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Effect of Body Positioning on Gastrointestinal Tolerance in Very-Low-Birth-Weight Preterm Infants Fed Enriched Breast Milk in a NICU in Yazd, Iran

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ABSTRACT

Background: Feeding preterm infants with unfortified breast milk can lead to growth delays and nutritional deficiencies. To address this while promoting breastfeeding, commercial human milk fortifiers are commonly used. However, gastrointestinal intolerance, including gastric residue, remains a significant concern in these infants. This study investigates the impact of body positioning on gastrointestinal tolerance in very low birth weight (VLBW) preterm infants fed enriched breast milk.

Methods: A crossover clinical trial was conducted on 60 VLBW preterm infants admitted to the NICUs of Shahid Sadoughi Hospital in Yazd, Iran, in 2023. Infants were divided into two groups (n=30 each) via convenience sampling. In Group 1, infants were first placed in the prone position after feeding, followed by the right lateral position, with gastrointestinal tolerance assessed 3 hours post-feeding using a standardized checklist. Group 2 followed the reverse order.

Results: The majority (86.7%) of infants exhibited effective tolerance, with minimal gastric residuals (<20%) before and after feeding. No statistically significant differences in gastrointestinal outcomes were detected between the prone and right lateral positions ($p > 0.05$). These findings do not establish equivalence between the two positions, but they suggest that both may be considered as options in NICU feeding management.

Conclusion: The present study detected no significant difference in gastrointestinal tolerance between prone and right lateral positioning in VLBW infants, with no observed increase in adverse effects such as vomiting or abdominal distension. The results indicate that both positions may be acceptable for clinical use; however, formal equivalence has not been demonstrated. Further studies with larger samples and equivalence designs are needed before the two positions can be considered fully interchangeable.

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Introduction

Premature babies are those born before 37 weeks of pregnancy. In recent decades, with the growth of medical-nursing and health services, the survival rate of newborns has increased significantly[1]. One of the most important indicators of the health of any society is the birth rate of premature babies. Despite the significant progress that has been made in identifying the science of prematurity, the birth rate of these babies is increasing[2]. When a premature baby is born, the abundant sources of nutrients that have nurtured the growth and development of the fetus up until that point are suddenly halted. It is crucial for nutrient delivery to be swift in order for the infant to achieve rapid growth and develop a body composition resembling that of a full-term fetus[3]. Premature infants with very low birth weight (less than 1500 grams) who are exclusively breastfed face heightened risks due to their small size[4]. Premature babies have low reserves of calcium and phosphate and require large amounts of minerals, and in order to achieve proper skeletal growth, the importance of meeting the nutritional needs of these babies increases[5]. Human milk is considered the optimal source of nutrition for infants and plays a crucial role in any nutritional regimen aimed at supporting gut health. It contributes significantly to enhancing host defenses, aiding in digestion and nutrient absorption, promoting neural development, maintaining proper function of the digestive system, and supporting the mental well-being of the mother[6]. However, it is important to note that human milk, while beneficial, may not fully meet the intricate nutritional requirements of extremely low birth weight and premature infants[7]. After the second and third week of life, there is a noticeable decrease in the concentration of key nutrients such as protein, calcium, phosphorus, and magnesium. Consequently, the standard practice of fortification, which involves adding a fixed amount of commercial breast milk fortifier, has become widespread[8]. In order to mitigate these drawbacks and simultaneously promote the consumption of breast milk among very low birth weight preterm infants, a commercial breast milk fortifier is utilized. This fortifier, among its many functions, elevates the calcium and phosphorus levels in the final feedings provided to very low birth weight infants[9]. The commercial breast milk fortifier, containing essential nutrients such as fat, calcium, phosphorus, magnesium, sodium, potassium, iron, vitamin A, and vitamin D, is known for enhancing the nutritional content of breast milk[10]. Since 2012, an HMF-based human milk enhancer has been approved and made available to the public, and the use of this milk has been introduced as a salvage treatment[8]. Babies born before 34 weeks of pregnancy are at a heightened risk of aspiration and suffocation due to the underdeveloped coordination between sucking, swallowing, and breathing. Feeding for these infants typically commences with gavage and lavage techniques. Consequently, a considerable proportion of infants admitted to the neonatal intensive care unit encounter challenges in tolerating feeding and processing milk[11].

