

## Research Article

# Feeding VLBW Infants with Mother's Own Milk in Southern Brazil: Every Week Counts – an Observational Study

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**Abstract**

**Objectives:** To investigate whether changing maternal milk expression routine reduces exclusive mother's own milk (MOM) feedings rate at discharge for very low birth weight infants.

**Methods:** Prospective observational cohort study with historic control, including infants with gestational age  $\leq 30$  weeks and/or birth weight  $\leq 1500$ g. Patients were divided in two groups, according to maternal milk expression routine: at the hospital and at home (Group 1) or only at the hospital (Group 2). Main outcome was type of feeding at discharge (exclusive MOM, any MOM or formula). Independent variables were evaluated using Student's *t* test, Mann-Whitney, and Fisher's exact test in univariate model. Variables with  $p < 0.05$  were included in a logistic regression model.

**Results:** We followed 433 patients up until discharge, 147 in Group 1 and 286 in Group 2. Group 2 received prenatal steroids more frequently, had lower gestational age, higher frequency of enterocolitis and higher post menstrual age at discharge. They also received less exclusive MOM (48/147 vs 157/286,  $p = 0.01$ ). There was no difference regarding formula. In logistic regression model, only post menstrual age remained independently associated with exclusive MOM feeding failure at discharge. Every additional week of hospitalization reduced in 10% the chance of receiving exclusive MOM feedings at discharge (OR 0.89; CI 0.83-0.96;  $p=0.05$ ).

**Conclusion:** Reducing maternal milk expression and longer hospital stay are associated with reduction of exclusive MOM feeding at discharge. Each additional week of hospitalization reduced the chance of exclusive MOM feeding at discharge by 10%.

**ABBREVIATIONS**

MOM: Mother's Own Milk; VLBW: Very Low Birth Weight; PMA: Post Menstrual Age; BPD: Bronchopulmonary Dysplasia; NICU: Neonatal Intensive Care Unit; ROP: Retinopathy of Prematurity; EUGR: Extra Uterine Growth Restriction

**INTRODUCTION**

Mother's own milk (MOM) is recommended as the preferred type of feeding for preterm infants. There is a large body of evidence demonstrating biologic, nutritional and developmental advantages of MOM for the preterm population [1-3]. Human milk has been recognized as a protective element in reducing the risk of morbidities linked to oxidative stress, such as bronchopulmonary dysplasia (BPD) [4], necrotizing enterocolitis (NEC) [5], retinopathy of prematurity (ROP) [6], intraventricular hemorrhage (IVH) and late onset sepsis [3,7,8].

Despite being highly desirable, mothers face challenges in initiating and maintaining milk production when they give birth

prematurely [9]. Mothers of very premature infants, who are unable to breastfeed, must rely on milk expression to provide feedings to their infants and therefore become dependent on milk expression devices until their infants are able to breastfeed. Mothers must be supported by specialized neonatal intensive care unit (NICU) multi professional teams for lactation routines while often times facing the emotional challenges of having their child in critical status or even life-or-death condition. One of the factors previously identified as a barrier to sustained milk expression and production among mothers of preterm infants is the dependency of milk expression devices for long periods of hospital stay. Mothers must adapt to the artificial mechanical stimuli of breast-pumps to stimulate milk production as their infants are not able to directly breastfeed [10]. The routine use of electric pumps for milk expression should begin at least 12 hours after birth and be repeated approximately eight to twelve times a day until milk production is well established [11,12]. Thereafter, a routine of six to eight times a day has been deemed necessary to sustain maternal milk supply [13].

At Hospital Moinhos de Vento, a private hospital in Southern Brazil with a 27 bed, level III NICU, the rates of initiation of MOM expression are close to 100%. In Brazil, breastfeeding is the preferred initial feeding by most of the mothers regardless of socio economic status. There is a strong cultural tradition in breastfeeding and the desire of the mothers to provide milk for their infant is a cultural trait, with very rare instances where mothers decide not to do so.

