

## Feeding Practices and Nutritional Evolution of Preterm Infants during Hospitalization: a Longitudinal Study

Tafnes Laís Pereira Santos de Oliveira<sup>1</sup>, Kennia Kiss Borges Santos Silva<sup>2</sup>, Andressa Laís Ferreira Silva<sup>1</sup>, Camylla Sinezia dos Santos Paiva Alves Pereira<sup>3</sup>, Isabella da Costa Ribeiro<sup>1</sup>, Matheus Santos de Sousa Fernandes<sup>1\*</sup>, Jéssica de Oliveira Campos<sup>2</sup>, Flaydson Clayton Silva Pinto<sup>1</sup>, Jenyffer Medeiros Campos Guerra<sup>1</sup>, Sandra Cristina da Silva Santana<sup>2</sup>, Antonio Flaudiano Bem Leite<sup>4</sup> and Michelle Figueiredo Carvalho<sup>2</sup>

### Abstract

**Objectives:** To compare feeding practices and anthropometric variables between preterm infants, according to the degree of prematurity, during hospitalization until hospital discharge, and to correlate these practices with nutritional evolution.

**Methods:** Prospective study with 44 premature infants admitted to a referral hospital for the care of high-risk newborns, in the interior of Pernambuco, between 2016 and 2017. The data analyzed were obtained by consulting medical records to compare birth characteristics, feeding practices, and anthropometric measurements between preterm infants  $\leq 33$  and  $\geq 34$  weeks of gestational age.

**Results:** Parenteral nutrition and the start of full enteral nutrition were similar between groups. Premature infants with a gestational age  $\geq 34$  weeks had an earlier onset and shorter use of enteral nutrition (1; 0-2 vs. 0; 0-1,  $p=0.002$  and 25; 5-36 vs. 7; 1-24,  $p<0.0001$ , respectively), started oral feeding earlier (7.5; 2-32 vs. 4.5; 1-24,  $p=0.019$ ), and had a higher prevalence of exclusive breastfeeding at hospital discharge (56.2% vs. 76.2%,  $p=0.0017$ ). Those with a gestational age  $\leq 33$  weeks presented a greater need for human milk fortification (57.0% vs. 16.0%,  $p<0.0001$ ) and longer hospital stay (31; 10-55 vs. 12.5; 3-55,  $p=0.0001$ ). There was a positive correlation between the start of enteral nutrition and the hospitalization time ( $r=0.410$ ,  $p=0.007$ ).

**Conclusion:** Physiological maturity seems to influence dietary practices and nutritional evolution during the hospitalization of premature infants. The start of enteral nutrition, as observed in this study, is positively correlated with the length of hospital stay. These findings may contribute to improvement in nutritional care for premature infants.

**Keywords:** Nutrition; Enteral nutrition; Parenteral nutrition; Oral feeding; Premature; Neonatal ICU

- 1 Federal University of Pernambuco, Pernambuco, Brazil
- 2 Federal University of Pernambuco, Academic Center of Vitória de Santo Antão, Pernambuco, Brazil
- 3 Tricentennial Hospital, Vitória de Santo Antão, Pernambuco, Brazil
- 4 Department of Health, Vitória de Santo Antão, Pernambuco, Brazil

**\*Corresponding author:**

Matheus Santos de Sousa Fernandes

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✉ theusfernandes10@hotmail.com

Tel: +62274489726

Federal University of Pernambuco, Pernambuco, Brazil.

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### Introduction

The World Health Organization (WHO) [1] defines a premature infant as any newborn born before the 37<sup>th</sup> week of gestational age. It is estimated that 15 million premature children are born worldwide each year, representing 1 in 10 births. In Brazil, the prevalence of prematurity increased from 9.2% in 2010 [1] to 11.5% in 2011 [2]. The scientific and technological progress of neonatal care, associated with more humanized care, has allowed the survival of newborns (NBs) with ever lower gestational ages (GA) and birth weights [3]. However, prematurity is still a major public health problem and is the greatest risk factor for infant morbidity and mortality [4].

