BREASTFEEDING MEDICINE
Volume 13, Number 2, 2018

DOI: 10.1089/bfm.2017.0159

Milk Volume at 2 Weeks Predicts Mother's Own Milk Feeding at Neonatal Intensive Care Unit Discharge for Very Low Birthweight Infants

Rebecca Hoban,[1,2] Harold Bigger,[1] Michael Schoeny,[3] Janet Engstrom,[3] Paula Meier,[1,3] and Aloka L. Patel[1,3]

Abstract

Objective: This study sought to determine the maternal prepregnancy, pregnancy, and delivery risk factors that predicted coming to volume (CTV; achieving pumped mother's own milk [MOM] volume ≥500 mLs/day) and the continuation of MOM provision through to discharge from the neonatal intensive care unit (NICU) in mothers and their very low birthweight (VLBW; <1,500 g at birth) infants.
Study Design: Secondary analysis of prospectively collected data from 402 mothers of VLBW infants admitted to an urban NICU, including detailed MOM pumping records for a subset (51%) of the cohort. Analyses included inverse probability weighting, multivariate regression, and chi-square statistics.
Results: In this high-risk cohort (51.2% black, 27.1% Hispanic, 21.6% white/Asian; 72.6% low income; 61.4% overweight/obese prepregnancy), CTV by day 14 was the strongest predictor of MOM feeding at NICU discharge (odds ratio [OR] 9.70 confidence interval [95% CI] 3.86–24.38, $p < 0.01$.). Only 39.5% of mothers achieved CTV by postpartum day 14, an outcome that was predicted by gestational age at delivery (OR 1.41, 95% CI 1.15–1.73, $p < 0.01$), being married (OR 3.66, 95% CI 1.08–12.39, $p = 0.04$), black race (OR 7.70, 95% CI 2.05–28.97, $p < 0.01$), cesarean delivery (OR 0.22, 95% CI 0.08–0.63, $p = 0.01$), and chorioamionitis (OR 0.14, 95% CI 0.02–0.82, $p = 0.03$).
Conclusion: Continued provision of MOM at NICU discharge can be predicted in the first 14 postpartum days on the basis of achievement of CTV. We posit that CTV can serve as a quality indicator for improving MOM feedings in the NICU and that lactation support resources should target this early critical postbirth period.

Keywords: human milk, mother's own milk, lactogenesis, VLBW, neonatal, pregnancy, maternal

Introduction

High-dose mother's own milk (MOM) feedings through to discharge from the neonatal intensive care unit (NICU) represent an essential part of a bundle of best practices to reduce potentially preventable NICU morbidities, their sequelae, and associated costs in very low birthweight (VLBW; <1,500 g) infants.[1] However, a global barrier to achieving this outcome is insufficient volumes of MOM. Insufficient MOM volume has its origins in the first 2 weeks postpartum, a critical period during which the mammary epithelial cells appear to undergo programming processes that regulate long-term MOM synthesis.[2,3] We have previously referred to this early phase of lactation as *coming to volume* (CTV), which we have defined as achieving a threshold daily MOM volume of ≥500 mL/day by postpartum day 14.[2,3]

Healthy mothers with exclusively breastfeeding term infants typically experience CTV between 4 and 7 days postpartum.[4] However, impaired CTV in healthy populations has been associated with predisposing risk factors, including primparity,[4,5] cesarean delivery,[6,7] and prepregnancy overweight and obesity.[8,9] Most importantly, impaired CTV predicts early cessation of exclusive and any breastfeeding in otherwise healthy populations.[10]

Little is known about CTV in mothers of preterm VLBW infants. However, these mothers are over-represented in the risk categories mentioned earlier for impaired CTV, and they also experience mammary gland immaturity,[11,12] stress

[1]Section of Neonatology, Department of Pediatrics, Rush University Medical Center, Chicago, Illinois.
[2]Division of Neonatology, Department of Paediatrics, The Hospital for Sick Children, Toronto, Canada.
[3]College of Nursing, Rush University Medical Center, Chicago, Illinois.

associated with the infant's NICU admission,[13] breast pump dependency, and prepregnancy and pregnancy-related health problems and delivery complications that may result in blood loss, inflammation, or other secondary morbidities. These conditions directly impact the regulation of lactation processes as well as early pumping behaviors. Although some data suggest that impaired CTV is merely delayed or temporary in these vulnerable mothers,[14] other data show that it predicts long-term insufficient MOM volume in this population.[15,16]

Understanding the origins of insufficient MOM volume in mothers of VLBW infants is central to prioritizing evidence-based lactation care. Thus, the purposes of this study were to identify previously unreported maternal predictors of CTV based on prepregnancy, pregnancy, and delivery factors that are common sources of morbidity in mothers who deliver VLBW infants and to determine whether CTV predicts continued MOM provision through to NICU discharge.