Within that context, 80% of very low birth weight infants (VLBW) were being discharged home from NICU receiving some amount of MOM, 30% of them being on exclusive MOM (2006 to 2011, unpublished data). In 2011, a change in human milk processing occurred as the newly build NICU could no longer accommodate a milk depot capable of pasteurization. Because of concerns with safety delivering unpasteurized MOM collected at home to premature infants and the inability to standardize the milk collection methods at home (collection containers, storage and labeling) the mothers were instructed by the NICU lactation team to only express milk while at the hospital. They were no longer instructed to collect and bring milk from home. The potential significant change in frequency of milk expression given the new instructions raised concerns on the NICU lactation team in regards to maintenance of adequate milk supply and warranted close monitoring of the outcomes.

The aim of this study is to address whether the changes in maternal milk expression routine as a result of changes in the milk depot process had an impact in exclusive MOM feedings rates at discharge for very low birth weight infants. Secondary effects on neonatal morbidity were also observed.

## MATERIALS AND METHODS

### Study cohort

This prospective cohort study enrolled all inborn or out born infants admitted to the Neonatal Intensive Care Unit at Hospital Moinhos de Vento, Porto Alegre, Brazil between March 2006 and March 2016 with birth weight  $\leq 1500$ g and/or gestational age (GA)  $\leq 30$  weeks. Exclusion criteria were absolute contraindication for use of MOM according to WHO guidelines [14], diagnosis of any genetic syndrome or death during hospitalization in the NICU.

The Hospital Moinhos de Vento NICU offers lactation consultants, education and milk expression equipment that is shared by the mothers on a scheduled basis (two hospital grade breast pumps, located at a common lactation room inside the NICU). All mothers receive education on the importance of mother's milk, operation of the pumps, milk handling and storage. Mothers can stay at NICU for as long as they wish, but they are encouraged to take breaks during daytime and go home at night to rest. When the preterm infants reach 34 weeks postmenstrual age (PMA) and are clinically stable, their mothers are offered to start breastfeeding. Until 2011, maternal milk expression routine consisted of milk expression utilizing hospital grade equipment as well as home personal equipment. Once milk was collected, it was stored and delivered at the NICU milk depot to be pasteurized and then offered to their preterm infant.

Mothers providing expressed breast milk to their VLBW premature infants in the NICU were divided into two groups

for comparisons and the main outcome was type of feeding at infant's hospital discharge. Group 1 consisted of VLBW infants/mothers dyads, admitted to the NICU between March 2006 and March 2011. During that period of time mothers were instructed by the NICU lactation team to routinely perform milk expression at their convenience, utilizing a shared hospital grade pump at the hospital or their own manual or electric pump at home. After collection, the milk was delivered at the hospital milk depot and pasteurized prior to its utilization for infant feedings. Group 2 consisted of VLBW infants/mothers dyads admitted to the NICU between April 2011 to March 2016. During that period of time, due to changes in the logistic capacity of the milk depot leading to inability to pasteurize the milk, mothers were instructed to only express their milk utilizing the shared hospital grade breast milk pump during the day time at the hospital. Those mothers were no longer permitted to bring milk expressed at home, restricting their expression times only during periods they were visiting at the hospital and infants received unpasteurized MOM. A schedule for the 2 available hospital pumps utilization was created and mothers managed to adapt to the new instructed routine. During both periods, only MOM was offered to preterm infants since our institution does not provide donor human milk. All mothers were offered lactation counseling and education provided by the NICU lactation team.

All patients were followed until hospital discharge, feeding type at discharge was defined as the most frequent type of feeding recorded up to 72 hours prior to discharge date. The study protocol was approved by Hospital Moinhos de Vento institutional review board. NICU staff participating in the study obtained a general informed consent from parents or legal guardians for clinical data collection from the medical records.

