Early Pumping Behaviors Predict Pumped Milk Volume, Achievement of Secretory Activation and Coming to Volume in Breast Pump-Dependent Mothers of Preterm Infants

Clarisa Median-Poeliniz
`Clarisa_MedinaPoeliniz@rush.edu`

Rush University Medical Center https://orcid.org/0000-0002-6593-0458
Rebecca Hoban
Seattle Children's Hospital https://orcid.org/0000-0001-9457-8791
Marisa Signorile
University Health Network
Judy Janes
Steve Fan
Ted Rogers Computational Program, Peter Munk Cardiac Centre
Paula P. Meier
Rush University

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Abstract

Objective: Pumping studies in mothers of preterm infants are limited by self-reported pumping behaviors and non-objective measures of pumped milk volume and secretory activation (SA). Study Design: Non-randomized observational study of first 14 days postpartum in 29 mothers of preterm infants. Smart pumps measured and stored pumping behaviors and pumped milk volume. Selective ion electrodes measured sodium and sodium:potassium ratio to determine SA. Generalized estimating equations, cluster analyses and multivariate regression were used. Results: SA was delayed (median 5.8 days) and impermanent. Each additional daily pumping increased odds of SA within 2 days by 48% (p=.01). High-intensity pumping mothers (N=17) had greater daily and cumulative pumped milk volume than low-intensity pumping mothers (N=12). Pumping variables showed daily changes in the first week, then plateaued. Conclusion: The first week postpartum is critical for optimizing pumping behaviors. Accurate, objective measures of pumping behaviors, pumped milk volume and SA are a research priority.

Introduction

Mothers of preterm infants cared for in the neonatal intensive care unit (NICU) initiate lactation and provide mothers' own milk (MOM) at rates that approach or exceed those for healthy populations.[1] However, these high rates are not sustained through to NICU discharge, with insufficient MOM volume cited as a primary reason.[1] Lack of MOM at NICU discharge deprives preterm infants of critical nutritional and bioactive components in MOM, including neuroprotective, immunomodulatory and metabolic programming mechanisms that are associated with high-dose, long-duration MOM feedings.[2] High-dose pasteurized donor human milk (PDHM) is an inferior substitute, so understanding the origins of insufficient MOM is a research priority.[3]

Insufficient MOM volume in this population can often be traced to the first 14 days postpartum, a critical timeframe that includes the achievement of secretory activation (SA*; lactogenesis II, milk coming in*) and coming to volume (CTV; 500 mL/day of pumped MOM), both of which predict MOM feedings at NICU discharge in very low birthweight (VLBW; <1500 grams birthweight) preterm infants.[4-7] There is strong evidence that the mammary gland undergoes programming during this early post-birth window, during which interventions to optimize long-term MOM volume may be most effective.[8,9] However, preterm infants require only small MOM volumes during feed advancement, so insufficient MOM often goes undetected until later in the NICU hospitalization. The same MOM volume that allowed exclusive MOM feedings during the first two weeks post-birth—often as little as 150 mL/day--becomes insufficient MOM volume later as infants' feeding requirements increase, making it appear that the problem occurs later in the NICU hospitalization than it actually does.

A universal unmodifiable risk factor in mothers of preterm infants is breast pump-dependency, meaning that the pump completely replaces the breastfeeding infant for MOM removal and the regulation of lactation processes.[9] In healthy breastfeeding dyads, effective, efficient and frequent MOM removal by infant stimulates suckling-induced prolactin release and the personalization of autocrine/paracrine mechanisms that control MOM *supply and demand*.[9] However, in breast pump-dependency, *maternal pumping behaviors* are clinically unlinked from infant feeding "demands" and are entirely reliant on mothers who often are sick themselves and overwhelmed with the NICU admission. Nonetheless, these maternal pumping behaviors*,* including frequency of daily pumping sessions, total daily minutes spent pumping, and inter-pump intervals have been associated with achievement of SA and CTV and represent an opportunity for intervention.[4-7] However, our understanding of maternal pumping behaviors from previous studies is limited by the use of maternal self-report via milk diaries or logs, which are known to be subjective, incomplete, and often inaccurate, especially during the very early post-birth period. [5,6]

The purpose of this study was to leverage innovative breast pump technology to characterize the relationship between maternal pumping behaviors and lactation outcomes including achievement of SA and CTV in mothers of preterm infants <34 weeks of gestation admitted to the NICU. Specifically, we sought to measure three pumping behaviors (number of pumping sessions, minutes spent pumping and longest interval between pumping sessions) each day during postpartum days 1 to 14, and to determine their relationships to the achievement of SA (measured with MOM biomarkers of sodium [Na] and sodium-to-potassium [Na-to-K] ratios; Na:K) and CTV as well as daily and cumulative pumped MOM volume.