Materials and Methods

This study is a secondary analysis of a prospective cohort study of 430 VLBW infants and their mothers for whom inclusion and exclusion criteria have been previously detailed.[17] Cohort enrollment took place in the level III NICU at Rush University Medical Center between February 2008 and December 2012, and mothers provided signed informed consent for themselves and their infants. Both the original cohort study and this secondary analysis were approved by the Rush University Institutional Review Board.

Measures

For this analysis, prospectively collected maternal and infant characteristics, including complete health and demographic data ($n = 402$ mothers), were accessed from the cohort study database. Maternal characteristics included: age, marital status, race/ethnicity (non-Hispanic black [black], non-Hispanic white [white], Hispanic, and Asian), low income status (yes/no for maternal eligibility for Special Supplemental Nutrition Program for Women, Infants, and Children [WIC]), formal education attained (<high school, high school, trade school/some college without attainment of a bachelor's degree, and ≥bachelor's degree), and previous breastfeeding experience (yes/no). Seven mothers who were Asian were re-categorized as white given similar sociodemographic characteristics and breastfeeding rates.[18]

Maternal lactation risk factors that had been obtained from the medical record during the prospective cohort study were organized within three categories: prepregnancy health factors, pregnancy complications resulting in an indication for delivery, and labor and delivery factors. These lactation risk factors were not mutually exclusive, and most mothers had more than one risk factor. Prepregnancy health factors included body mass index (normal [<25] or overweight/obese [≥25]),[19] and diagnoses of hypertension or type 2 diabetes listed in the medical record.

Pregnancy complications included: multiple gestation, pre-eclampsia/eclampsia, premature rupture of membranes (PROM), placental abruption, fetal heart rate abnormalities/poor biophysical profile, intrauterine growth restriction, uterine abnormalities or cerclage, chorioamnionitis, and preterm labor. Labor and delivery factors included spontaneous labor, induced labor, and cesarean delivery.

Prospectively collected infant data extracted from the cohort study database included birth weight (BW), gestational age at delivery (GA; marker of mammary gland immaturity), and daily intake (mL) of MOM and formula from birth through to NICU discharge. The variable *MOM feeding at NICU discharge* was determined based on the type of feedings received on the last full day of NICU hospitalization (12 AM–11:59 PM), and it was categorized into the mutually exclusive categories of *any MOM* or *no MOM*. Donor human milk was not used.

As standard practice in our NICU, mothers are strongly encouraged, but not required, to keep detailed pumping records to assist with lactation support. Similarly, completion of pumping records was encouraged but not a requirement of the cohort study. Reasons for noncompletion were not collected. A subset of the 402 mothers in the study ($n = 205$; 51%) provided detailed MOM pumping data, including self-recorded timing and volume of MOM pumping sessions during the first 14 postpartum days. Mothers were taught by study staff how to record date, time, and duration of pumping session, as well as how to visually assess and record pumped MOM volume from marked pumping containers. The remaining 197 mothers did not provide pumping records during the first 14 postpartum days.

The 205 pumping records were used to determine whether mothers experienced CTV, defined as a total pumped MOM volume ≥500 mL/day for at least one 24-hour period during the first 14 days postpartum.[2] If mothers had incomplete records that stopped before day 14 and had not yet experienced CTV ($n = 6$), they were presumed not to have achieved CTV by day 14.

Data analysis

Descriptive statistics included frequencies, percentages, and mean ± SD. Characteristics of mothers with and without MOM pumping data (Table 1) were compared by chi-square and independent *t* tests to determine the best approach for statistical adjustment and weighting of the 205 MOM pumping records so that the records reflected the total study sample of 402 mothers. Significant differences in mothers who provided and did not provide MOM pumping records were noted, especially for sociodemographic characteristics and delivery indications.

Because these differences suggested that completion of pumping logs was nonrandom, we performed the following steps. First, we conducted a logistic regression in which the completion of pumping data was regressed on the following variables: sociodemographic factors, GA, prepregnancy health factors, pregnancy complications, and labor and delivery factors (Table 1). Using the results of this regression, we applied inverse probability weighting methods[20] to reduce bias that was introduced by analyzing only the sample with available pumping data.

