



**Comparative analysis of the effects of early breastfeeding versus formula feeding on the growth and development of preterm infants**

**Análisis comparativo de los efectos de la lactancia materna temprana frente a la alimentación con fórmula en el crecimiento y desarrollo de bebés prematuros**

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**Abstract**

This study aims to compare the effects of early breastfeeding and formula feeding on the growth and developmental outcomes of preterm infants over 24 months. A comparative longitudinal study was conducted involving 100 preterm infants divided into two groups: breastfeeding and formula feeding. Growth parameters (weight, length, head circumference) were monitored at regular intervals, and developmental outcomes were assessed using the Bayley Scales of Infant and Toddler Development. Statistical analyses, including repeated measures ANOVA and regression models, were applied. Both groups exhibited similar growth trajectories, with formula-fed infants demonstrating slightly higher weight, length, and head circumference values, though these differences were not statistically significant ( $p > 0.05$ ). Developmental assessments showed comparable results across cognitive, motor, and social-emotional domains, with breastfed infants scoring marginally higher in cognitive and social-emotional development at 24 months. Breastfeeding and formula feeding both support the growth and development of preterm infants effectively.

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**Resumen**

Este estudio tuvo como objetivo comparar los efectos de la lactancia materna temprana y la alimentación con fórmula en el crecimiento y los resultados de desarrollo de bebés prematuros durante un período de 24 meses. Se realizó un estudio longitudinal comparativo con 100 bebés prematuros divididos en dos grupos: lactancia materna y alimentación con fórmula. Se monitorearon parámetros de crecimiento (peso, longitud, circunferencia de la cabeza) en intervalos regulares, y los resultados del desarrollo se evaluaron utilizando las Escalas de Desarrollo Infantil y del Bebé de Bayley. Se aplicaron análisis estadísticos, incluidos ANOVA de medidas repetidas y modelos de regresión. Ambos grupos mostraron trayectorias de crecimiento similares, con los bebés alimentados con fórmula mostrando valores ligeramente más altos de peso, longitud y circunferencia de la cabeza, aunque estas diferencias no fueron estadísticamente significativas ( $p > 0.05$ ). Las evaluaciones del desarrollo mostraron resultados comparables en las áreas cognitiva, motora y socioemocional, con los bebés amamantados obteniendo puntajes ligeramente más altos en desarrollo cognitivo y socioemocional a los 24 meses. Tanto la lactancia materna como la alimentación con fórmula apoyan eficazmente el crecimiento y desarrollo de los bebés prematuros.

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## Introduction

Preterm birth, defined as delivery before 37 weeks of gestation, represents a significant global health challenge and is a leading cause of neonatal morbidity and mortality. It affects approximately 11 % of all live births worldwide, placing millions of infants at increased risk for both short- and long-term health complications<sup>1-4</sup>. The survival and development of these vulnerable infants are intricately linked to the quality of care they receive during the neonatal period, particularly with respect to nutrition. Adequate and timely nutritional intervention is essential for promoting optimal growth, brain development, and physiological maturation during this critical time of early life<sup>5-8</sup>.

Due to the immaturity of their gastrointestinal and neurological systems, preterm infants have distinct nutritional requirements compared to full-term newborns. Early nutritional support not only influences immediate growth parameters such as weight, length, and head circumference but also contributes significantly to long-term cognitive, motor, and social-emotional development<sup>9-11</sup>. Emerging research highlights the importance of nutrient-enriched feeding strategies in the neonatal intensive care unit (NICU), especially during the first 1000 days of life, a period considered critical for brain development<sup>12,13</sup>.

Breastfeeding is widely recognized as the gold standard for infant nutrition. Human milk contains not only the macronutrients and micronutrients necessary for physical growth but also a complex array of bioactive compounds, including immunoglobulins, enzymes, hormones, long-chain polyunsaturated fatty acids, and human milk oligosaccharides, which collectively support neurodevelopment, immune function, and gastrointestinal health<sup>14-16</sup>. Studies have demonstrated that preterm infants who receive

breast milk shows improved brain volume, enhanced functional connectivity, and better performance on cognitive assessments later in life<sup>17,18</sup>.