Being born prematurely predisposes the NB to nutritional risk,

since at birth there is a sudden interruption of the nutritional supply to the fetus during the phase of greatest speed of growth and development [5]. Thus, the preterm newborn (PTNB) is harmed, partly or totally, depending on the gestational age,

becoming more vulnerable to nutritional deficits, due to the high metabolic demand, inadequate nutritional reserves, immaturity of the physiological systems, and high presence of morbidity [6]. This condition requires complex adaptation to the extrauterine environment, which in many cases makes specialized care in the neonatal intensive care unit (NICU) necessary [7].

Neonatal nutrition plays a key role in the survival and growth and development processes of preterm infants [7]. According to the American Academy of Pediatrics (AAP), preterm nutrition aims to provide nutrients to achieve a postnatal growth rate, in anthropometric and body composition terms, similar to that of a normal fetus of the same gestational age [8]. However, this is still a significant challenge [6]. Review studies show that the nutritional and metabolic impact resulting from eating practices, whether appropriate or not, established in the initial period of life have repercussions in the short and long term [5-7]. Thus, nutritional care for preterm infants should have an emphasis on the assessment of nutritional practices and infant growth.

The aim of this study was to compare feeding practices and anthropometric variables between preterm infants  $\leq 33$  and  $\geq 34$  weeks of gestational age admitted to a referral hospital for the care of high-risk newborns, as well as to correlate these practices with nutritional evolution.

## Methods

This is a prospective longitudinal study carried out in the neonatal unit of a public hospital of reference in the care of high-risk newborns, in the city of Vitória de Santo Antão-PE. The study includes a convenience sample of 44 PTNBs of both sexes, hospitalized in the referred service, during the period from May 2016 to May 2017.

Newborns with GA less than 37 weeks, premature births according to the WHO classification [1] were included in the study. Exclusion criteria were the presence of congenital malformations, maternal or neonatal death shortly after delivery, laboratory-confirmed congenital infections, genetic disorders, inborn errors of metabolism, neuropsychomotor diseases, and babies whose mothers were unable to breastfeed due to illness or use of medications and/or illicit toxic substances that contraindicate this practice.

Data collection was performed using a form prepared by properly trained researchers, which was completed based on the review of the patients' medical records. The information was collected at three moments: in the first 24 h postpartum, weekly during the period of stay in the neonatal unit, and at hospital discharge.

The variables of interest were grouped as follows:

a) clinical birth variables: sex; birth weight (g); gestational age (full weeks); and nutritional status at birth, according to the classification of Fenton and Kim [9].

b) feeding practices: start and duration of enteral nutrition (days of life), start of full enteral nutrition (FEN) (150 ml/kg/day supply) [10] (days of life), start and duration of parenteral nutrition (days of life), start of oral feeding (days of life), type of milk in the first week of hospitalization, use of breast milk additive, start of

breastfeeding on the free breast (days of life), and type of food at hospital discharge [11]. The premature infant was considered in enteral nutrition when they received food via a tube and the beginning of oral feeding when the PTNB started nutritional suction through stimulus with the breast, cup, or bottle feeding.

c) nutritional evolution: % of physiological weight loss, being adequate when less than 15%; [12] mean daily weight gain (g/day), adequate when  $\geq 25$  g/d, [12] being calculated only for premature infants who spent more than a week in the neonatal unit, considering that in the first week of life physiological weight loss occurs; recovery of birth weight, being adequate when occurring between the 10th and 21st day of life [12] and length of hospital stay (days).

Premature infants were divided into two sample groups according to their physiological maturity, given their relationship with the establishment of nutritional behaviors: newborns of gestational age  $\leq 33$  weeks, including extreme, severe, and moderate premature infants; and premature infants of gestational age  $\geq 34$  weeks, including late preterm infants, according to the criteria of the Brazilian Society of Pediatrics (BSP) [13].

This study was approved by the Ethics Committee from the Federal University of Pernambuco (number 1692730). The parents of the infants signed a written informed consent form.