Using these weighted data, we conducted a series of bivariate and multivariate analyses to determine the predictors of CTV by postpartum day 14 (CTV by day 14). An additional multivariate regression, using the variable of CTV by day 14 as well as the significant predictors of CTV themselves were entered into the analyses to determine the extent

to which each variable predicted MOM feeding at NICU discharge. Analyses were performed by using SAS software (SAS Institute, Inc., Cary, North Carolina). SAS Proc SurveyLogistic was used for all analyses that incorporated sampling weights. Type 1 error was set at $p < 0.05$.

Results

Characteristics of the sample

Mothers who provided ($n = 205$) and did not provide ($n = 197$) pumping log data had several dissimilar characteristics (Table 1), so the pumping data were weighted to reflect the entire cohort of 402 mothers. Mothers who provided pumping data were older, more educated, and less likely to be low income and black. In addition, mothers who provided pumping data were significantly more likely to have experienced PROM. Although nearly all (98%) of the 402 mothers provided some MOM for their infants, mothers who provided pumping data were more likely to have infants receiving MOM feedings at NICU discharge (51.7% versus 14.7%, $p < 0.01$).

Of the six mothers with incomplete pumping records who were presumed not to have experienced CTV, four had MOM volumes below 150 mL/day at the time of record discontinuation (mean 8.8 days) and the remaining two had MOM volumes <375 mL/day on day 12.

CTV by day 14

Of the many socioeconomic and prepregnancy health factors, pregnancy complications, and labor/delivery factors evaluated, few retained significance as predicting CTV by day 14 in multivariate analysis: marital status, race/ethnicity, chorioamnionitis, cesarean delivery, and GA (Table 2). Unweighted models are available in Supplementary Tables S1 and S2 (Supplementary Data are available online at www.liebertpub.com/bfm).

MOM feeding at NICU discharge

In the multivariate model (Table 3), only maternal age and achievement of CTV by day 14 were significant predictors of MOM feeding at NICU discharge. Achievement of CTV by postpartum day 14 was the strongest predictor of MOM feeding at discharge (odds ratio [OR] 9.70, 95% confidence interval 3.86–24.38). Of mothers who achieved CTV by day 14, 75.3% provided MOM at NICU discharge, versus 36.3% of mothers who did not achieve CTV ($p < 0.001$). Unweighted models are available in Supplementary Tables S1 and S2.

Discussion

To our knowledge, this is the first study to report predictors of achieving and not achieving CTV and to describe the relationship between CTV and continued MOM feeding through to NICU discharge in breast pump-dependent mothers of VLBW infants. In this primarily minority, low income cohort, we found that achievement of CTV by postpartum day 14 was the strongest predictor of the infant's receiving MOM feedings at NICU discharge, with an odds ratio of 9.70. This strong relationship suggests that the achievement of CTV can be incorporated as an early quality indicator for evidence-based NICU benchmarks that target the increased use of MOM at the time of NICU discharge.

Although CTV and its definition as ≥500 mLs of pumped MOM by postpartum day 14 may seem novel, we have previously published a detailed description of this phase of lactation and its specific importance for breast pump-dependent

Table 1. Characteristics of Mothers With and Without Pumping Data

Characteristic, n *(%) or mean ± SD*	*Pumping data (n = 205)*	*No pumping data (n = 197)*	p
Sociodemographic			
Maternal age (years)	28.8 ± 6.2	25.3 ± 6.3	<0.01*
Low socioeconomic status	120 (58.5)	172 (87.3)	<0.01*
Married	105 (51.2)	49 (24.9)	<0.01*
Race/ethnicity			
White/Asian	54 (26.3)	33 (16.8)	<0.01*
Hispanic	75 (36.6)	34 (17.3)	
Black	76 (37.1)	130 (66.0)	
Highest education completed			
<High school	27 (13.2)	41 (20.8)	<0.01*
High school	51 (24.9)	54 (27.4)	
Trade or <BA/BS	75 (36.6)	79 (40.1)	
BA/BS or higher	52 (25.4)	23 (11.7)	
Previous breastfeeding experience			
No (primiparous)	119 (58.0)	101 (51.3)	0.06
No (multiparous)	28 (13.7)	45 (22.8)	
Yes	58 (28.3)	51 (25.9)	
Prepregnancy health factors			
Prepregnancy BMI, kg/m^2	28.5 ± 7.2	28.7 ± 7.8	0.73
Prepregnancy overweight/obese (BMI ≥25)	126 (61.5)	121 (61.4)	0.87
Hypertension	20 (9.8)	17 (8.6)	0.70
Type II diabetes	4 (2.0)	4 (2.0)	0.96
Pregnancy and infant characteristics			
Multiple gestation	39 (19.0)	24 (12.2)	0.06
Infant male sex	114 (55.6)	101 (51.3)	0.38
Infant gestational age (weeks)	27.8 ± 2.5	28.2 ± 2.4	0.08
Infant birth weight (grams)	1,036 ± 246	1,064 ± 261	0.26
Pregnancy complications			
Multiple gestation	37 (18.0)	22 (11.2)	0.05
Pre-eclampsia/eclampsia	47 (22.9)	59 (29.9)	0.11
Premature rupture of membranes	59 (28.8)	37 (18.8)	0.02*
Placental abruption	12 (5.9)	22 (11.2)	0.06
Fetal heart rate abnormalities/poor biophysical profile	30 (14.6)	31 (15.7)	0.76
Intrauterine growth restriction	13 (6.3)	15 (7.6)	0.62
Uterine abnormalities/ cerclage	16 (7.8)	7 (3.6)	0.07
Chorioamnionitis	25 (12.2)	21 (10.7)	0.63
Preterm labor	68 (33.2)	66 (33.5)	0.94
Labor and delivery factors			
Spontaneous onset of labor	123 (60.0)	104 (52.8)	0.15
Induction of labor	20 (9.8)	18 (9.1)	0.83
Cesarean delivery	126 (61.5)	126 (64.0)	0.61
Coming to volume			
By day 14	81 (39.5)	N/A	N/A