Nonetheless, exclusive breastfeeding is not always feasible for mothers of preterm infants. Maternal health complications, stress, lactation difficulties, and limited access to lactation support often result in inadequate milk supply, leading to the need for supplementation or substitution with formula. Preterm formulas are specifically designed to address the elevated nutritional needs of preterm infants and are fortified with higher levels of protein, calories, vitamins, and minerals<sup>19</sup>. Some evidence suggests that formula feeding may lead to faster short-term growth<sup>20</sup>, yet concerns persist regarding its association with higher risks of necrotizing enterocolitis and the absence of critical neuroprotective and immunological factors found in breast milk<sup>21,22</sup>.

Although numerous studies have explored the individual benefits of breastfeeding and formula feeding, few have provided comprehensive, head-to-head comparisons of their impact on both growth trajectories and developmental outcomes in preterm populations. This gap in the literature leaves clinicians and parents with limited evidence-based guidance when making critical decisions about feeding strategies in the NICU and during early infancy<sup>12,13</sup>.

Therefore, the objective of this study was to conduct a longitudinal comparative analysis of early breastfeeding versus formula feeding in preterm infants, focusing on their effects on physical growth and developmental outcomes over a 24-month period. By examining validated growth indicators and standardized developmental assessments, this research aims to generate evidence that supports informed nutritional decision-making for preterm infants during a

critical stage of life.

## Materials and methods

This study employed a comparative longitudinal design, a widely used approach in pediatric and neonatal research, to assess the effects of early breastfeeding versus formula feeding on growth and developmental outcomes in preterm infants<sup>9-11</sup>. Two cohorts of preterm infants one predominantly breastfed and the other predominantly formula-fed were followed from birth until 24 months of corrected age to evaluate differences in physical growth and neurodevelopmental progression.

The study population consisted of preterm infants born at less than 37 weeks of gestation, with birth weights ranging from 500 to 2500 g. These inclusion criteria align with international definitions of preterm birth and low birth weight<sup>23</sup>. Infants were enrolled if they were medically stable and able to tolerate enteral feeding within the first week of life, which is consistent with clinical guidelines for initiating neonatal nutrition<sup>22</sup>. Exclusion criteria included the presence of major congenital anomalies, gastrointestinal conditions impairing oral feeding, or significant metabolic and endocrine disorders, all of which are known to influence feeding tolerance and developmental trajectories<sup>19</sup>.

Growth parameters weight, length, and head circumference were recorded at baseline (within the first week of life), then monthly for the first six months, and subsequently every two months until 24 months corrected age. Measurements were interpreted using the Fenton growth chart, a validated tool specifically designed to assess growth in preterm infants<sup>24</sup>.

Developmental progress was evaluated using the Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III), a standardized and widely

recognized tool for assessing early cognitive, motor, and social-emotional development<sup>25,26</sup>. Assessments were conducted at 6, 12, and 24 months of corrected age by trained developmental specialists.

The primary independent variable was feeding type, classified as either breastfeeding (exclusive or predominantly breast milk) or formula feeding (exclusive or predominantly preterm formula). Dependent variables included continuous measures of physical growth (weight, length, and head circumference) and domain-specific BSID-III scores (cognitive, motor, and social-emotional development).

Statistical analyses were conducted using repeated measures ANOVA to assess growth trajectories across time between groups. Independent t-tests were used to compare group means at specific time points. Multiple linear regression models were employed to evaluate developmental scores while adjusting for potential confounders such as gestational age and birth weight<sup>12,13</sup>. Chi-square tests were used for comparisons involving categorical variables.

The study was conducted in accordance with ethical principles outlined in the Declaration of Helsinki<sup>27</sup>. Written informed consent was obtained from the parents or legal guardians of all participants. The research protocol was reviewed and approved by the institutional ethics committee, and all data were anonymized and securely stored to protect participant confidentiality.

## Results

The growth trajectories of preterm infants in both breastfeeding and formula-feeding groups were analyzed using weight, length, and head circumference measurements collected at eight time points: baseline (0 months), 1, 2, 3, 6, 12, 18, and 24 months. Table 1 and Figure 1.