One of the most concerning issues in infant feeding is the occurrence of gastric residuals or aspirations prior to feeding, along with various symptoms associated with intolerance. Gastric residuals or pre-feeding aspirates refer to the retention of food in the stomach from a previous feeding, which is observed at the commencement of the subsequent feeding session[12]. When gastric residue exceeds 25% to 50% of the prior feeding volume, it raises concerns about diminished gastric motility, potentially hindering the neonate's ability to properly absorb nutrients. Significant amounts of gastric residue are perceived by caregivers as indicative of food intolerance, prompting them to administer tailored treatment protocols[12,13]. Defining feeding tolerance presents a challenge for caregivers of infants. Research suggests that feeding tolerance is influenced by various factors, including the volume and color of residual stomach contents,

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stool patterns, presence of blood in stools, vomiting, abdominal distension, and tenderness[14]. Additionally, gastric emptying is impacted by factors such as gestational and postnatal age, the types of formula and nutrient combinations used, medications, and sleeping positions[15]. Supportive nursing care pertaining to nutrition plays a crucial role in enhancing the nutritional status of low-birth-weight infants. This form of care entails fundamental considerations such as food quantity, formula composition, feeding intervals, and prevention of complications associated with gastric residue[16]. The positioning of the infant post-feeding is also recognized as a significant factor influencing gastric emptying. Neonatal positioning is a non-intrusive and non-pharmacological intervention rooted in the comprehension of human anatomy and nursing expertise[17].

In recent years, there has been a significant focus on determining the optimal body position for premature infants. Advancements in neonatal care technology have enhanced our understanding of the crucial role body position plays in various physiological functions for premature infants[18]. In clinical settings, the impact of varying body positions on the evolution of gastric residuals in very low birth weight premature infants has not been comprehensively addressed. Additionally, the prevalent practice of employing fortified breast milk for very low birth weight infants persists in Iran, with limited investigation and understanding of the subject. Given the limited understanding of the digestive tolerance of fortified milk in very low birth weight premature infants and the sparse research on the impact of diverse conditions, particularly on the tolerance of fortified breast milk, this study seeks to explore the influence of body condition on gastrointestinal tolerance. The investigation involved conducting gastrointestinal studies on very low birth weight preterm infants who were fed enriched breast milk and hospitalized in the neonatal intensive care unit.

Materials and Methods

This crossover clinical trial (Registration Code: IRCT20230328057781N1) evaluated 60 very low birth weight (VLBW) infants admitted to the neonatal intensive care unit (NICU) at Shahid Sadoughi Hospital, Yazd, between June and November 2023. Inclusion criteria included a gestational age of 26–33 weeks, nasogastric tube feeding, a birth weight of 1000–1500 grams, absence of congenital anomalies, breastfeeding status, clinical stability, and medical clearance for supine positioning. Medical records were reviewed, and infants were randomly assigned to either the prone or right-side-lying group through computer-generated randomization. Each infant received enriched breast milk prior to being positioned accordingly. Gastrointestinal tolerance was assessed three hours post-feeding using a structured checklist, followed by a resting period dedicated to breastfeeding. Data collection tools included a demographic questionnaire capturing variables such as gender, gestational age, and birth weight, alongside a gastrointestinal tolerance checklist. The checklist evaluated factors including the baby's position (Group A: prone, Group B: right-side lying), daily milk intake, gastric residuals exceeding or below 20% of the milk volume three hours post-feeding, and clinical signs such as vomiting and abdominal distension. Acknowledging that a dichotomous threshold of <20% may have limited discriminatory ability—given that 86.7% of infants fell below this threshold—the present study also recorded raw residual volumes in milliliters to enable future continuous analysis. This threshold was selected based on prior NICU protocols, but the authors recognize that alternative definitions (e.g., residual >50% of feed volume or presence of bilious residuals) might yield different results. This comprehensive methodology ensures robust data collection and facilitates the comparison of gastrointestinal tolerance between the two positioning groups. By obtaining informed consent from the parents of the baby and