*$p < 0.05$.
BA/BS, bachelor of arts/bachelor of science; BMI, body mass index.

Table 2. Predictors of Coming to Volume by Day 14

Characteristic, n = *205*[a]	*OR (95% CI)*	p
Sociodemographic factors		
Maternal age (years)	0.98 (0.90–1.07)	0.70
Low socioeconomic status	1.25 (0.44–3.50)	0.67
Married	3.66 (1.08–12.39)	0.04*
Race/ethnicity (white is reference)		0.01*
Hispanic	1.70 (0.51–5.64)	0.38
Black	7.70 (2.05–28.97)	<0.01*
Highest education (<high school is reference)		0.10
High school	3.33 (0.49–22.60)	0.22
Trade or <BA/BS	1.10 (0.15–8.23)	0.92
BA/BS or higher	0.89 (0.11–7.24)	0.91
Previous breastfeeding experience (yes is reference)		0.11
No (primiparous)	1.02 (0.36–2.92)	0.97
No (multiparous)	0.24 (0.05–1.11)	0.07
Prepregnancy health factors		
Prepregnancy overweight/obese (BMI ≥25)	0.44 (0.18–1.11)	0.08
Hypertension	0.56 (0.10–3.05)	0.51
Pregnancy complications		
Multiple gestation	1.31 (0.35–4.93)	0.69
Pre-eclampsia/eclampsia	0.70 (0.17–2.86)	0.62
Premature rupture of membranes	1.90 (0.44–8.18)	0.39
Placental abruption	4.17 (0.87–20.05)	0.07
Fetal heart rate abnormalities or poor biophysical profile	1.59 (0.42–5.95)	0.49
Intrauterine growth restriction	0.47 (0.06–3.54)	0.46
Uterine abnormalities/ cerclage	1.93 (0.56–6.63)	0.30
Chorioamnionitis	0.14 (0.02–0.82)	0.03*
Preterm labor	0.41 (0.08–2.03)	0.28
Labor and delivery factors		
Induction of labor	1.26 (0.26–6.03)	0.77
Cesarean delivery	0.22 (0.08–0.63)	0.01*
Gestational age (weeks)	1.41 (1.15–1.73)	<0.01*

[a]Results weighted to reflect entire cohort of 402 mothers.
*$p < 0.05$.
CI, confidence interval; OR, odds ratio.

Table 3. Predictors of Infant Receiving Mother's Own Milk Feedings at Neonatal Intensive Care Unit Discharge