METHODS

Design and Setting

This was a non-randomized observational study for which serial data were collected daily between postpartum days 1 and 14 for breast pump-dependent mothers of preterm infants (<34 weeks of gestation) cared for in the Rush University Medical Center NICU between October 2019 and October 2020. Researchers who measured outcome variables (pumped MOM volume, MOM biomarkers) were blinded to maternal pumping behaviors. All mothers received personalized lactation care, including breast pump type recommendations and usage instructions as previously detailed by this team.[4,6,10,11]

Standard clinical practice also included access to NICU-based breastfeeding peer counselors who proactively attempt to speak to mothers daily during the first 14 postpartum days.[11]

Subjects

Maternal and infant inclusion criteria were: infant gestational age <34 weeks; anticipated NICU hospitalization ≥14 days; maternal decision to provide MOM; no use of hormonal contraception or galactagogues; English- or Spanish- speaking; singleton infant without severe medical complications or congenital anomalies. Mothers who met inclusion criteria were invited to participate either antepartum or postpartum, depending upon clinical status. Of the 51 mothers approached, 35 were enrolled. Three were made ineligible after enrollment and complete data were available for 29 (Figure 1). The institutional review board at Rush University Medical Center approved this study.

Measures

Maternal and infant characteristics. Maternal and infant characteristics were extracted from the electronic medical record and included maternal gravida and para status, birth mode, antepartum and intrapartum medical complications, and pre-pregnancy height and weight. Infant characteristics included birth weight, gestational age at delivery, and sex. Questionnaires described in prior published research by this team were used to collect demographic information such as maternal race (non-Hispanic black, non-Hispanic white, Hispanic, Asian), age, education, and low-income status (yes/no for maternal eligibility for Special Supplemental Nutrition Program for Women, Infants, and Children [WIC]), as well as mothers' self-reported medical and lactation histories.[4,6]

Pumping behaviors: Pumping behaviors were recorded and stored electronically using an innovative adaptation of the Medela Symphony Breast Pump (Smart Pump, Medela AG, Switzerland) (Supplementary Figure 1). This adaptation consisted of a novel software program incorporating digital hardware that captured and recorded each daily pumping session and minutes pumped per session as well as pumping pressures, changes in pumping pressures and type of breast pump suction pattern. These data were stored on encrypted password protected computer USB flash drives until the study's end for each mother, at which time they were downloaded into a customized computer software program compatible with Microsoft Excel. To ensure that all pumping behaviors were measured, each mother had a total of 3 Smart Pumps assigned and programmed with her study ID for the 14-day study period: one each for the mother-baby unit hospitalization, the NICU, and in-home use. The Smart Pump recorded pumping behaviors beginning at 0000 AM and ending at 1159 PM. The following variables were calculated from Smart Pump data: daily and cumulative minutes spent pumping, number of pumping sessions and inter-pump intervals (time between the end of one pumping session and the end of the next).

Pumped MOM volume: Pumped MOM volume was measured (nearest 0.1 g) for each breast separately for each pumping session during the 14-day study using a customized software application and hardware in the SMART Pump (Supplemental Figure 1). After pumping, the mother placed the filled MOM container on the integrated scale and was prompted to enter right or left breast and the container size (11 mL, 30 mL, 60 mL, 240 mL) being weighed. The Digital Interface Screen was configured to subtract the container weight from the measured MOM weight, using container weight data previously collected by this research team.[4] All auto-recorded data were stored in the Data Logger integrated in the SMART Pump. These data were used to measure daily and cumulative pumped MOM volume (mL) as well as achievement of CTV. Achievement of CTV (yes/no) was defined as having at least one daily (24-hour period) pumped MOM volume ≥500 mL by postpartum day 14.