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securing approval from the baby's physician, demographic information was gathered. Specialized neonatologists attended to very low birth weight premature infants to establish the initial feeding volume, a combination of breast milk and fortifier milk. The baby's optimal weight was determined based on gestational age, and individualized feeding plans were devised to outline the commencement of feeding, daily feeding rate increase, and the timeline for achieving full feeding (160 ml/kg/day). Oral-gastric tubes (OG Tub) were inserted for all premature infants under study. Exclusive breast milk feeding was provided to all infants throughout the study period, with a consistent feeding interval of three hours. Within 8 to 10 days, babies were fully transitioned to feeding based on birth weight. Upon reaching a feeding rate of 60-100 ml/kg/day, the addition of fortifier, specifically Aptamil fortified milk, commenced. Every three hours, infants received a feeding of either pure breast milk or a mixture of breast milk with fortifier. Gastric residual volume was measured using a 10 cc syringe, and various indicators of digestive tolerance, such as abdominal distention and vomiting, were assessed and documented based on a predefined checklist. The amount of milk administered to each infant was tailored to their individual weight, with both the volume consumed and any residual volume in the stomach measured in cubic centimeters.

Infants in the first group received their designated volume of fortified breast milk and were then positioned prone (Position A). After three hours, gastric residual volume was measured, and digestive tolerance indicators were recorded using a standardized checklist. During a subsequent rest period, the infants were initially fed unfortified breast milk. In the following feeding cycle, they received enriched breast milk and were positioned on their right side (Position B). Gastric residual volume was again assessed three hours post-feeding. The fortified breast milk feeding schedule included two daily sessions at 8:00 AM and 2:00 PM. Each infant underwent gastric residual assessment three hours after each feeding, with data systematically recorded on the checklist to ensure protocol compliance. In the second group, infants received their specified volume of enriched breast milk while positioned on their right side (Position B). Similar to the first group, residual gastric volumes and digestive tolerance parameters were measured and documented three hours post-feeding. Infants were placed in the prone position (Position A) during subsequent feedings, following the same feeding schedule. A three-hour washout period was implemented between feedings to minimize residual effects. Data collection involved repeated measurements and analyses over one week to assess tolerance under both positional conditions. This structured approach allowed for rigorous evaluation of gastrointestinal outcomes, ensuring the reliability and validity of the findings.

Sample size calculation: Sample size was calculated a priori using GPower software (version 3.1.9.7) for a two-sided McNemar's test for paired proportions (within-subject crossover comparisons). Based on prior literature reporting baseline gastrointestinal tolerance rates of approximately 80% in VLBW infants, an absolute difference of 15% (e.g., 80% vs. 95%) was considered clinically meaningful. With $\alpha = 0.05$ and power $(1-\beta) = 0.80$, the required sample size was calculated as 47 infants. To account for an anticipated 20% dropout or protocol violation rate, 60 infants were enrolled. Post-hoc analysis: With the obtained sample of 30 infants completing both periods of the crossover (60 infants total, each serving as their own control), the study had 80% power to detect an absolute difference of approximately 20 percentage points in tolerance rates. Smaller differences (10-15 percentage points) would require sample sizes exceeding 150 infants per group and were therefore not detectable in the present study.

Results

Of the 60 infants included in the study, 50% (n=30) were male, and 50% (n=30) were

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female. Among the participants, 13.3% (n=8) had a history of vomiting, while 46.7% (n=28) experienced bloating. Notably, 86.7% (n=52) demonstrated digestive tolerance. All infants (n=60) had less than 20% gastric residual volume before feeding, and 86.7% (n=52) maintained this level of residual volume three hours post-feeding. As shown in Table 1, a comparative analysis of gastrointestinal tolerance between the two positions (prone and right-side lying) in the first group revealed no statistically significant difference in tolerance frequency between the conditions ($p > 0.05$). These findings indicate no statistically significant difference in gastrointestinal tolerance frequency between the prone and right-lateral positions ($p > 0.05$ for all comparisons; Table 1). However, non-significant p-values do not confirm equivalence. The observed frequencies were identical for vomiting (13.3% vs. 13.3%), gastrointestinal tolerance (86.7% vs. 86.7%), and post-feeding residuals (13.3% vs. 13.3%), suggesting similar point estimates. Formal equivalence testing with pre-specified margins would be required to claim clinical equivalence.