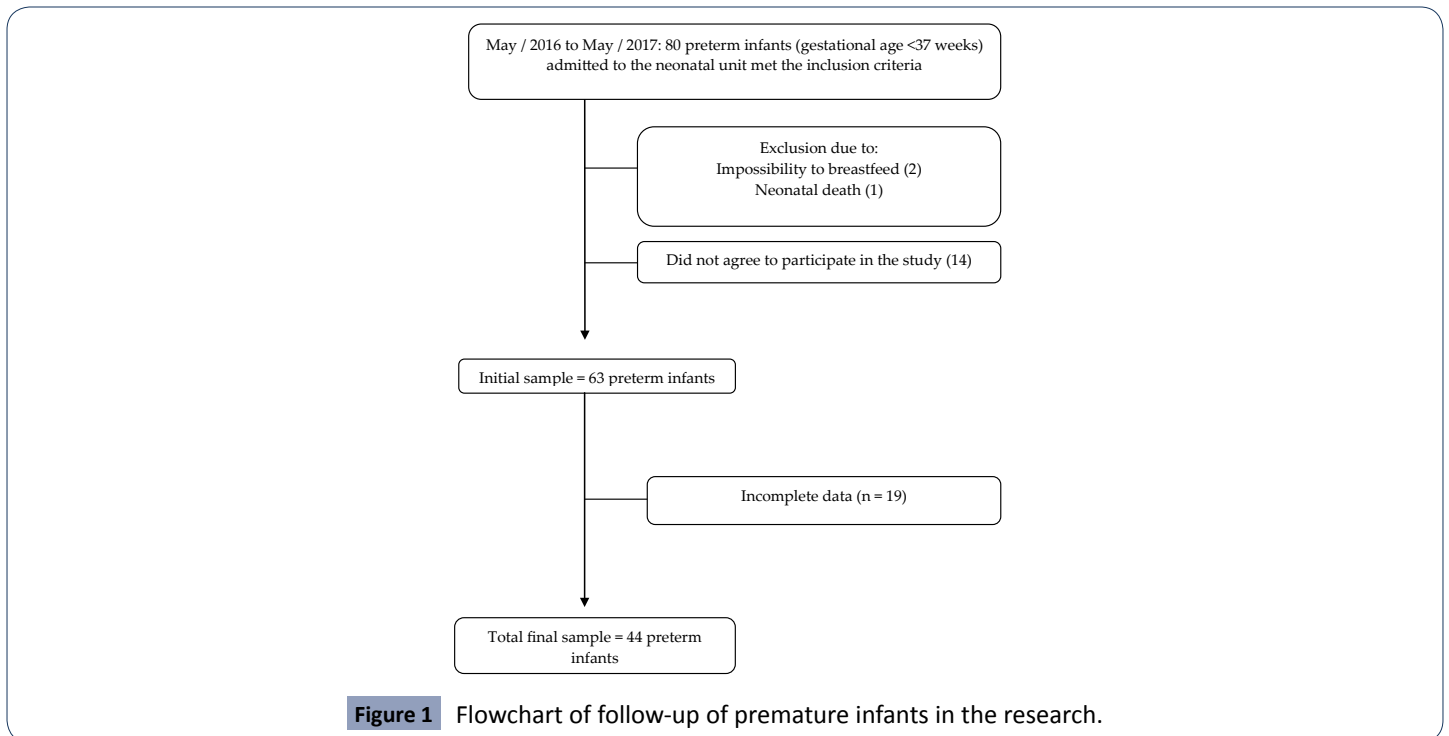
The data were organized in Microsoft Office Excel 2013 (Microsoft Corporation) and analyzed using GraphPad Prism 8 software (San Diego, USA). The distribution of variables was assessed using the Shapiro-Wilk test. Quantitative variables were expressed as mean and standard deviation, and compared by the Student's t test for independent samples, or as median and minimum and maximum values, compared by the Mann-Whitney test. Categorical variables were presented in absolute numbers and percentages and compared using the chi-square or Fisher's exact tests. Spearman's correlation test was used to study correlations between the variables of dietary practices and nutritional evolution. The level of significance adopted was 5% ( $p < 0.05$ ) for all tests.

