et al. similarly highlighted that preterm birth is a persistent public health concern, requiring standardized nutritional strategies to improve outcomes [14]. These findings align with our trial, emphasizing that structured early feeding protocols can be successfully implemented in resource-constrained NICUs.

International studies further strengthen the case for early initiation. Ofek Shlomai et al. showed that delaying feeding until exclusive maternal breast milk was available prolonged parenteral nutrition without added benefit [15]. Kwok et al. also concluded that early feeding is generally safe, enhances gastrointestinal adaptation, and is considered safe, with no observed rise in the risk of necrotizing enterocolitis (NEC) [16]. Consistent with these reports, our study observed no increase in NEC or sepsis among early-fed infants, confirming the safety of early initiation.

The multicenter Ethiopian study by Kebede et al identified barriers to early trophic feeding, such as respiratory distress and hemodynamic instability, which contributed to delayed feeding initiation [17]. Their earlier preprint reported similar challenges [18]. While such barriers are common in low-resource environments, our results indicate that with proper monitoring and standardized feeding protocols, early initiation can be achieved safely. This underscores the importance of training healthcare staff and adopting institutional guidelines to overcome clinical hesitation in initiating early feeding.

In terms of long-term implications, Skinner and Narchi highlighted that adequate early nutrition is strongly associated with improved neurodevelopmental outcomes in preterm infants [19]. Although our trial did not assess long-term growth or neurodevelopment, the observed

early clinical benefits—such as quicker weight regain and reduced hospitalization—may translate into improved long-term outcomes, consistent with these reviews.

This study has several strengths. Its randomized controlled design minimized bias and increased the reliability of the results. The use of strict inclusion criteria ensured homogeneity in study participants, and daily monitoring with standardized feeding protocols minimized variability in management. Furthermore, this trial adds important data from a South Asian NICU setting, where the burden of prematurity is among the highest globally.

Nevertheless, some limitations should be acknowledged. The study was conducted at a single center, which may restrict generalizability to other settings. The sample size, though statistically adequate, was relatively small and may not have been sufficient to detect rare adverse events such as NEC or sepsis. Follow-up was limited to in-hospital outcomes, preventing evaluation of long-term growth and neurodevelopmental trajectories. In addition, reliance on formula feeding in cases of insufficient breast milk could have influenced tolerance and outcomes.

CONCLUSION

This trial confirms that early trophic feeding is safe and effective in preterm neonates, leading to earlier weight regain, shorter parenteral nutrition, and reduced hospitalization without increasing adverse events. These findings are consistent with global and regional evidence and suggest that implementation of early feeding protocols could yield substantial clinical benefits, particularly in high-burden regions such as South Asia. Further multicenter studies with larger cohorts and long-term follow-up are recommended to consolidate these findings and assess their impact on neurodevelopmental outcomes.

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