### Maternal and neonatal data

All maternal and infant demographic and medical data were prospectively collected by two independent neonatologists, according to definitions of Vermont-Oxford Network [15]. Maternal and infant data included mother's age, years of education, any prenatal care, mode of delivery, multiples, gestational morbidities, antenatal steroids administration, gestational age (weeks), birth weight (grams and percentile), gender, SNAPPE-II score, neonatal morbidity such as late onset sepsis, necrotizing enterocolitis (NEC), severe retinopathy of prematurity (ROP stages 3 to 5), severe intraventricular hemorrhage (IVH grades III and IV), extra-uterine growth retardation (EUGR - weight below 10<sup>th</sup> percentile) at discharge, bronchopulmonary dysplasia (BPD need for oxygen or respiratory support at 36 weeks PMA), age at onset and at full enteral feeds (100 ml/kg/d), length of stay and PMA at discharge. Main outcome was type of feedings at hospital discharge defined as the most frequent type of feeding recorded up to 72 hours prior to discharge date. Feedings were classified as exclusive MOM, any MOM or formula. Breastfeeding at discharge was defined as any feedings directly at the mother's breast at least up to 72 hours prior to discharge date.

### Statistical analysis

As this was an observational study, proportions of sizes between groups were used to detect differences related to the outcome [16]. Considering sample sizes of Group 1 (n=147)

and Group 2 (n=286), the known proportion of 30% exclusive breastfeeding in the first group, an error of 0.05 and expecting reduction in main outcome, our study had 80% power to detect a difference up to 17.6% in Group 2. For group comparisons of continuous data, Student's t tests were performed. When data were skewed, Mann-Whitney tests were applied. For comparison of categorical data Fisher's exact test was used. Description data are presented as numbers with percentages, medians with interquartile range, or means with standard deviations or 95% confidence intervals. Data were initially analyzed in univariate models. Variables with  $p < 0.05$  were included in a logistic regression model. For regression, dependent variable was dichotomized in patients who received exclusive MOM and any MOM or formula on discharge. Results were considered statistically significant when two-sided  $p$  was  $< 0.05$ . Statistical analysis was performed with IBM SPSS for Mac software (version 20, SPSS Inc., Chicago, IL).

## RESULTS

### Study subjects

During the study period, there were 492 eligible subjects for the study. Of those, 433 were followed up to NICU hospital discharge (Figure 1). There were no differences in the number of deaths among the 2 groups (15/162 in Group 1 vs. 34/320 in Group 2,  $p=0.75$ ). All mothers received prenatal care. Demographic and clinical characteristics are presented in Table (1). Maternal and neonatal characteristics were similar for both groups, except for slightly higher maternal education, higher exposure to antenatal steroids and lower gestational age at birth among infants in Group 2. There were no significant differences in clinical morbidities between the groups, including illness severity scores, despite infants in Group 2 having slightly lower GA, longer length of hospital stay and a higher PMA at discharge. Cases of necrotizing enterocolitis were 2.7% and 7.7% in Groups 1 and 2, respectively. The difference was not statistically significant, however represented a clinically relevant concern for the unit.

### Feeding outcomes at discharge

The overall rate of any MOM at discharge was 93.9% (407/433). All patients who were discharged on any MOM were also breastfed at least once a day. Only 5 (1.1%) patients who survived never received any human milk, due to mother's illness or choice not to provide MOM. Infants in Group 2 were discharged home on exclusive MOM less frequently than Group 1 (48/147 in Group 1 vs. 57/286 in Group 2,  $p<0.01$ ). In addition, infants in Group 2 took longer time to achieve full enteral feeds. The rate of infants who were discharged on formula was similar in both groups (Table 2).