## Results

During the study period, 80 preterm newborns were potentially eligible, however, after exclusion of 36, the final sample contained 44 premature infants (**Figure 1**). Premature infants were divided into two groups:  $\leq 33$  ( $n=19$ ) and  $\geq 34$  weeks of gestational age ( $n=25$ ). All clinical birth variables were different between groups (**Table 1**).

**Table 2** presents the eating practices during hospitalization. The groups were similar regarding parenteral nutrition practices and the beginning of full enteral nutrition. On the other hand, it was noted that premature infants with GA  $\geq 34$  weeks had an earlier onset (0; 0-1 versus 1; 0-2 days,  $p=0.002$ ) and shorter time of use (7; 1-24 versus 25; 5-36 days of life,  $p < 0.0001$ ) of enteral nutrition, started oral feeding earlier (4.5; 1-24 versus 7.5; 2-32 days of life,  $p=0.019$ ), and evolved earlier to the free maternal breast (7; 1-26 versus 18; 3-34 days of life,  $p=0.0006$ ).

In the first week of hospitalization, almost all preterm infants (97.6%) were receiving breast milk (exclusive or mixed).



**Table 1** Characteristics of preterm infants according to gestational age. Vitória de Santo Antão, Pernambuco, Brazil, 2017 (n=44).

Variables	≤ 33 weeks (n=19)	≥ 34 weeks (n=25)	p-value
Sex (n, %)			
Boys	12 (63.2)	11 (44.0)	0.010
Girls	7 (36.8)	14 (56.0)	
Birth weight (g in mean ± SD)	1669 ± 362.9	2078 ± 415.5	0.001
Gestational age (weeks in median, min-max)	31 (27-33)	35 (34-36)	<0.0001
Nutritional status at birth (n,%)			
Small for gestational age (SGA)	1 (5.3%)	7 (28.0%)	<0.0001
Appropriate for gestational age (AGA)	17 (89.4%)	18 (72.0%)	
Large for gestational age (LGA)	1 (5.3%)	0 (0.0%)	

SD: standard deviation

**Table 2** Characteristics of feeding practices during the hospitalization of premature infants according to gestational age. Vitória de Santo Antão, Pernambuco, Brazil, 2017.

Variables	≤ 33 weeks (n=19)	≥ 34 weeks (n=25)	p-value
Parenteral nutrition			
Start (days of life in median, min-max)	2 (1-4) <sup>a</sup>	2 (1-4) <sup>b</sup>	>0.9999
Duration (days in mean ± SD)	5.8 ± 2.1 <sup>c</sup>	5.7 ± 0.6 <sup>d</sup>	0.922
Enteral nutrition			
Start (days of life in median, min-max)	1 (0-2)	0 (0-1) <sup>e</sup>	0.002
Start FEN (days of life in median, min-max)	9.0 ± 4.0 <sup>f</sup>	7.5 ± 2.9 <sup>g</sup>	0.341
Duration (days in mean ± SD)	25 (5-36) <sup>h</sup>	7.0 (1-24) <sup>i</sup>	<0.0001
Oral feeding			
Start oral feeding(days of life in median, min-max)	7.5 (2-32) <sup>j</sup>	4.5 (1-24) <sup>k</sup>	0.019
Start FMB (days of life in median, min-max)	18 (3-34) <sup>l</sup>	7 (1-26) <sup>m</sup>	0.0006
Type of milk (oral / tube) in the 1 <sup>st</sup> week of life (n,%)			
Infant formula	1 (5.3%)	0 (0.0%)	0.024
Breast milk	7 (36.8%)	7 (30.4%)	
Mixed	11 (57.9%)	16 (69.6)	
Use of breast milk additive (n,%)	11 (57.0%)	4 (16.0%)	<0.0001
Type of food at hospital discharge (n,%)			
Infant formula	2 (12.5%)	2 (9.5%)	0.0017
Exclusive breastfeeding	9 (56.2%)	16 (76.2%)	
Mixed breastfeeding	5 (31.3%)	3 (14.3%)	

FEN: full enteral nutrition; FMB: Free maternal breast; SD: standard deviation.