As presented in Table 2, a comparative analysis of gastrointestinal tolerance between the first and second time periods in the second group (right-side and prone positions) demonstrated no statistically significant differences in tolerance frequency between the two conditions ($p > 0.05$). These results demonstrate no statistically significant differences between the two time periods for either positioning strategy ($p > 0.05$ for all variables; Table 2). The absence of significant differences within each position over time suggests stability of the observed effects, but does not constitute proof of equivalence between positions.

Table 1. Comparison of gastrointestinal tolerance in the first and second period in the first group (right lateral abdomen)

Variable	Incidence	Stomach Position n (%)	Right Lateral Position n (%)	P-value
Vomiting	Yes	4 (13.3%)	4 (13.3%)	1.000
	No	26 (86.7%)	26 (86.7%)	
Flatulence	Yes	16 (53.3%)	15 (50.0%)	0.796
	No	14 (46.7%)	15 (50.0%)	
Gastrointestinal Tolerance	Yes	26 (86.7%)	26 (86.7%)	1.000
	No	4 (13.3%)	4 (13.3%)	
Leftover Food Before Feeding	Yes	0 (0%)	0 (0%)	N/A
	No	30 (100%)	30 (100%)	
Leftover Food After Feeding	Yes	4 (13.3%)	4 (13.3%)	1.000
	No	26 (86.7%)	26 (86.7%)	

* McNemar's test

Table 2. Comparison of gastrointestinal tolerance in the first and second period in the second group (right lateral abdomen)

Variable	Incidence	Stomach Position n (%)	Right Lateral Position n (%)	P-value
Vomiting	Yes	4 (13.3%)	3 (10.0%)	1.000
	No	26 (86.7%)	27 (90.0%)	
Flatulence	Yes	15 (50.0%)	13 (43.3%)	1.000
	No	15 (50.0%)	17 (56.7%)	
Gastrointestinal Tolerance	Yes	26 (86.7%)	26 (86.7%)	1.000
	No	4 (13.3%)	4 (13.3%)	
Leftover Food Before Feeding	Yes	0 (0%)	0 (0%)	N/A
	No	30 (100%)	30 (100%)	
Leftover Food After Feeding	Yes	4 (13.3%)	4 (13.3%)	1.000
	No	26 (86.7%)	26 (86.7%)	

* McNemar's test

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However, non-significant p-values do not constitute evidence of equivalence. The observed frequencies were identical for vomiting (13.3% vs. 13.3%), gastrointestinal tolerance (86.7% vs. 86.7%), and post-feeding residuals (13.3% vs. 13.3%), suggesting similar point estimates, but formal equivalence testing with pre-specified margins (±10% for tolerance rates) would be required to claim clinical equivalence.

Table 3 compares gastrointestinal tolerance in the prone position between Group A (prone during Period 1) and Group B (prone during Period 2). No statistically significant differences were observed for any variable (vomiting: 13.3% vs. 13.3%, p = 1.000; flatulence: 53.3% vs. 50.0%, p = 0.438; gastrointestinal tolerance: 86.7% vs. 86.7%, p = 1.000; post-feeding residuals: 13.3% vs. 13.3%, p = 1.000). These non-significant findings indicate the absence of a substantial carryover effect from the preceding positioning condition and confirm that outcomes in the prone position were not systematically influenced by the order of position administration.

Table 4 provides the symmetrical analysis for the right-side position, comparing Group A (right-side during Period 2) with Group B (right-side during Period 1). Again, no statistically significant differences were detected (vomiting: 13.3% vs. 10.0%, p = 1.000; flatulence: 43.3% vs. 43.3%, p = 0.605; gastrointestinal tolerance: 83.3% vs. 86.7%, p = 1.000; post-feeding residuals: 16.7% vs. 13.3%, p = 1.000). These findings symmetrically confirm the absence of carryover or period effects, supporting the validity of the within-subject comparisons presented in Tables 1 and 2.