### Logistic regression model

There was a greater proportion of NEC cases in Group 2. Because NEC diagnosis may significantly delay achievement of full enteral feedings, the association between NEC and longer time to reach full enteral feedings was investigated. Both these variables were related and we chose to input only the latest in the regression model. After logistic regression controlling for maternal education, GA  $< 28$  weeks, exposure to prenatal steroids, gender, time to reach full enteral feedings and PMA at

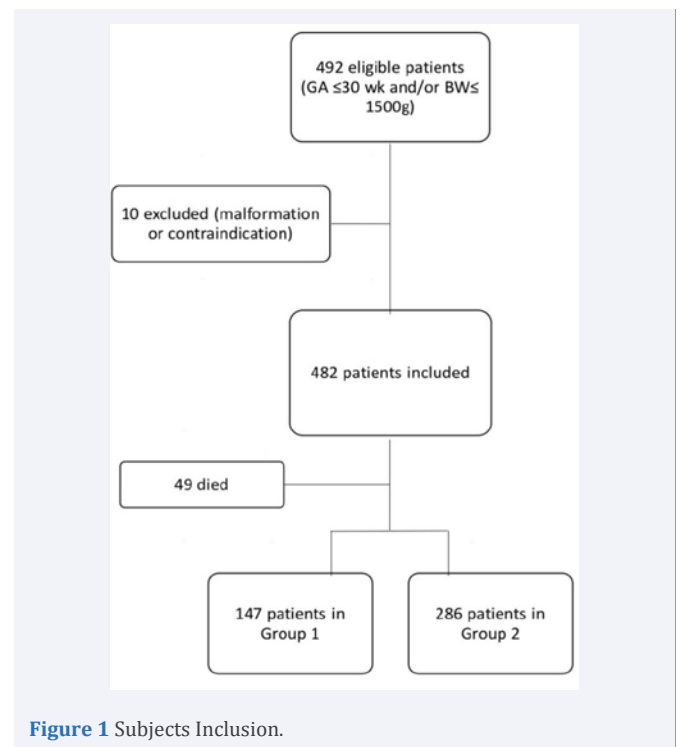


Figure 1 Subjects Inclusion.

discharge, only PMA remained independently associated with exclusive MOM feedings at discharge. Every additional week of hospitalization reduced in 10% the chance of receiving exclusive MOM at discharge (Table 3).

## DISCUSSION

In this observational cohort study of VLBW infants admitted to a single, private, 27 bed, level III NICU in southern Brazil, we found that changing the routine instructions for MOM expression and longer NICU hospitalization were associated with a decrease in rates of exclusive MOM feedings at infant NICU discharge. It was noted that for each additional week of hospitalization, there was a 10% reduction in the likelihood of a VLBW infant receiving exclusive MOM at their discharge. Despite such reduction, it is important to note that most of the patients (93.7%) received some MOM during their hospitalization and rates of discharge on any MOM remained preserved. Reports from the USA and Europe show rates of MOM availability for VLBW infants at discharge to be lower (50 to 86%), with wide variations regarding gestational ages and NICU practices [17-20]. In addition, it is worth to comment that in the present study all of the babies who received any MOM were being actually breastfed, at least once daily at the time of NICU discharge. Delfosse et al.[21], described the finding of higher provision of MOM in privately insured hospitals, however we are unaware of any literature describing MOM availability at private or public hospitals in Brazil.

In this study the reduction of exclusive MOM feedings at the time of VLBW infant NICU discharge occurred as a result of insufficient milk supply to attend the infants nutritional demands throughout hospital stay, which lead to the need for formula supplementation. It is possible that the changes in the routine of milk expression generated insufficient milk supply due to infrequent milk expression, a well-known factor associated

