ORIGINAL ARTICLE

Effect of early versus late trophic feeding initiation on high dependency unit stay in preterm infants: A non-randomised clinical trial

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Abstract

Objective: To evaluate the impact of early (<48 hrs) versus late (>72 hrs) initiation of trophic feeding in preterm infants on time to reach full enteral feeds and length of stay in the high dependency unit, and on the incidence of complications.

Method: The clinical trial was conducted at the Neonatal High Dependency Unit, Lady Reading Hospital, Peshawar, Pakistan, from July 30 to October 30, 2023, and comprised preterm infants with gestation age 28-36 weeks and birth weight 1-2.5kg. The subjects were divided into two groups. In group A, feeding was initiated at <48 hours of birth, while in group B, feeding was initiated after 72 hours of birth. Feeding was given at 12ml/kg/day and advanced with incremental increase in both the groups. The neonates were assessed for success of trophic feeding and development of complications. Stay in the high dependency unit was also documented. Data was analysed using SPSS 23.

Results: Of the 240 preterm infants, 141(58.8%) were boys and 99(41.3%) were girls. There were 120(50%) neonates in group A with mean gestational age 31.65±2.04 weeks, and 120(50%) in group B with mean gestational age 3117±2.46 weeks. There was no significant difference between the groups with respect to gender, gestational age and birthweight (p>0.05). The mean stay in high dependency unit was 6.14±2.74 days in group A compared to 12.07±4.11 days in group B (p<0.001). There was no significant difference between the groups concerning complications (p>0.05).

Conclusion: Early initiation of trophic feeding in preterm neonates had a significant positive impact without any significant increase in the risk of complications.

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Introduction

Preterm births have been increasing worldwide over the past two decades due to advances in obstetric practices and neonatal care. The World Health Organisation (WHO) defines a preterm infant as one born before 37 weeks of gestation.[1] In the postnatal period, nutrition and timing of initiation of enteral feed is crucial for achieving optimal growth and development in infants, especially in preterm and low-birthweight (LBW) babies.[2]

Intolerance to feed is a major issue in preterm infants and is characterised by residual gastric volume of >50% at the time of the second feed, vomiting, abdominal distension, or a combination of these.[3] Enteral feeding supports gut development in preterm infants, and reduces the risk of infections and sepsis. Delaying enteral feeds does not increase the risk of common complications, like necrotising enterocolitis. Proper and adequate nutrition is essential for growth and development of preterm infants and to improve their immunity, while poor nutrition leads to restricted growth, which can have a significant impact on neuro-behavioural development. Preterm infants with poor nutrition are at a risk of psychomotor and cognitive disorders, including a higher incidence of conditions, like cerebral palsy (CP) and autism.[4]

Trophic feeding involves administering small amounts of enteral feeds that are not only beneficial for nutritional purposes, but also stimulate mucosal enzymes activity, release hormones, improve blood flow, gut motility and microbial flora of the gastrointestinal tract (GIT) of preterm babies. This further decreases the incidence of complications, including hyperbilirubinaemia, gut mucosal atrophy, infections, cholestasis and metabolic complications.[5] Enteral fasting during the neonatal period can be disadvantageous, as enteral feeds promote gastrointestinal hormone secretion and motility, contributing to the physiological, endocrine and metabolic maturation of GIT.[6] Studies have shown that higher protein and calories intake in the early neonatal period is associated with higher intelligence quotient (IQ) score at 18 months of age. Conversely, delayed introduction of

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feeds may impair the functional adaptation of the immature GIT, leading to reduced enzyme production and prolonged dependence on parenteral nutrition, which, in turn, increases the risk of sepsis and necrotising enterocolitis as well as vitamin and mineral deficiencies.[7]

In a study, babies who were started enteral feeding earlier were found to achieve well-sustained feeding earlier (18 days) than those in whom feeding was initiated late (21 days).[8] A clinical trial conducted in 2020 also reported that the early feeding group reached full feeds faster, and had a shorter mean hospital stay than the late feeding group.[9]

The current study was planned to evaluate the impact of early (<48 hrs) versus late (>72 hrs) initiation of trophic feeding in preterm infants on time to reach full enteral feeds and length of stay in the high dependency unit (HDU), and on the incidence of complications.