Characteristic, n = *205*[a]	*OR (95% CI)*	p
Sociodemographic factors		
Maternal age (years)	1.11 (1.02–1.21)	0.02*
Low socioeconomic status	0.47 (0.16–1.42)	0.18
Married	1.52 (0.56–4.15)	0.41
Race/ethnicity (white is reference)		0.61
Hispanic	1.43 (0.37–5.43)	0.60
Black	0.77 (0.20–2.98)	0.71
Highest education (<high school is reference)		0.18
High school	0.24 (0.06–0.98)	0.05
Trade or <BA/BS	0.60 (0.14–2.51)	0.48
BA/BS or higher	0.48 (0.09–2.48)	0.38
Previous breastfeeding experience (yes is reference)		0.06
No (primiparous)	3.22 (1.22–8.51)	0.02
No (multiparous)	1.19 (0.33–4.28)	0.79
Prepregnancy health factors		
Prepregnancy overweight/ obese (BMI ≥25)	2.05 (0.71–5.90)	0.19
Hypertension	0.46 (0.10–2.07)	0.31
Pregnancy complications		
Multiple gestation	0.28 (0.07–1.10)	0.07
Pre-eclampsia/eclampsia	0.31 (0.07–1.31)	0.11
Premature rupture of membranes	1.58 (0.32–7.90)	0.57
Placental abruption	0.43 (0.08–2.32)	0.33
Fetal heart rate abnormalities or poor biophysical profile	3.31 (0.65–16.77)	0.15
Intrauterine growth restriction	0.46 (0.08–2.59)	0.38
Uterine abnormalities/ cerclage	0.85 (0.18–4.11)	0.84
Chorioamnionitis	0.46 (0.08–2.54)	0.38
Preterm labor	0.53 (0.13–2.22)	0.38
Labor and delivery factors		
Induction of labor	0.80 (0.16–3.88)	0.78
Cesarean delivery	1.06 (0.42–2.71)	0.90
Gestational age (weeks)	1.13 (0.92–1.39)	0.24
MOM		
Coming to volume by day 14	9.70 (3.86–24.38)	<0.01*

[a]Results weighted to reflect entire cohort of 402 mothers.
*$p < 0.05$.

mothers of VLBW infants.[3] Despite the fact that VLBW infants require far less than 500 mL of MOM a day in the first weeks of life, this volume is useful as a quality indicator for successful lactogenesis, as studies suggest that the mammary gland is programmed for long-term lactation during these early postpartum days, including increases in the numbers of secretory cells and prolactin receptors.[3]

Multiple studies have reported that mothers of premature, low birthweight (<2,500 g) and VLBW infants produce lower MOM volumes than mothers who breastfeed healthy infants.[15,16] However, few studies have focused on delineating critical postpartum periods during which these mothers are at the highest risk for MOM volume problems. In a classic study of 95 breast pump-dependent mothers of infants born ≤31 weeks GA, Hill et al.[16] reported that pumped MOM volume at the end of postpartum week 1 predicted MOM volume at postpartum week 6. These investigators concluded that interventions to prevent low MOM volume in this population should be targeted during the first postpartum week.

Two additional randomized studies in mothers of VLBW infants support the idea of early postpartum mammary gland programming. The interventions in both studies, which included pumping within the first postpartum hour[21] and electric breast pump use versus hand expression during the first seven postpartum days,[22] were short-term, but had a measurable impact on pumped MOM volume weeks thereafter.

A recent retrospective record review of 85 mothers and their infants born ≤32 weeks GA also revealed that pumped MOM volumes below the sample median on postpartum day 4 predicted formula use at NICU discharge.[23] Thus, our finding that CTV by day 14 predicts the continuation of MOM feedings through to NICU discharge is consistent with other studies, postulating an early critical window for establishment of long-term adequacy of pumped MOM volume in this population.

CTV encompasses the short but vital period between the onset of secretory activation and the achievement of a threshold MOM volume ≥500 mLs per day.[2] This period is fraught with difficulties for both healthy and vulnerable populations, resulting in high rates of unplanned early weaning,[24] low pumped MOM volumes,[2] and/or lack of exclusive MOM feeding.[10] Several randomized and observational studies have linked maternal demographic characteristics, prepregnancy, pregnancy, and delivery risk factors with delayed onset of lactation (e.g., delayed lactogenesis II) and/or MOM supply concerns during the first two postpartum weeks in otherwise healthy populations.[4–9] However, little research has focused on the timing-specific impact of these maternal risk factors when they occur in breast pump-dependent mothers of premature infants.

Multivariate model predictors of achieving CTV by day 14 in our population included black race and being married, whereas predictors of not achieving CTV included chorioamnionitis, cesarean delivery, and lower GA. However, it is likely that cesarean delivery served as a proxy variable for other maternal prepregnancy, pregnancy, and delivery risk factors that were not mutually exclusive with respect to each other or with cesarean delivery. Thus, mothers could have had one or more of these risk factors, which increase the likelihood of cesarean delivery.[25,26] One previous retrospective study reported that cesarean delivery increased the odds (4.3-fold) of low pumped MOM volume on postpartum day 4 in 85 mothers of premature infants born ≤32 weeks GA, and that pregnancy-induced hypertension predicted cesarean delivery.[23] Thus, cesarean delivery may serve as a marker for other maternal risk factors that potentially influence pumped MOM volume.