MOM biomarkers of SA: Daily MOM samples (1.0 mL each) were collected on postpartum days 1-14 and stored at -20^0 C until Na and K concentrations were measured in duplicate using selective ion electrodes (Horiba; Japan), as described by this team and others.[4,6,12-14] Na and K concentrations were measured in parts per million, then subsequently divided by the molecular weights for Na (22.9 g/mMol) and K (39.0 g/mMol).

Daily MOM biomarkers were used to calculate daily values for Na and Na:K ratio, daily rates of change in Na and Na:K ratio, *achievement of SA* (yes/no; defined as Na £16 mMol and/or Na:K ratio <0.8), and reversal of SA, defined as having at least 1 daily MOM sample with Na >16 mMol and/or Na:K ratio >0.8 on a day after achievement of SA.

Data Analysis

All statistical analyses assumed a significance level of 5% and were conducted using R v4.0.3.[15] Sample characteristics were summarized with descriptive statistics. Continuous data were expressed as mean +/- SD. Between-group differences were assessed using Fisher's exact tests for categorical variables and *t*-tests or the Mann–Whitney U test, as appropriate, for continuous variables. Generalized estimating equations (GEE) with an independent working correlation matrix were employed to predict achievement of: 1) SA in the next 2 days as a function of pumping behaviors, and 2) CTV in the next 2 days as a function of Na concentration.[16] Coefficients with the corresponding 95% CIs and p values were estimated from the robust sandwich variance estimator. Next, we applied a cluster analysis to the three longitudinal pumping variables (number of daily pump sessions, number of daily minutes spent pumping and longest inter-pump interval) to identify mother subpopulations. The Calinski-Harabasz criterionwas used to identify the optimal number of clusters for the k-means algorithm, with higher Calinski-Harabasz values indicating well-separated clusters.[17] The resulting two clusters were used to compare pumping behaviours, biomarkers of SA, and daily volume of pumped milk, using linear mixed effects models with random patient-specific intercepts. Differences in the time profiles of the variables were compared using F-tests. Finally, we explored the association between 2 separate pumping behaviors, namely, above average number of daily pumping sessions (>4) and above average number of daily minutes pumped (>75) with common maternal co-morbidities (prepregnancy BMI >30, delivery blood loss >500 mL, preeclampsia (yes/no) and diabetes (yes/no) using multivariable logistic regression.

Results

Characteristics of Mothers and Infants

Maternal-infant characteristics are summarized in Table 1. The sample was predominantly Black race (52%), delivered by Cesarean section (59%), and reported a mean of 3 co-morbidities per subject. Common co-morbidities included pre-eclampsia (41%), infection (31%), excessive blood loss (24%) gestational diabetes (21%) and psychiatric diagnoses (21%). Of the 29 mothers, 55% had a BMI > 30, and 66% had intrapartum/postpartum blood loss > 500 mL

Changes in Pumping Behaviors, MOM Volume and MOM Biomarkers for Postpartum Days 1–14

Figures 2 and 3 depict time-dependent changes in pumping behaviors, pumped MOM volume and MOM biomarkers between birth and postpartum day 14 for the 29 mothers. The data reveal statistically significant changes in daily pumping behaviors for postpartum days 1–5, plateauing thereafter. Daily *rates of change* (mean incremental increase or decrease from previous day) in pumping behaviors were significantly different for days 1–5 versus days 6–14 as follows: total minutes spent pumping (16.4 minutes ± 8.5 vs 0.49 minutes ± 5.55), number of pumping sessions (0.8 times ± 0.5 vs 0.015 times ± 0.21) and the longest inter-pump interval (0.61 hours ± 0.85 vs 0.01 hours ± 0.22). Daily rate of change in pumped MOM volume increased from postpartum day 1 to 8, with little change between postpartum days 9–14 (47.29 mL ± 41.41 vs -9.57 mL ± 45.14, respectively). Statistically significant daily rates of decrease in Na concentration and the Na:K ratio occurred between days 1–8, with minimal change between days 9–14 (Na: -1.02 mMol ± 1.49 vs 0.07 mMol ± 0.53; Na:K: -0.04 ± 0.17 vs 0.01 ± 0.04).