Patients and Methods

The non-randomised clinical trial was conducted at the Neonatal HDU of Lady Reading Hospital, Peshawar, Pakistan, from July 30 to October 30, 2023. After approval from the institutional ethics review committee, the sample size was calculated in the light of literature[8] with 95% confidence level and 80% power using the WHO calculator.[10] The sample was raised using consecutive non-probability sampling technique. Those included were preterm infants of either gender with gestation age 28-36 weeks and birth weight 1-2.5kg, and postnatal age <3 days at the time of admission to hospital. Those excluded were neonates with major congenital anomaly, those on inotropic drug support, and preterm infants with severe respiratory distress.

For the purpose of the study, trophic feeding was defined as the method of enteral feeding when preterm LBW neonate had no coordinated swallowing. It was given as a small amount of feed through either nasogastric or orogastric tube.

HDU was a part of neonatology where intensive care was provided to high-risk preterm LBW babies, although it did not include advanced life support, like ventilator, extracorporeal membrane oxygenation (ECMO), etc. Preterm was defined as an infant delivered before 37 weeks of gestation.

The preterm infants were allocated according to their date of birth into two groups. In group A, trophic feeding was initiated early (<48hrs postnatal age) at 12ml/kg/day in the form of 1-2ml every 2 hourly with an incremental increase each day in the same way. In group B, it was initiated late (>72hrs postnatal age) in the same amount and with a similar increase each day. The neonates were assessed for success of trophic feeding and development of complications. Stay in HDU was documented along with the other data.

Data was analysed using SPSS 23. Frequencies and percentages were calculated for categorical variables. Mean±standard deviation were calculated for numerical variables. Independent sample t-test was used to compare the HDU stay between the groups. Chi-square test was used to compare the incidence of complications in the groups. P<0.05 was considered statistically significant.

Results

Of the 240 preterm infants, 120(50%) were in each of the two groups (Figure 1). Overall, there were 141(58.8%) boys and 99(41.3%) girls (Figure 2). Neonates in group A had mean gestational age 31.65±2.04 weeks, while those in group B had mean gestational age 3117±2.46 weeks. There

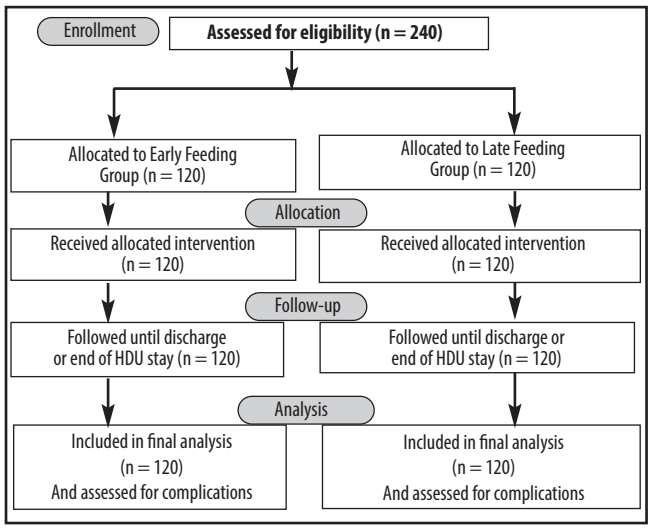

Figure-1: Consolidated standards of reporting trials (CONSORT) diagram.[23]

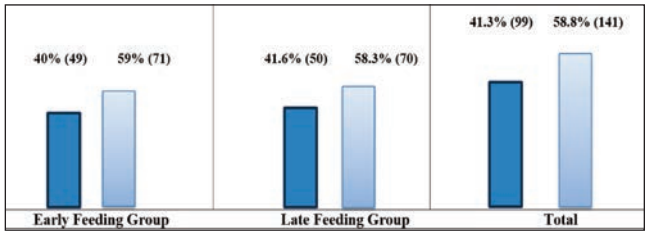

Figure-2: Gender distribution in the study groups.

Table-1: Intergroup comparison of baseline characteristics (n+240).

Clinical Characteristics	Early feeding group Group A	Late feeding group Group B	*p*-value
Gestational			
Mean age (weeks)	31.65±2.04	31.17±2.46	
Median (Range)	32 (28-36)	31.5 (28-36)	0.106
Mean Weight (grams)	1892±271	1848±311	0.243

SD: Standard deviation.

Table-2: Intergroup comparison of duration of HDU stay.