<sup>a</sup>: n=7; <sup>b</sup> n=3; <sup>c</sup>: n=6; <sup>d</sup>: n=4; <sup>e</sup>: n=22; <sup>f</sup>: n=16; <sup>g</sup>: n=10; <sup>h</sup>: n=16; <sup>i</sup>: n=22; <sup>j</sup>: n=15; <sup>k</sup>: n=23; <sup>l</sup>: n=18; <sup>m</sup>: n=23.

Premature infants with gestational age  $\geq 34$  weeks presented less need for fortified human milk, when compared to PTNB with GA  $\leq 33$  weeks (16.0% versus 57.0%,  $p < 0.0001$ ). Premature infants with GA  $\geq 34$  weeks presented a higher prevalence of exclusive breastfeeding at the time of hospital discharge (76.2% versus 56.2%,  $p = 0.0017$ ), as shown in Table 2.

In the assessment of nutritional evolution and length of stay in the neonatal unit (Table 3), no difference was found in the mean daily weight gain between the groups. However, the percentage of weight loss on the 7<sup>th</sup> day of life ( $9.6 \pm 3.8\%$  versus  $6.8 \pm 3.6\%$ ,  $p = 0.021$ ), recovery of birth weight ( $16.4 \pm 3.7$  versus  $12.0 \pm 4.6$  days,  $p = 0.025$ ), and length of hospital stay (31; 10-55 versus 12.5; 3-55 days,  $p = 0.0001$ ) were longer in the group of premature infants with GA  $\leq 33$  weeks compared to those with GA  $\geq 34$  weeks.

Table 4 shows the study of correlations between variables related to dietary practices and nutritional evolution. There was a positive correlation between the beginning of enteral nutrition and the length of hospital stay ( $r = 0.410$ ,  $p = 0.007$ ).

**Table 3** Characteristics of the nutritional evolution of preterm infants according to gestational age. Vitória de Santo Antão, Pernambuco, Brazil, 2017.

Variables	$\leq 33$ weeks (n=19)	$\geq 34$ weeks (n=25)	p-value
Weight loss on the 7th day of life (% in mean $\pm$ SD)	$9.6 \pm 3.8^a$	$6.8 \pm 3.6^b$	0.021
Mean daily weight gain (g in mean $\pm$ SD)	$6.1 \pm 3.0^c$	$9.5 \pm 8.7^d$	0.145
Recovery of birth weight (days of life in mean $\pm$ SD) <sup>e</sup>	$16.4 \pm 3.7^e$	$12.0 \pm 4.6^f$	0.025
Length of stay (days in median, min-max)	31 (10-55)	12.5 (3-55)	0.0001

SD: standard deviation  
<sup>a</sup>: n= 18; <sup>b</sup>: n=22; <sup>c</sup>: n=18; <sup>d</sup>: n=11; <sup>e</sup>: n=13; <sup>f</sup>: n=14

**Table 4** Correlation between variables related to dietary practices and nutritional evolution. Vitória de Santo Antão, Pernambuco, Brazil, 2017.

Related variables	r	p-value
Start of PN (days of life) and daily weight gain (g)	-0.193	0.669
Start of EN (days of life) and recovery of birth weight (days of life)	0.052	0.821
Start of EN (days of life) and length of stay (days)	0.410	0.007
Start of FMB (days of life) and daily weight gain (g)	0.207	0.288
Start of oral feeding (days of life) and recovery of birth weight (days of life)	0.058	0.800
Daily weight gain (g) and length of stay (days)	0.230	0.238
Physiological weight loss (%) and length of stay (days)	0.086	0.626

PN: parenteral nutrition; EN: enteral nutrition; FMB: free maternal breast.