Relationship between Pumping Behaviors and Achievement of SA and CTV.

Achievement of SA was documented in 27 of the 29 mothers, occurring at a median of 5.8 days [4.30, 8.23] postpartum. None of the mothers achieved SA prior to postpartum day 4. Each additional daily pumping session increased the odds of achieving SA within the next 2 days by 48% ($p = .01$). In contrast, neither total daily minutes spent pumping (OR 1.00 [0.69, 1.46], $p = .85$) nor longest inter-pump interval (OR 0.99 [0.87, 1.13], $p = .89$.) was associated with achievement of SA. Of the 27 mothers who achieved SA, 14 (42.4%) reversed SA at least once in the 14-day period. Of these 14 mothers, 4 re-achieved and subsequently maintained SA for the remainder of the study. Of the remaining 10 mothers, 4 never achieved SA again and 6 fluctuated between achievement and non-achievement of SA for the remainder of the study. Of the 29 mothers, 13 achieved CTV. Higher Na concentrations reduced the odds of achieving CTV, with each 1 mMol increase in Na reducing the odds of CTV within the next 2 days by 18% (OR 0.82 [0.70, 0.97], $p = .02$).

Cluster Analysis: High Intensity Versus Low Intensity Pumping Groups

For our data, the Calinski-Harabasz criterion[17] for 2, 3, and 4 clusters were 13.13, 9.50, and 7.64 respectively. Having also considered the limited sample size, we used two clusters for this analysis: high intensity (HIPG; N = 17) and low intensity (LIPG; N = 12) pumping groups (Fig. 4). Compared to mothers in the LIPG, HIPG mothers pumped more frequently per day (5 ± 2 times vs 2 ± 2 times, $p < .001$), for more total minutes per day (105 ± 53 minutes vs 46 ± 31 minutes, p < .001) and with shorter daily inter-pump intervals (5.5 ± 1.7 hours vs 7.5 ± 3.2 hours per day, p < .001). For both groups, these pumping behaviors showed increasing rates of change between postpartum days 1 and 5, followed by a plateau from days 5 through 14. Table 2 shows that the two groups of mothers were statistically similar with the exception that HIPG mothers were older and had longer previous breastfeeding/MOM provision experiences than

LIPG mothers. Although the incidence of co-morbidities was not significantly different between the two groups, the HIPG had higher proportions of mothers with diabetes, PCOS, hemorrhage, blood transfusions, and psychiatric diagnoses. In contrast, the LIPG had a slightly greater proportion of mothers with pre-eclampsia.

Differences in Pumped MOM Volume, Achievement of SA and CTV for HIPG and LIPG Groups

Figure 5 demonstrates that HIPG mothers had significantly greater mean daily pumped MOM volume over the 14-day study period. For both groups, pumped MOM volume increased between postpartum days 1 and 8, thereafter plateauing in the HIPG and decreasing in the LIPG. The 14-day cumulative mean pumped MOM volumes for the HIPG and LIPG were 4,769 ± 3,154 mL and 2,582 ± 1,492 mL, respectively (*p* = .02). While daily Na concentration and Na:K was higher in LIPG than HIPG consistently (*p* = .07 for Na; 0.39 for Na:K), the differences did not warrant statistical significance most likely due to limited sample size. All mothers in the HIPG achieved SA, whereas 10 of 12 mothers (83%) in the LIPG achieved SA *(p* = .16). Of the 17 mothers in the HIPG, 9 (53%) achieved CTV, whereas 4 of 12 mothers (33%) in the LIPG achieved CTV (*p* = .45).

Impact of Maternal Co-Morbidities on Pumping Behaviors

Mothers with pre-eclampsia were significantly less likely to pump > 75 minutes per day (OR 0.651, *p* = 0.05) and > 4 times daily (OR 0.591, *p* = 0.017) than mothers without pre-eclampsia. In contrast, maternal diabetes was significantly associated with > 75 daily minutes of pumping (OR = 1.79, p = 0.04), whereas BMI > 30 (OR = 1.25, *p* = 0.38) and blood loss > 500 mL (OR = 1.36, *p* = 0.24) were not significantly associated with either daily pumping frequency or daily pumping minutes.