Duration of HDU stay (Days)	Early feeding group Group A (n=120)	Late feeding group Group B (n=120)	*p*-value
Mean±SD	6.14±2.74	12.07±4.11	<0.001
Median (Range)	5(12)	12(17)	

HDU: High dependency unit, SD: Standard deviation.

Table-3: Intergroup comparison of complications.

Complications	Early feeding (Group A)	Late feeding (Group B)	*p*-value (0.736)
	[n (%)]	[n (%)]	
1. **Feed intolerance**	8/120 (6.7)	6/120 (5)	(0.783)
2. **Necrotising enterocolitis**	3/120 (2.5)	2/120 (1.7)	(1.00)
3. **Sepsis**	2/120 (1.7)	6/120 (5)	(0.281)

was no significant difference between the groups with respect to gender, gestational age and birthweight (p>0.05) (Table 1).

The mean stay in high dependency unit was 6.14±2.74 days in group A compared to 12.07±4.11 days in group B (p<0.001) (Table 2).

No significant differences were observed between the groups in terms of the incidence of complications (Table 3).

Discussion

Preterm birth is a significant cause of neonatal deaths and one of the leading causes of mortality in children aged less than five years. Preterm birth complications remained the top cause of under-5 child mortality globally in 2022, accounting for about one million neonatal deaths.[11] An approximately13.4 million births were preterm in 2020, accounting for 9.9% of total births worldwide.[12] Of total preterm births globally in 2014, 81.1% were reported in sub-Saharan African and South Asian countries, like India, China, Nigeria, Bangladesh, Indonesia and Pakistan.[13]

For proper care of preterm infants, achieving adequate growth is crucial. Proper nutrition is not only essential for optimal growth, but also for neurological development. Determining the best feeding practices for preterm infants poses a significant challenge as their immature gastrointestinal system may not tolerate early feeds, and lead to feeding difficulties. Contrary to this, a lack of early enteral feed initiation may impair gastrointestinal motility by reducing hormonal activity, intestinal mucosal growth, and nutrient absorption. This can further contribute to feeding intolerance and prolonged hospital stays.[14]

In the current clinical trial, the effects of early and late trophic feeding initiation were compared and assessed in preterm infants with respect to an important neonatal outcome in resource-limited settings; the length of HDU stay. The infant's clinical characteristics were similar in both groups with no significant differences between the early and late feeding groups. However, the early initiation of trophic feeding had a significant impact on HDU stay, resulting in early discharge from the unit.

This shorter HDU stay was mainly due improved blood flow, gut motility and early stimulation of gut microbial flora of these preterm babies, and reduced dependence on parenteral nutrition. The results align with earlier studies.[15,16] Moreover, early feeding is linked to improved milestones and shorter neonatal intensive care unit (NICU) stays.[17]

The current study supports the benefits of trophic feeding in the form of improved weight-gain, better milk tolerance, a lower incidence of sepsis, and earlier hospital discharge, consistent with findings reported by a prospective follow-up study.[18]

The shorter average HDU stay in the current study was associated with early trophic feeding. This was supported by Pratiwi et al. in 2023, who found that trophic feeding significantly reduces the length of hospital stay among neonates.[19]

In the current study, there were no significant differences between the two groups concerning complications, such as feeding intolerance, necrotising enterocolitis and sepsis. Similar results were reported by Muguruza et al. in 2025.[20]

A systematic review in 2021 demonstrated that the interval between bolus feed, whether short or long, did not significantly impact feeding tolerance or clinical outcomes in very preterm infants, reinforcing the idea that feeding initiation timing may have a greater influence than frequency alone.[21] Additionally, Parker et al. in 2021 emphasised in their state-of-the-science review that early enteral initiation was essential to optimise growth and neurodevelopmental outcomes in very LBW infants.[22]

The current study has limitations of being a single-centre research. Large, multicentre randomised controlled trials (RCTs) are highly recommended to validate the current results, and to study other aspects of early trophic feeding on neonates and hospital resources.

Conclusion

Early initiation of trophic feeding in preterm infants was associated with a significantly shorter HDU stay without increasing the risk of complications.

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Author Contribution:

RM: Research question, ethical approval, trial registration, design, data analysis, writing, final review and willing to take responsibility.

AK: Research question, design, data interpretation, drafting, critical review and willing to take responsibility.

AM: Design, data compilation, drafting and final review.

ZR: Design, data analysis, writing, review and willing to take responsibility.

AA: Design, data compilation, drafting, final review and willing to take responsibility.