## Discussion

In the present study, we compared feeding practices and anthropometric variables among preterm newborns admitted to a neonatal unit in the interior of Pernambuco, according to the degree of prematurity, and correlated these practices with nutritional evolution.

The nutrition of preterm newborns has been widely discussed in the literature and it is noted that the nutritional practices in the NICU vary between hospitals [5-7,14,15]. In our study, PN and EN started in the first days of life, similar to what was observed in premature infants admitted to an NICU in northeastern Brazil [16]. There is sufficient evidence that parenteral nutrition in the first days of life prevents the initial loss of protein and hypoglycemic peaks, and maintains the growth of organs and tissues [6]. Enteral nutrition meanwhile promotes the functional and structural integrity of the gastrointestinal tract, favoring maturation of motor activity and resulting in rapid weight gain and obtention of full enteral nutrition earlier [14]. Late onset of FEN is seen as a risk factor for increased morbidity and mortality in the perinatal period and beyond [7].

The time required to achieve FEN was adequate (up to 14 days of life) [10]. Menezes et al. [16] followed the clinical evolution of 137 preterm infants in a public maternity hospital in the northeastern region of Brazil and also observed that babies reached FEN by the second week of life ( $10 \pm 5$  days of life). However, the authors did not specify the volume of diet needed to achieve FEN.

Oral feeding in the neonatal period requires the coordination of suction, swallowing, and breathing movements, which takes place around the 34<sup>th</sup> week of GA. Before this, it is necessary to use enteral nutrition probes for feeding [17,18]. In our research, the beginning of oral feeding and the free maternal breast were earlier among premature GI  $\geq 34$  weeks, who also passed less time using enteral nutrition. Scochi et al [19] identified a negative correlation between GI at birth and the duration of the food transition to oral route, showing that the more immature PTNBs make the transition in a longer time. It is worth noting that this factor alone should not be decisive for the beginning of oral feeding, as the clinical stability and neurological maturity of the PTNB should also be evaluated [18].

The food of choice for the PTNB is their own mother's milk [8]. In the first week of life, almost all preterm infants were already receiving breast milk (exclusive or mixed). The advantages of offering breast milk to premature infants are well established in the literature, such as the provision of intestinal maturation factors and antioxidants, immunological protection, pain relief, interaction between mother and child, reduced risk of rehospitalization after discharge, and prevention of necrotizing enterocolitis and delayed sepsis [5-7,20,21].

The continuous supply of nutrition through fortified breast milk is important during neonatal hospitalization since human milk as the only source of nutrition does not fully meet the nutritional needs of very premature babies with birth weight  $< 1,500$  g [5]. Although it is possible to supply the energy and protein needs with larger amounts of milk without additives, this does not necessarily meet the needs for calcium, phosphorus, or other micronutrients [6]. Due to premature GA  $\leq 33$  weeks being more vulnerable to nutritional deficits, greater use of breast milk additive was observed in this group. Martins and Krebs [22], when studying the effects of the use of additives in the mother's own human milk in PTNB infants  $\leq 34$  weeks hospitalized in a neonatal unit, confirmed that the premature infants in the intervention group presented better growth, with a significant increase in

length and head circumference.

Maintaining exclusive breastfeeding until hospital discharge is a major challenge faced by mothers of preterm infants, since the deprivation of spontaneous contact between mother and child arouses a feeling of anxiety, fear, and uncertainty regarding the newborn's survival. In addition to witnessing their children's daily struggle for life, they need to be persistent to overcome this difficult experience, seeking to remain calm, within the possibilities, so as not to interfere with milk production [23]. Maciel, Almeida and Braga [24] emphasize the importance of humanized and educational assistance with mothers, stating that when education is properly offered, it can reconstruct meanings and dispel some myths, thus being able to promote breastfeeding.