Discussion

To our knowledge this is the first study to describe the relationship between pumping behaviors and lactation outcomes in breast pump-dependent mothers of preterm NICU infants during the early postpartum period using accurate, objective measures. Previous studies have been limited by maternal self-report of pumping behaviors, pumped MOM volume and achievement of SA, data that are often incomplete and inaccurate during this stressful time for NICU mothers.[5,6,18]

Our innovative methods, especially the use of Smart pump technologies and MOM biomarkers of SA, have the potential to advance both practice and research in this field.

For the cohort, time-dependent changes in pumping behaviors and lactation outcomes were confined to the first 5-8 days postpartum, with little variability thereafter. The achievement of SA (median 5.8 days) was delayed when compared to the typical 72 hours postpartum for healthy breastfeeding dyads.[19] Even more concerning is that of the 27/29 mothers who achieved SA, over half reversed it at least once during the 14-day study. Our cluster analysis clearly differentiated HIPG and LIPG by pumping behaviors. HIPG mothers had greater daily pumped MOM volume, greater cumulative pumped MOM volume, and were more likely to achieve SA and CTV than LIPG mothers, demonstrating the critical role of early and frequent pumping in the first postpartum days. Additionally, mothers with pre-eclampsia pumped significantly less frequently than did mothers without pre-eclampsia, but this was not the case with other morbidities, begging the question as to whether this outcome is modifiable with targeted interventions for this group of mothers. These findings have multiple actionable implications for practice and research.

Pumping Behaviors

Recommendations for daily pumping frequency, minutes and inter-pump intervals for breast pump-dependent mothers of NICU infants during the early days postpartum have historically been based on behaviors for healthy breastfeeding dyads.[9] These behaviors consist of early, frequent breastfeeds with minimal MOM intake, and the use of a uniquely human sucking pattern prior to achievement of SA.[9,20-23] These feeding behaviors are thought to have a programming role in the regulation of subsequent lactation processes, including increases in the number of secretory cells and prolactin receptors in the mammary gland.[8,24] Based on these studies, mothers of preterm NICU infants have been instructed to pump every 2-3 hours or 8-12 daily prior to achievement of SA.[1,4,6,12,25] However, we could not locate a study enrolling mothers of preterm NICU infants in which this target was actually achieved by more than a handful of outliers,[24,26] with most studies reporting an average of 4-5 daily pumping sessions during the early postpartum period.[6,24,25,27] Per study methods, these mothers were *educated to pump every 2-3 hours*, but results either fell short of this target or pumping behaviors were not reported.[12,25,27,28] In our study, mothers were educated to pump a minimum of 8 times daily, but our electronically-measured pumping data indicate that 12 of our 29 mothers fell into the LIPG, which on average pumped £4 times and <75 minutes daily. Even mothers in the HIPG did not achieve a mean of 8 pumping sessions daily.

Given the literature in this field, it is clear that most mothers of NICU infants do not or cannot comply with current pumping recommendations during the early postpartum period despite receiving guidance. Both Mago-Shah et al,[25] and Hoban et al.[6] reported that ³5 daily pump sessions during the first 5 postpartum days was highly associated with the achievement of CTV. Thus, research priorities in this field include the development of evidence-based guidelines specific to breast pump-dependent mothers of NICU infants as well as prioritizing the improvement of breast pumps and breast pump suction patterns that optimize efficiency without sacrificing effectiveness of MOM removal.[9] Quality improvement initiatives should target modifiable barriers to pumping frequency, especially lack of ready access to a hospital-grade electric breast pump in the postpartum unit and NICU so that mothers can pump without lengthy delays. Similarly, educational sheets and videos such as that those in the PROVIDE compendium can standardize information for both families and staff about the importance and techniques of early, frequent, effective and efficient pumping behaviors.[29] A “takeaway” talking point from our study is that each additional daily pumping session increases the odds of SA achievement in the next 2 days by almost 50%. This is an actionable message for NICU mothers and staff and should be leveraged in quality improvement initiatives.