Table 3. Comparison of gastrointestinal tolerance according to similar conditions of the two groups

Variables	Incidence	First Group in Stomach Position N (%)	Second Group in Stomach Position N (%)	P-value
Vomiting	Yes	4 (13.3%)	4 (13.3%)	1.000
	No	26 (86.7%)	26 (86.7%)	
Flatulence	Yes	16 (53.3%)	15 (50.0%)	0.438
	No	14 (46.7%)	15 (50.0%)	
Gastrointestinal Tolerance	Yes	26 (86.7%)	26 (86.7%)	1.000
	No	4 (13.3%)	4 (13.3%)	
Leftover Food Before Feeding	Yes	0 (0%)	0 (0%)	N/A
	No	30 (100%)	30 (100%)	
Leftover Food After Feeding	Yes	4 (13.3%)	4 (13.3%)	1.000 *
	No	26 (86.7%)	26 (86.7%)	

* Fisher's exact test

Table 4. Comparison of gastrointestinal tolerance according to side position in two groups

Variable	Incidence	First Group in Stomach Position n (%)	Second Group in Stomach Position n (%)	P-value
Vomiting	Yes	4 (13.3%)	3 (10.0%)	1.000
	No	26 (86.7%)	27 (90.0%)	
Flatulence	Yes	13 (43.3%)	13 (43.3%)	0.605
	No	17 (56.7%)	17 (56.7%)	
Gastrointestinal Tolerance	Yes	25 (83.3%)	26 (86.7%)	1.000
	No	5 (16.7%)	4 (13.3%)	
Leftover Food Before Feeding	Yes	0 (0%)	0 (0%)	N/A
	No	30 (100%)	30 (100%)	
Leftover Food After Feeding	Yes	5 (16.7%)	4 (13.3%)	1.000*
	No	25 (83.3%)	26 (86.7%)	

* Fisher's exact test

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Discussion

This study explored gastrointestinal tolerance in preterm infants based on body positioning during feeding, focusing on the stomach (prone) and right-side positions. The findings highlight critical considerations for feeding practices in NICUs and provide evidence for optimizing digestive outcomes in vulnerable populations. Our study included an equal representation of male and female infants (50% each). While 13.3% of infants reported a history of vomiting and 46.7% experienced bloating, the majority (86.7%) exhibited effective gastrointestinal tolerance during the study. Gastric residuals before and after feeding were minimal, with less than 20% residual volume in all infants prior to feeding and 86.7% achieving the same standard post-feeding. This suggests that the feeding protocols and body positions used were effective in promoting gastric emptying and minimizing intolerance. Within both groups (prone and right-lateral positions), gastrointestinal tolerance across two distinct time periods showed no statistically significant differences ($p > 0.05$). This indicates **consistency in digestive outcomes over time** for each position individually.

Between the prone and right-lateral positions, the final measurements also showed no statistically significant differences ($p > 0.05$). **However, it is important to note that non-significant findings do not demonstrate equivalence.** The present study was designed to detect differences, not to establish equivalence. The sample size (n=60 per group for within-group comparisons; n=30 per group for between-group comparisons) may have been insufficient to detect small but clinically meaningful differences. Similarly, comparisons between the side and stomach positions revealed no significant differences in gastrointestinal tolerance. However, the absence of statistically significant differences does not underscore interchangeability; rather, it indicates that the present study failed to detect a difference. To claim interchangeability or equivalence, a formal equivalence trial with pre-specified equivalence margins (e.g., ±10% difference in tolerance rates) and a sample size calculated for equivalence (not for difference) would be required. The present study was designed to detect differences and lacks the statistical power to conclude equivalence. In 2013, Alinejad-Naine et al. conducted a review study to evaluate the benefits and drawbacks of various positioning techniques for newborns. The review encompassed 16 research articles and three specialized books on neonatal care. The study concluded that proper positioning of premature infants supports optimal developmental and neurological outcomes, leading to improved clinical and therapeutic results[19].

Several studies align with the findings of the present study on gastrointestinal tolerance and body positioning in preterm infants. Khatony et al. (2019) similarly reported no statistically significant differences in gastric residuals or digestive tolerance between different positions[20]. The consistency of non-significant findings across independent studies strengthens the evidence that any true difference between positions, if present, is likely small. However, as with the present study, Khatony et al. did not perform formal equivalence testing. Therefore, while the cumulative evidence suggests clinical similarity, confirmation through equivalence trials would strengthen this conclusion. The study by Gozen et al. (2022) was carried out under the hypothesis that lying on the right side leads to less stomach residue compared to lying on the left side. While the study assessed four different positions, it found that prone and right-side positions had the lowest residual volumes, aligning with the present findings[21]. Kaur et al. (2018) reported similar results, noting that prone and right-side positions were comparable and superior to the left-side position in reducing residuals, mirroring the findings of the present study[22]. Yayan et al. (2018) highlighted the effectiveness of the prone and right-side positions in reducing