We speculate that an underlying mechanism to explain the negative impact of maternal morbidities on CTV may be the presence of inflammation, seen with both cesarean delivery and chorioamionitis, as well as with preterm birth.[27–29] Since inflammation interrupts the closure of mammary epithelial tight junctions,[30,31] downregulates lactose synthesis, and decreases milk volumes in in vitro and animal models,[32,33] we hypothesize that these inflammatory conditions may pose additional challenges to the already ''at-risk'' immature mammary gland in mothers who deliver at an early GA,[11,12] itself a negative predictor of CTV.

To date, the majority of interventions to improve CTV and pumped MOM volume have been primarily focused on behavioral and motivational approaches such as breast pump type and use, skin-to-skin holding, and the integration of breastfeeding peer counselors.[3,15,34–36] However, future research addressing the mechanisms by which these maternal risk factors impact the physiology of CTV may lead to targeted interventions for women with specific risk factors.

Our study has several strengths, including the large racially, ethnically, and socioeconomically diverse sample, and the prospective collection of data, including maternal health and intrapartum conditions. The use of documented pumped MOM volumes to measure CTV through the first two postpartum weeks is a particular strength of our study, as most studies on this topic have used infant feeding data as a proxy variable for pumped MOM volume.[37,38] Premature and/or VLBW infants require very small volumes of human milk during the first 2 weeks of life to receive exclusive MOM feedings, often only 150–200 mLs per day.[39] Thus, early exclusive MOM feedings may be accomplished even though mothers of these infants have not achieved CTV, which potentially leads to later insufficient MOM volume as feeding requirements increase and resultant discontinuation of exclusive or any MOM provision. Thus, the use of infant feeding rather than pumped MOM volume data makes the results of these studies difficult to interpret.

Although the use of pumped MOM volumes is a strength of this study, we acknowledge that these measures were self-recorded and may be subject to maternal error. Although mothers were taught how to visually measure and record their MOM volumes from marked containers after pumping, the MOM was not measured directly by the study team. In addition, if pumping records were incomplete and mothers had not yet CTV ($n=6$), it was assumed that they did not CTV. Thus, we may have underestimated rates of successful CTV, although the volumes recorded by these mothers before discontinuation of record keeping suggest that this assumption is accurate.

In addition, MOM feedings at discharge were measured by using infant feeding data records rather than daily pumped MOM volume. Although MOM feeding data are more likely to reflect pumped MOM volumes at NICU discharge than during the first two postpartum weeks, it is possible that some mothers in our study were no longer pumping but had sufficient frozen MOM for partial or exclusive MOM feedings at discharge, although this suggests an adequate MOM supply before discontinuation of pumping. Another limitation of our study is the low number of mothers in our cohort with diabetes, which limits our analysis of the impact of this risk factor and CTV. Previous studies in mothers of term and premature infants have revealed delayed onset of lactation and/or insufficient MOM volumes in the presence of maternal diabetes.[40]

Finally, the subset ($n=205$) of mothers who maintained pumped MOM volume records was more educated, less likely to be low income, more likely to be white, and more likely to have experienced PROM than the subset ($n=197$) of mothers who did not. Although we corrected for these differences by using propensity score-weighting, it is possible that some confounding findings remain. The higher rates of continued MOM provision through to NICU discharge in the pumping record group, as well as their willingness to keep records, suggest that these mothers may have been more highly motivated to provide MOM, and may have had

different pumping behaviors, which were not analyzed in this study.

Although maternal length of stay was not measured, higher rates of PROM suggest that this group of mothers was likely to have been hospitalized for days to weeks before preterm delivery. We hypothesize that a longer hospitalization would allow more time for prenatal education on the importance of MOM for preterm infants and result in higher motivation to provide both pumping records and long-term MOM than mothers who had an unexpected or urgent preterm delivery. Overall, however, the fact that only 39.5% of highly motivated mothers with strong lactation support were able to CTV 2 weeks after preterm delivery sheds light on the scale of this problem, as the rate in a typical mother is likely even lower.

In summary, we found that multiple maternal pregnancy and delivery risk factors negatively affected CTV in this diverse urban cohort of mothers, and that CTV was, by far, the strongest predictor of MOM feeding at NICU discharge. We speculate that these maternal risk factors manifest in higher rates of cesarean delivery, hence the strength of this predictor in the multivariate model for CTV by day 14. Overall, the high percentage of mothers who experience a delay in or failure to CTV is concerning from a public health standpoint. Mothers and providers should be educated regarding early mammary gland programming and the importance of optimal pumping behavior to maximize MOM volumes in the first 14 days postpartum as an intervention to improve long-term lactation outcomes.