Pumping Behaviors, Maternal Co-Morbidities and Achievement of SA and CTV

Mothers who deliver preterm infants are often sick themselves with a multitude of risk factors associated with delayed and/or impaired achievement of SA, as exemplified by the mothers in our study with an average of 3 co-morbidities each. Our finding of delayed and/or impaired achievement of SA in this breast pump-dependent population is consistent with conclusions from a recent integrative review of all previous studies using MOM biomarkers to measure SA.[30] Although the mechanisms for delayed/impaired SA are not well-elucidated, two broad explanations are possible and may be mutually dependent. First, from a biological perspective, early lactation problems in this population may be partially or wholly attributable to disrupted and/or interrupted secretory differentiation.[19,30] Secretory differentiation is incomplete at the time of preterm birth, and several studies suggest disrupted secretory differentiation in the presence of inflammatory processes, such as those due to obesity, pre-eclampsia, diabetes and other metabolic health problems that are common in this population.[7,19,31,32] Secondly, mothers with multiple co-morbidities and their associated treatments may be seen as “too sick to pump” by hospital staff and family members, so are not encouraged or assisted with pumping. Thus, underlying biologic problems may be exacerbated by lack of timely mammary gland stimuli. For example, our mothers with pre-eclampsia pumped significantly less frequently than mothers without pre-eclampsia despite this NICU’s approach of engaging family members to assist with pumping when necessary, such as when mothers are being treated with magnesium. This finding raises the question of whether delayed SA in this population may be partially modifiable with increased pumping frequency and effectiveness. Thus, a research priority is understanding the role of optimal pumping behaviors in partially mitigating the immaturity and metabolic/inflammation-based lactation risk factors common among breast pump-dependent mothers of preterm NICU infants.

The measurement of daily Na and Na:K ratios, compared to the typical one-time measurement in other studies,[30] allowed us to detect the lack of permanence in achievement of SA among breast pump-dependent mothers of preterm NICU infants, previously reported only by Hoban et al.[6]Over half of our sample reversed SA at least once after it had been achieved, indicating a lack of permanence in paracellular pathway closure.[19] In nearly all instances, these reversals were associated with interruptions in daily pumping frequency that are common in NICU mothers. For example, mothers in our study reported several reasons for interrupted pumping frequency including misplaced pump tubing, extended outpatient medical appointments due to maternal co-morbidities, and “deciding that they could stop pumping altogether because they had so much frozen MOM.” The subgroup of mothers who achieved and reversed SA multiple times underscores the importance of serial MOM Na measurements in practice and research.

Rethinking the Critical Window of Postpartum Days 1-14

Our data reveal that changes in pumping behaviors were confined to the first 5-6 postpartum days with little change in pumped MOM volume, Na and Na:K ratio and after postpartum day 8. Similar findings have been reported by Hoban et al,[6] Mago-Shah et al,[25] and Medina-Poeliniz et al,[7] all suggesting that the critical window may be 7 rather than 14 postpartum days as previously thought.[5,8,24] Healthy, exclusively breastfed infants typically consume 500-600 mL of MOM by postpartum days 4-7.[20,21,33,34] Two randomized studies of breast pump-dependent mothers of preterm NICU infants reported similar mean volumes of pumped MOM[12,24] within the first 7 postpartum days in mothers assigned to a specific breast pump[12] or breast pump suction pattern.[24] Thus, rigorous research using accurate measures of pumping behaviors, pumped MOM volume, and achievement of SA and CTV should elucidate whether intense lactation care should target the first 7 versus 14 postpartum days. This information has actionable staff utilization and cost implications so that NICU lactation care can be optimally effective and efficient.

Study Strengths and Limitations

A primary strength of our study is the use of electronically measured and stored pumping behaviors and MOM volumes using Smart pump technology, data that have previously been provided by maternal self-report and which are the most incomplete during the early postpartum period among NICU mothers. Additionally, our daily measures of MOM Na and Na:K ratios provided an accurate measure of achievement of SA as well as allowing us to report the lack of permanence in SA achievement in this population. Although relatively small, our racially and ethnically heterogenous sample is typical of NICU mothers with respect to co-morbidities that can impact lactation outcomes. We surmise that other maternal co-morbidities may be associated with pumping frequency and lactation outcomes, but our sample size did not permit further analysis of the impact of incremental morbidities on these variables.