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gastric residuals and improving digestive tolerance, in line with the present study[17]. Halemani et al.'s (2022) systematic review and meta-analysis provides a comprehensive examination of the effects of various body positions on gastric residual volume in preterm infants[23]. The findings from their study are broadly consistent with the current results, underscoring the clinical utility of both prone and right-side lying positions relative to the supine position. Halemani et al. emphasize that prone and right-side positions are well-tolerated by preterm infants, with fewer incidences of adverse effects when compared with supine positioning. In line with this, the current study found that 86.7% of participants exhibited effective digestive tolerance. However, the present study extends these findings by directly comparing prone and right-lateral positions, revealing no significant differences in outcomes between them – a comparison not explicitly addressed in the Halemani et al. review[23].

While most studies reviewed align with the current study's findings, a few exhibit contrasts that are important to highlight. Sajadi et al. (2019) found that prone positioning reduced gastric residual volume significantly and recommended it as the optimal post-feeding position[24]. However, this contrasts with the current study, which found no statistically significant differences in digestive tolerance or gastric residuals between the prone and right-side positions. The difference may arise from timing since Sajadi et al. measured residuals at multiple intervals (30, 60, and 90 minutes) compared to the single 3-hour post-feeding measurement in the present study. Jebreili et al. (2017) observed statistically significant reductions in gastric residual volumes in both prone and right-side positions 1–2 hours after feeding, unlike the current study, which found no significant differences[25]. The variation might stem from differences in timing and the use of enriched breast milk in the present study versus standard breast milk in Jebreili et al.'s work. Sandhu et al. (2012) emphasized the role of fortified breast milk in improving digestive outcomes and reducing complications, complementing the current findings but providing a stronger emphasis on nutritional intervention rather than positioning alone[26].

The present study defined gastrointestinal tolerance primarily based on gastric residual volume below 20% of the prior feed. With 86.7% of infants maintaining this threshold post-feeding, a ceiling effect was observed that may have reduced the statistical power to detect positional differences. Future studies should evaluate gastric residual volume as a continuous outcome (milliliters or percentage of feed volume) or employ alternative definitions of feeding intolerance, such as residual volume exceeding 50% of the previous feed, the presence of bilious or vomiting episodes, or composite clinical scores. The use of a liberal threshold may explain why no positional differences were detected, even if physiologically relevant differences exist at earlier time points or with stricter criteria.

All reviewed studies corroborate the equivalency of these positions in improving gastric emptying and reducing residuals, aligning with the current study's conclusions. Prone and right-side positions are consistently highlighted as effective and practical for NICU feeding protocols, particularly in reducing adverse outcomes like vomiting and bloating. Differences in the timing of gastric residual volume assessments (e.g., 30, 60, 90 minutes vs. 3 hours post-feeding) account for minor statistical variations, though the clinical implications remain aligned. Incorporating enriched breast milk and evaluating developmental outcomes further strengthens the clinical recommendations. The findings suggest that healthcare providers may consider alternating between prone and right-side-lying positions given the absence of evidence for a difference in this sample; however, this recommendation is provisional pending confirmatory equivalence trials. The present data do not constitute proof of safety or efficacy equivalence, and clinicians should remain aware that small but clinically

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meaningful differences (e.g., 10-15% absolute difference in tolerance rates) could not be excluded given the sample size. Parents can be assured of the safety and efficacy of both positions, encouraging active participation in care routines under professional supervision. Ongoing research on infant positioning, combined with increasing awareness and knowledge dissemination, remains crucial. Nurses and healthcare professionals must continuously update their knowledge and skills to provide optimal care in NICU settings.