The frequency of exclusive breastfeeding at hospital discharge can vary between 10% and 56.2% [16,25]. In our study, the prevalence of exclusive breastfeeding at hospital discharge was higher in premature infants with GA > 34 weeks (76.2%). However, a study carried out with PTNB of GI < 32 weeks found that the mother's own breast milk supply on the 7th postnatal day is associated with EBF at 36 weeks corrected GA (OR=1.18 per 10 mL/kg of breast milk; 95% CI=1.06-1.32), showing that it is possible to achieve good exclusive breastfeeding rates in these premature babies [26].

Expectations regarding the postnatal growth of the PTNB are that there will be an initial weight loss, followed by recovery of birth weight. The intensity and duration of these phases is inversely proportional to the GA and the birth weight and directly proportional to the severity of the newborn's condition, also being influenced by the nutritional practice [7,27]. During the first weeks of life, preterm infants have high energy expenditure [16], using their limited body reserves to maintain energy production and, consequently, their vital functions, at the expense of growth [6].

Our data showed that physiological weight loss and birth weight recovery occurred as expected in both groups, being longer among premature infants with GA ≤ 33 weeks, who also had lower birth weight. A study carried out with 61 preterm infants suitable and small for gestational age (birth weight below 1,500 grams or gestational age < 32 weeks) admitted to a NICU in Rio de Janeiro, also showed a similar evolution of postnatal growth among preterm infants suitable for gestational age, who also had a gestational age < 32 weeks (29 ± 1.3 weeks) [28].

The length of hospital stay can be considered an indicator of severity for PTNB. Lima et al [29] demonstrated that the increase of one day in the length of hospital stay for very low birth weight preterm infants increased the chance of growth restriction of the head circumference and weight at discharge (z score ≤ -2 for corrected age), by 3 % and 2%, respectively. In our study, premature infants with GA ≤ 33 weeks also stayed longer in the neonatal unit. However, the period was lower than that found by Abranches et al [28] when studying premature infants with GA < 32 weeks suitable for gestational age (39.7 ± 13.8 days). A

possible explanation for this finding is that the physiological skills considered essential for hospital discharge are reached by most preterm infants at around 36 to 37 weeks of corrected age. Thus, the lower the GA, the greater the time to achieve these skills, which implies a prolonged stay in the neonatal unit [12].

The correlation observed between the start of enteral nutrition and the length of hospital stay demonstrated that the later the premature infant starts enteral nutrition, the longer the hospital stay. This correlation was also observed in other studies carried out in Brazil [25] (r=0.41; p<0.026) and in Spain [30] (r=0.409; p<0.001). It should be noted that a correlation does not necessarily imply a causal relationship. However, a review study showed that early enteral nutrition strategies, in addition to being well tolerated by low weight preterm infants, result in a rapid recovery of lost weight and reduced hospitalization time [7].

## Conclusion

Premature infants with lower GI spent more time on enteral nutrition; started the transition to oral feeding and free maternal breast later; and showed a greater need for fortified breast milk, lower frequency of EBF at hospital discharge, and longer hospital stay. The initial weight loss, recovery of birth weight, and days necessary to reach NEP occurred within the expected ranges in both groups, although this was more accentuated among premature GI ≤ 33 weeks. In the current study, the early onset of enteral nutrition was correlated with a shorter hospital stay.

The definition of sample groups according to the degree of prematurity allows a closer look by the professional to detect the group at greatest risk and adopt nutritional strategies that promote growth in the appropriate standards. It is noted that in the routine of the NICU in question, practical measures are already taken, whose benefits to the PTNB are scientifically proven, such as the establishment of nutrition in the first 24 hours of life, and use of human milk and breast milk additives.

The present study brings valuable information contributing to the improvement in nutritional care for PTNBs. However, it also has limitations. The lack of quantitative variables in the diet and clinical profile of the premature infants made it impossible to assess the influence on nutritional evolution. Finally, the continuity of studies of this nature are recommended with expansion of the studied sample and which allow follow-up after hospital discharge, in order to understand the influence of neonatal nutrition on the long-term growth process.

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