**Table 1 Growth data for breastfeeding vs. formula feeding groups**

Time point (months)	Weight (g) (breastfeeding)	Weight (g) (formula feeding)	Length (cm) (breastfeeding)	Length (cm) (formula feeding)	Head circumference (cm) (breastfeeding)	Head circumference (cm) (formula feeding)
0	1800	1850	42	4	30	31
1	2200	2250	46	47	32	33
2	2700	2750	50	51	34	35
3	3200	3300	54	55	36	37
6	5000	5200	60	61	39	40
12	7500	7600	70	71	44	45
18	9000	9200	80	81	46	47
24	11000	11500	90	91	48	49

Figure 1 provides a visual comparison of the weight, length, and head circumference growth trajectories across the breastfeeding and formula-feeding groups. Both groups demonstrated consistent increases in growth parameters over time, with the formula-fed group exhibiting marginally higher values for weight, length, and head circumference at most inter-

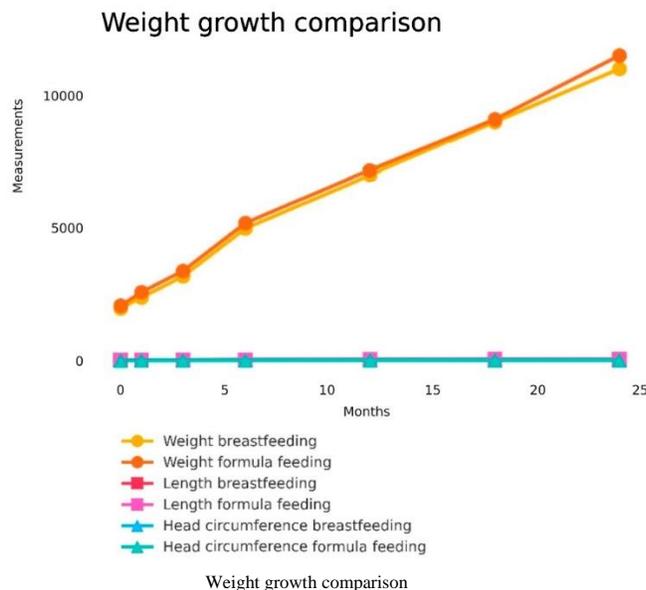
vals. However, these differences were not statistically significant ( $p > 0.05$ ).

The developmental outcomes of preterm infants were assessed at 6, 12, and 24 months using the Bayley Scales of Infant and Toddler Development (BSID). Measurements included cognitive, motor, and social-emotional domains. Table 2.

**Table 2 Developmental outcomes (BSID scores) for breastfeeding vs. formula feeding groups**

Time point (months)	Cognitive development (breastfeeding)	Cognitive development (formula feeding)	Motor development (breastfeeding)	Motor development (formula feeding)	Social-emotional development (breastfeeding)	Social-emotional development (formula feeding)
6	85	84	80	79	83	82
12	90	89	85	84	88	87
24	100	98	95	93	95	94

**Figure 1 Head circumference growth comparison**



## Discussion

This study compared the effects of early breastfeeding and formula feeding on the growth and developmental outcomes of preterm infants over a 24-month period. The findings indicate that both feeding practices effectively support physical growth and early development, with no statistically significant differences in measured parameters such as weight, length, and head circumference. These outcomes contribute to the growing body of evidence suggesting that both feeding strategies can be viable under appropriate clinical guidance<sup>17</sup>.

The observed growth trajectories are consistent with previous studies showing that formula-fed preterm infants may exhibit slightly higher weight and length gains in early months, although such differences often lack statistical significance<sup>20</sup>. The current findings suggest that advances in the nutritional formulation of preterm-specific formulas have narrowed the gap in growth outcomes between formula-fed and breastfed preterm infants.

Despite these improvements, breastfeeding continues to be the recommended practice due to its long-term health benefits and unique biological components. Breast milk is rich in long-chain polyunsaturated fatty acids, oligosaccharides, and immunoglobulins, which contribute not only to physical growth but also to the development of the immune system and central nervous system<sup>28</sup>. Moreover, human milk has been consistently associated with a lower incidence of necrotizing enterocolitis, a life-threatening condition in preterm infants<sup>21</sup>.

In terms of developmental outcomes, the study found that both groups showed comparable progress across cognitive, motor, and social-emotional domains. However, breastfed infants demonstrated slightly higher cognitive and social-emotional scores at 24

months. This observation aligns with findings from longitudinal studies indicating modest but consistent neurodevelopmental advantages in breastfed preterm infants, which are often attributed to neuroprotective compounds present in breast milk<sup>5</sup>.