Limitations for this research

This study focused on the prone and right-side feeding positions, limiting its generalizability as other clinically relevant positions (e.g., left-side and supine) were excluded. Gastric residual volumes were measured only once, three hours post-feeding, which may underestimate positional effects compared to studies assessing multiple intervals. The exclusive use of enriched breast milk restricts comparisons with unfortified milk or formula, as milk composition could influence outcomes. A limited sample size and demographic homogeneity further constrain the findings' applicability across diverse NICU populations. Short-term observations fail to capture long-term impacts on growth and gastrointestinal health. Additionally, the study's focus on digestive tolerance omitted other important outcomes like respiratory complications, neurodevelopment, or sleep patterns. Conducted in a single NICU, findings may reflect institutional practices, limiting external validity. Several methodological limitations inherent to the crossover design warrant acknowledgment. First, potential carryover effects cannot be entirely excluded. The interval between the two positional interventions was three hours. Given the crossover nature of the study and the use of fortified breast milk, the possibility of residual effects from the first intervention persisting into the second period remains. Future studies would benefit from a longer washout period or a formal assessment of carryover effects using appropriate statistical tests (e.g., Hill's–Armitage approach). Second, reporting of crossover methodology requires further transparency. In crossover studies, consideration of period effects, sequence effects, and potential carryover effects is essential for accurate interpretation. These aspects were not formally assessed in the current analysis. Future research should evaluate period and sequence effects, as unaccounted temporal changes or order-related biases could influence the results. Addressing these methodological considerations would substantially strengthen the transparency and rigor of future investigations in this area. Future research should address these limitations—including carryover effects, period/sequence effects, longer washout periods, and multi-center designs—to enhance the clinical relevance and generalizability of the findings.

This study focused on the prone and right-side feeding positions, limiting its generalizability as other clinically relevant positions (e.g., left-side and supine) were excluded. Gastric residual volumes were measured only once, three hours post-feeding, which may underestimate positional effects compared to studies assessing multiple intervals. The exclusive use of enriched breast milk restricts comparisons with unfortified milk or formula, as milk composition could influence outcomes. A limited sample size and demographic homogeneity further constrain the findings' applicability across diverse NICU populations. Short-term observations fail to capture long-term impacts on growth and gastrointestinal health. Additionally, the study's focus on digestive tolerance omitted other important outcomes like respiratory complications, neurodevelopment, or sleep patterns. Conducted in a single NICU, findings may reflect institutional practices, limiting external validity. Future research should address these limitations to enhance the clinical relevance and generalizability of the findings.

Future Directions

Investigating the four major positions (prone, supine, right-side, and left-side) across varying time intervals post-feeding (e.g., 30,

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60, 120, 180 minutes). Larger sample sizes and multicenter trials to enhance the generalizability of findings. Integration of enriched breast milk protocols with positioning interventions to explore synergistic effects on growth and feeding tolerance. This comprehensive review underscores the importance of evidence-based feeding strategies in the NICU, providing a foundation for tailored, effective neonatal care.

Conclusion

This study found no statistically significant difference between prone (stomach) and right-side positions regarding gastrointestinal tolerance and gastric residual volumes in preterm infants. The observed rates of vomiting, abdominal distension, and residual volumes were similar between the two positions. However, the absence of a significant difference does not confirm that the positions are equally effective; equivalence would require a specifically designed trial. The use of enriched breast milk added a consistent nutritional context, and the results suggest that both prone and right-side lying may be safe positioning options during feeding management. Healthcare providers may consider either position based on clinical judgement and individual infant needs, but the current data do not support treating them as fully interchangeable without further evidence. Future research should employ larger sample sizes, multiple measurement time points, and equivalence designs to definitively establish comparability, and should also examine other positions and long-term outcomes to further refine evidence-based feeding protocols in neonatal care.

Conflict of Interest

The authors declare no conflict of interest.

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Ethical Considerations

The research protocol was thoroughly evaluated and approved by the ethics committee at Shahid Sadoughi University of Yazd (IR.SSU.REC.1402.001).

Author's Contribution

Conceptualization, M.P., Z.P., and M.H.L.; methodology, M.P., Z.P., and M.H.L.; formal analysis, M.P., and Z.P.; investigation, M.P., Z.P., and M.H.L.; resources, M.P., and Z.P.; data curation, M.P., and Z.P.; writing—original draft preparation, M.P., Z.P., and M.H.L.; writing—review and editing, M.P., Z.P., and M.H.L.; supervision, Z.P., and M.H.L. All authors have read and agreed to the published version of the manuscript.

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