Acknowledgments

Research reported in this publication was supported by the Eunice Kennedy Shriver National Institute Of Child Health & Human Development of the National Institutes of Health under Award Number R03HD081412. Research reported in this publication was supported by the Eunice Kennedy Shriver National Institute Of Child Health & Human Development of the National Institutes of Health under Award Number R03HD081412. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Ethics/Consent Statement

Written consent was obtained from all subjects for participation in the original cohort study.

Disclosure Statement

All authors made substantial contributions to the study design, analysis, and interpretation of data, and drafting and revising the article. All approved the final version to be published.

References

1. Meier PP, Patel AL, Bigger HR, et al. Human milk feedings in the neonatal intensive care unit. In: Diet and Nutrition in Critical Care, Rajendram R, Preedy VR, Patel VB, eds. New York: Springer-Verlag, 2015, pp. 807–822.
2. Meier PP, Patel AL, Hoban R, et al. Which breast pump for which mother: An evidence-based approach to individualizing breast pump technology. *J Perinatol* 2016;36:493–499.
3. Meier PP, Engstrom JL, Janes JE, et al. Breast pump suction patterns that mimic the human infant during breastfeeding: Greater milk output in less time spent pumping for breast pump-dependent mothers with premature infants. *J Perinatol* 2012;32:103–110.
4. Chen DC, Nommsen-Rivers L, Dewey KG, et al. Stress during labor and delivery and early lactation performance. *Am J Clin Nutr* 1998;68:335–344.
5. Sievers E, Haase S, Oldigs HD, et al. The impact of peripartum factors on the onset and duration of lactation. *Biol Neonate* 2003;83:246–252.
6. Dewey KG, Nommsen-Rivers LA, Heinig MJ, et al. Risk factors for suboptimal infant breastfeeding behavior, delayed onset of lactation, and excess neonatal weight loss. *Pediatrics* 2003;112(3 Pt 1):607–619.
7. Evans KC, Evans RG, Royal R, et al. Effect of caesarean section on breast milk transfer to the normal term newborn over the first week of life. *Arch Dis Child Fetal Neonatal Ed* 2003;88:F380.
8. Rasmussen KM, Hilson JA, Kjolhede CL. Obesity may impair lactogenesis II. *J Nutr* 2001;131:3009S–3011S.
9. Nommsen-Rivers LA, Chantry CJ, Peerson JM, et al. Delayed onset of lactogenesis among first-time mothers is related to maternal obesity and factors associated with ineffective breastfeeding. *Am J Clin Nutr* 2010;92:574–584.
10. Brownell E, Howard CR, Lawrence RA, et al. Delayed onset lactogenesis II predicts the cessation of any or exclusive breastfeeding. *J Pediatr* 2012;161:608–614.
11. Russo J RI. Development of the human breast. *Maturitas* 2004;49:2.
12. Cregan MD, De Mello TR, Kershaw D, et al. Initiation of lactation in women after preterm delivery. *Acta Obstet Gynecol Scand* 2002;81:870–877.
13. Lau C, Hurst NM, Smith EO, et al. Ethnic/racial diversity, maternal stress, lactation and very low birthweight infants. *J Perinatol* 2007;27:399–408.
14. Henderson JJ, Hartmann PE, Newnham JP, et al. Effect of preterm birth and antenatal corticosteroid treatment on lactogenesis II in women. *Pediatrics* 2008;121:e92–e100.
15. Parker LA, Sullivan S, Krueger C, et al. Effect of early breast milk expression on milk volume and timing of lactogenesis stage II among mothers of very low birth weight infants: A pilot study. *J Perinatol* 2012;32:205–209.
16. Hill PD, Aldag JC, Chatterton RT, et al. Comparison of milk output between mothers of preterm and term infants: The first 6 weeks after birth. *J Hum Lact* 2005;21:22–30.
17. Hoban R, Bigger H, Patel AL, et al. Goals for human milk feeding in mothers of very low birth weight infants: How do goals change and are they achieved during the NICU hospitalization? *Breastfeed Med* 2015;10:305–311.
18. Jones KM, Power ML, Queenan JT, et al. Racial and ethnic disparities in breastfeeding. *Breastfeed Med* 2015;10:186–196.
19. Center for Disease Control, Division of Nutrition, Physical Activity, and Obesity. Defining adult overweight and obesity. CDC Division of Nutrition, Physical Activity, and Obesity Home: Overweight and Obesity: Adult Overweight and Obesity. www.cdc.gov/obesity/adult/defining.html (accessed March 30, 2016). Updated 2012.
20. Seaman SR, White IR. Review of inverse probability weighting for dealing with missing data. *Stat Methods Med Res* 2011;22:278—295.
21. Parker LA, Sullivan S, Krueger C, et al. Association of timing of initiation of breastmilk expression on milk volume