Although formula feeding meets nutritional requirements and supports typical developmental trajectories, it lacks certain bioactive substances naturally found in breast milk, such as growth factors and enzymes that support neural development. These missing components may explain the marginal cognitive benefits observed among breastfed infants<sup>6</sup>.

From a clinical perspective, the results support the continued promotion of breastfeeding in neonatal care. However, when breastfeeding is not possible due to maternal illness, low milk supply, or other challenges formula feeding remains a practical and effective alternative. It is important for healthcare providers to offer individualized support and consider supplemental options such as donor milk or human milk fortifiers to optimize nutritional care<sup>19</sup>.

Finally, while this study offers valuable insights, further research is needed to investigate the long-term cognitive, emotional, and behavioral outcomes associated with early feeding practices. Future studies should also examine the effects of mixed feeding and fortified breast milk to provide a more.

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## Conflicts of interest

The author declares that there is no conflict of interest regarding the publication of this article.

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## Ethical considerations

The study was approved by the institutional ethics committee, and written informed consent was obtained from the parents or legal guardians of all participants. All procedures were conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.

## Research limitations

This study has several limitations that should be considered when interpreting the results. i) Sample size. The relatively small sample size of 100 infants limited the statistical power of the study. While sufficient to detect moderate differences between groups, the sample may not have been large enough to identify subtle effects of feeding method on growth and neurodevelopmental outcomes. Similar concerns have been reported in previous studies, where small cohorts often reduced the ability to detect clinically meaningful differences in preterm populations<sup>23</sup>. ii) Duration of follow-up. Although a 24-month follow-up captures early developmental outcomes, it may not be sufficient to observe long-term differences, especially in cognitive, behavioral, and academic performance. Research suggests that neurodevelopmental disparities associated with early nutrition may not fully manifest until later in childhood, particularly in executive functioning and learning capacity<sup>24</sup>. iii) Socioeconomic and environmental factors. While the

study controlled for some variables, it did not fully account for the influence of socioeconomic status, maternal education, parental involvement, and home environment all of which can affect both feeding choices and developmental trajectories. These factors are known to play a substantial role in shaping outcomes in preterm infants<sup>11</sup>. iv) Feeding practice classification. Infants were categorized as either breastfed or formula-fed, but variations such as mixed feeding (combination of breast milk and formula) or use of human milk fortifiers (HMFs) were not documented. Studies have shown that these variations can significantly influence growth and development, and their omission may confound the results<sup>25</sup>. v) Single-Center study design. This research was conducted at a single institution, limiting the generalizability of the findings. Multicenter studies are recommended to account for regional differences in healthcare practices, feeding protocols, and population demographics, which can impact infant outcomes<sup>26</sup>.

This study explored the comparative effects of early breastfeeding versus formula feeding on the growth and development of preterm infants over a 24 month. The results indicate that both feeding methods adequately support physical growth, with no statistically significant differences in weight, length, or head circumference between the groups. Similarly, both groups showed comparable developmental outcomes in cognitive, motor, and social-emotional domains, though breastfed infants exhibited slightly higher scores in cognitive and social-emotional development. While breastfeeding remains the gold standard due to its immunological benefits, formula feeding can serve as an effective alternative for preterm infants when breastfeeding is not possible. The findings suggest that healthcare providers can confidently recommend either feeding method, based on individual circumstances, without compromising the

growth or developmental trajectory of preterm infants. However, future research with larger sample sizes and extended follow-up periods is necessary to explore potential long-term differences, particularly in cognitive development.

### Data availability

The data supporting the findings of this study are not publicly available due to their technical specificity and field-sensitive nature, but they are available from the corresponding author upon reasonable academic request and for non-commercial research purposes.

### Publication permissions

The author reviewed and approved the final version of the manuscript and gave consent for its publication.

### Use of artificial intelligence in writing

No generative artificial intelligence tools were used in the writing of this manuscript. All content was produced by the author.

### Image generation disclosure

No AI-based tools were used for image creation. Figures in this article were created using scientific data visualization software. No AI-generated images were used without direct human oversight.

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