**Table 1:** Maternal and neonatal demographic and clinical characteristics.

Characteristic	Group 1 n = 147	Group 2 n = 286	p
Mother's age (years; mean ± SD)	32.5 ± 5.3	33 ± 4.7	0.44
Maternal education (years; mean ± SD)	13.9 ± 1.9	14.3 ± 2.2	0.04
Twins, n (%)	45 (30.6)	98 (34.3)	0.45
Pre-eclampsia, n (%)	64 (42.2)	128 (44.8)	0.68
Prenatal steroids, n (%)	104 (70.7)	257 (89.9)	< 0.001
Birth weight (grams; mean ± SD)	1.160 ± 263	1.122 ± 263	0.1
Gestational age (weeks; mean ± SD)	29.7 ± 2.4	29 ± 2.6	0.012
Gestational age <28 weeks, n (%)	24 (16.3)	79 (27.6)	0.008
Male sex, n (%)	60 (40.8)	155 (54.2)	0.01
Small for gestational age, n (%)	31 (21.1)	51 (17.8)	0.4
SNAPPE-II score, median (IQR)	9 (0-19)	10 (0-25)	0.09
Late onset sepsis, n (%)	39 (26.5)	84 (29.4)	0.5
ROP ≥ Stage 3, n (%)	1 (0.9)	4 (1.5)	1
IVH ≥ Grade III, n (%)	2 (1.4)	12 (4.1)	0.15
BPD at 36 weeks PMA, n (%)	8 (5.4)	26 (9.2)	0.19
Necrotising enterocolitis, n (%)	4 (2.7)	22 (7.7)	0.05
Length of stay, median number of days (IQR)	49 (39-62)	59 (42-88)	<0.001
PMA (weeks) at discharge, median (IQR)	37 (36-38)	38 (36-39)	<0.001

**Abbreviations:** SD: Standard Deviations; IQR: Interquartile Range; ROP: Retinopathy of Prematurity; IVH: Intraventricular Hemorrhage; BPD: Bronchopulmonary Dysplasia; PMA: Post Menstrual Age

**Table 2:** Feeding outcomes during hospital stay and at discharge.

Characteristic	Group 1 n = 147	Group 2 n = 286	p
Age (days) at onset of enteral feedings, median (IQR)	2 (1-3)	2 (1-4)	0.50
Age (days) at full enteral feedings, median (IQR)	10 (7-13)	10 (8-16)	0.01
<b>At discharge</b>			
Exclusive MOM, n (%)	48 (32.7)	57 (19.9)	0.01
Any MOM, n (%)	90 (61.2)	212 (74.1)	0.04
Formula, n (%)	9 (6.1)	17 (5.9)	0.94

**Abbreviations:** IQR: Interquartile Range

**Table 3:** Independent variables significantly associated with exclusive MOM feeding for very low birth weight infants at NICU discharge.

Independent Variables	Adjusted OR	95% CI	p
Gestational age < 28 weeks	0.78	0.53-1.14	0.2
Prenatal steroids	1	0.64-1.58	0.9
Maternal education	1.05	0.96-1.14	0.22
Male gender	1	0.74-1.45	0.8
PMA at discharge	0.89	0.83-0.96	0.05
Age at full enteral feeds	0.99	0.96-1.02	0.57

**Abbreviations:** OR: Odds Ratio; CI: Confidence Intervals; PMA: Post Menstrual Age

with decreased milk production [9]. The impact of restricting milk expression to daytime at the hospital may have altered the potential for MOM availability in Group 2.

For a mother, the experience of providing milk for her infant in the NICU is largely different from breastfeeding a healthy, term infant. The decision and motivation to artificially express breast milk is frequently based on the belief that her own milk might attenuate the infant's specific health vulnerabilities. Premature mothers also have a different physiology of milk production [22]. They have less time during gestation to develop their mammary glands and might have reduced neuro-hormonal stimulus of oxytocin and prolactin due to lack of maternal-infant contact.

Finally, they are highly dependent on staff support, and being able to provide milk might make them feel more connected to a baby they can hardly touch. The experience of pumping, instead of putting the baby to the breast can be frustrating. Maternal perceptions of the milk expression experience during the 2 time periods studied were not evaluated. We intend to investigate whether simply instructing mothers to continue same milk expression routine, discarding or donating milk expressed at home would have had a different impact on the outcomes.