and timing of lactogenesis stage II among mothers of very low-birth-weight infants. *Breastfeed Med* 2015;10:84–91.
22. Lussier MM, Brownell EA, Proulx TA, et al. Daily breastmilk volume in mothers of very low birth weight neonates: A repeated-measures randomized trial of hand expression versus electric breast pump expression. *Breastfeed Med* 2015;10:312–317.
23. Murase M, Nommsen-Rivers L, Morrow AL, et al. Predictors of low milk volume among mothers who delivered preterm. *J Hum Lact* 2014;30:425–435.
24. Chapman DJ, Perez-Escamilla R. Does delayed perception of the onset of lactation shorten breastfeeding duration? *J Hum Lact* 1999;15:107–111; quiz 137–139.
25. Lorthe E, Quere M, Sentilhes L, et al. Incidence and risk factors of caesarean section in preterm breech births: A population-based cohort study. *Eur J Obstet Gynecol Reprod Biol* 2017;212:37–43.
26. McClelland S, Gorfinkle N, Arslan AA, et al. Factors associated with cesarean delivery rates: A single-institution experience. *Matern Health Neonatol Perinatol* 2017;3:8.
27. Kääpä P, Koistinen E. Maternal and neonatal C-reactive protein after interventions during delivery. *Acta Obstet Gynecol Scand* 1993;72:543–546.
28. Kim CJ, Romero R, Chaemsaithong P, et al. Acute chorioamnionitis and funisitis: Definition, pathologic features, and clinical significance. *Am J Obstet Gynecol* 2015;213(4 Suppl):S29–S52.
29. Nadeau-Vallee M, Boudreault A, Leimert K, et al. Uterotonic neuromedin U receptor 2 and its ligands are upregulated by inflammation in mice and humans, and elicit preterm birth. *Biol Reprod* 2016;95:72.
30. Nguyen DD, Neville MC. Tight junction regulation in the mammary gland. *J Mammary Gland Biol Neoplasia* 1998; 3:233–246.
31. Symons DB, Wright LJ. Changes in bovine mammary gland permeability after intramammary exotoxin infusion. *J Comp Pathol* 1974;84:9–17.
32. Kester HJ, Sorter DE, Hogan JS. Activity and milk compositional changes following experimentally induced streptococcus uberis bovine mastitis. *J Dairy Sci* 2015;98: 999–1004.
33. Kobayashi K, Kuki C, Oyama S, et al. Pro-inflammatory cytokine TNF-α is a key inhibitory factor for lactose synthesis pathway in lactating mammary epithelial cells. *Exp Cell Res* 2016;340:295–304.
34. Meier PP, Engstrom JL, Rossman B. Breastfeeding peer counselors as direct lactation care providers in the neonatal intensive care unit. *J Hum Lact* 2013;29:313–322.
35. Meier PP, Engstrom JL, Hurst NM, et al. A comparison of the efficiency, efficacy, comfort, and convenience of two hospital-grade electric breast pumps for mothers of very low birthweight infants. *Breastfeed Med* 2008;3:141–150.
36. Hurst NM, Valentine CJ, Renfro L, et al. Skin-to-skin holding in the neonatal intensive care unit influences maternal milk volume. *J Perinatol* 1997;17:213–217.
37. Omarsdottir S, Adling A, Bonamy AKE, et al. Predictors of sustained maternal milk feeds in extremely preterm infants. *J Perinatol* 2015;35:367–372.
38. Pineda RG. Predictors of breastfeeding and breastmilk feeding among very low birth weight infants. *Breastfeed Med* 2011;6:15–19.
39. Dutta S, Singh B, Chessell L, et al. Guidelines for feeding very low birth weight infants. *Nutrients* 2015;7:423–442.
40. Hartmann P, Cregan M. Lactogenesis and the effects of insulin-dependent diabetes mellitus and prematurity. *J Nutr* 2001;131:3016S–3020S.

Address correspondence to:
Rebecca Hoban, MD, MPH
Division of Neonatology
Department of Paediatrics
The Hospital for Sick Children
555 University Avenue
Toronto, ON M5G 1X8
Canada

E-mail: rebecca.hoban@sickkids.ca