Other authors have raised concern about the challenges of maintaining MOM supply for infants with long hospitalizations [23-25]. Similarly, in the present study infants in Group 2 had

significantly higher length of stay as compared to Group 1, representing an additional obstacle to maintenance of MOM supply to that cohort. Despite that, rates of infant being discharge on formula were surprisingly the same on Group 2 (5,9%), suggesting that the impact of the milk depot process changes affected maternal milk volume production rather than maternal cessation of milk expression.

All neonatal morbidities associated with oxidative stress were not different between the 2 groups. These findings were in agreement with Flacking et al.[26], one of the few studies observing that neonatal morbidities did not influence duration of breastfeeding. Despite not statistically significant, NEC rates were increased during the second period of time studied. Group 2 had NEC rates almost 3 times higher than Group 1 (2.7% vs 7.7%) and this finding generated a clinical concern worth to be further investigated within our NICU. Studies have suggested that pasteurization of human milk alters immunobiological properties that might confer protection against NEC [27-29]. Interestingly, in our study pasteurization was not performed prior to utilization of MOM for Group 2. There was a higher proportion of more immature infants in this group, which could justify higher rates of NEC, an effect that in theory could be have been counteracted by higher exposure to antenatal steroids [30], also noted on this group.

It does not appear that NEC directly impairs MOM at discharge, however infants with such morbidity may have had prolonged NPO status, longer time to reach full enteral feeds and possibly disturbance in gut microbiome [31] that might compromise long term feeding tolerance. Our study did not evaluate the specific impact of all abovementioned factors, however we speculate that a longer hospitalization associated to NEC diagnosis was possible on those patients and could have had an impact on longer maternal dependency to mechanical milk extraction. Future directions will be to investigate in depth the common denominator of all participants who developed NEC and MOM dose related associated factors before and after NPO status.

Maternal level of education was high in the population studied. All mothers had at least high school degree. Work by Sisk et al.[32], identified more than twelve years of education as a predictor of greater success in breastfeeding preterm infants. Despite a significant difference of approximately one more year favoring Group 2 it does not seem to be clinically relevant as all mothers had greater than 12 years of education. Socio-economic status of the population is assumed to be above average for the Brazilian population, as all mothers had private health insurance, which indicates high income in Brazil (data not shown).

We identify as a limitation to our study the analysis of MOM at discharge of VLBW infants admitted to a single, private, level III NICU, which is an isolated reality within a developing country characterized by large socio-economic disparities. The current analysis has limited external validity within Brazilian context. Another limitation is the lack of information about MOM volumes. Meier et al.[33], cite in their review of strategies to promote breastfeeding among preterm infants, that the most appropriate indicator for assessing the success of breastfeeding and for reducing morbidity in premature infants is the volume of breast milk received effectively during hospitalization. Although we did

not collect the volume of milk received during hospitalization, our overall efforts to promote MOM guaranteed some MOM to the majority of infants discharged (>90%), certainly a positive effect. Strategies to monitor maternal milk volumes production and better evaluation of infant's volumes of MOM intake are necessary and will be the focus of our future projects.

To our knowledge, this is the first study that describes the incidence of human milk administration at discharge in a cohort of VLBW in Brazil. Although conducted in a private NICU, which may not reflect the reality of all health services in the country, it is important to stress the need to support breastfeeding among mothers of preterm infants during their hospitalization for better maintenance of milk supply. Knowledge of characteristics of mothers and premature infants, and specific factors associated with failure in breastfeeding may help planning strategies to increase the number of preterm infants being discharged home on exclusive MOM.

## CONCLUSION

Restricting MOM expression routine to be performed only at hospital facilities and longer infant hospital stay are associated with reduction of exclusive MOM feedings for VLBW infants at discharge. Each additional week of infant hospitalization reduced the likelihood of exclusive MOM feeding at discharge by 10%. Milk expression education and instructed routines provided by hospital staff must take into account the high vulnerability of mothers of VLBW infants for milk volume insufficiency at discharge.

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