Summary and Conclusions

Our study underscores the importance of early pumping behaviors for mothers of preterm NICU infants and is consistent with recent studies suggesting that the critical interval for achievement of SA and CTV may be within the first 6-8 days versus the first 14 days postpartum. We found significantly delayed achievement of SA as well as reversal of previously-achieved SA in this sample of breast pump-dependent mothers, an outcome that would not have been noticed without daily Na and/or Na:K ratio data. Our findings have important implications for clinicians and researchers. For clinicians, quality improvement initiatives should target the very early postpartum period with respect to the use of lactation experts, rapid access to high-quality breast pumps, and daily monitoring of achievement of SA and CTV. For researchers, the incorporation of accurate and objective measures of lactation processes and outcomes should be the new standard for methodologies in this field of inquiry.

Declarations

Authors’ Contributions: Conceptualization/design: R.H., C.M.P., P.P.M. Supervision: P.P.M., Data curation: M.S., J.J., C.M.P., C.S.F. Writing of original draft: R.H., C.M.P., P.P.M. Writing, reviewing, and editing: R.H., C.M.P., J.J., M.S., C.S.F., P.P.M. All authors have read and agreed to the published version of the article.

Disclosure of potential conflict of interest:

Dr. Paula Meier serves as a consultant to Medela for educational activities. Dr. Rebecca Hoban holds a position on Medela's scientific advisory board.

References

1. Meier PP, Johnson TJ, Patel AL, Rossman B. Evidence-based methods that promote human milk feeding of preterm infants: An expert review. *Clinics in Perinatology*. 2017;44(1):1.
2. Patel AL, Johnson TJ, Meier PP. Racial and socioeconomic disparities in breast milk feedings in US neonatal intensive care units. *Pediatric Research*. 2020;89(2):344-352.
3. Meier PP. More evidence: Mothers’ own milk is personalized medicine for very low birthweight infants. *Cell Reports Medicine*. 2022;3(8):100710.
4. Hoban R, Patel AL, Medina Poeliniz C, Tat Lai C, Judy JE, Geddes D. et al. Human milk biomarkers of secretory activation in breast pump-dependent mothers of premature infants. *Breastfeeding Medicine*. 2018;13(5):352-360.
5. Hoban R, Bigger H, Schoeny M, Engstrom J, Meier P, Patel AL. Milk volume at 2 weeks predicts mother's own milk feeding at neonatal intensive care unit discharge for very low birthweight infants. *Breastfeeding Medicine*. 2018;13(2):135-141.
6. Hoban R, Medina Poeliniz C, Somerset E, Tat Lai C, Janes JE, Patel AL et al. Mother's own milk biomarkers predict coming to volume in pump-dependent mothers of preterm infants. *The Journal of Pediatrics*. 2021;228:44-52. e3.
7. Medina Poeliniz C, Hoban R, Schoeny EM, Engstrom LJ, Patel LA, Meier PP. Prepregnancy BMI is associated with time-dependent changes in secretory activation measures during the first 7 days postpartum in breast pump-dependent mothers of premature infants. *Breastfeeding Medicine*. 2021;17(2),173-181.
8. Meier PP, Patel AL, Hoban R, Engstrom JL. Which breast pump for which mother: An evidence-based approach to individualizing breast pump technology. *Journal of Perinatology*. 2016;36(7):493-499.
9. Krebs FN, Belfort BM, Meier PP, Mennella JA, O’Connor DL, Taylor SN, et al. Infant factors that impact the ecology of human milk secretion and composition—a report from “Breastmilk ecology: Genesis of infant nutrition (BEGIN)” working group 3. *The American Journal of Clinical Nutrition*. 2023;117(Suppl 1): S43-S60. https://dx.doi.org/10.1016/j.ajcnut.2023.01.021.
10. Meier PP, Patel AL, Bigger HR, Rossman B, Engstrom JL. Supporting breastfeeding in the neonatal intensive care unit: Rush Mother's Milk Club as a case study of evidence-based care. *Pediatric Clinics of North America*. 2013;60(1):209-226.

11. Meier PP, Engstrom JL, Rossman B. Breastfeeding peer counselors as direct lactation care providers in the neonatal intensive care unit. *Journal of Human Lactation*. 2013;29(1):313-322.
12. Yuan S, Li Q, Wang H, Xu X. The utilization of sodium concentration in human milk from pump-dependent mothers of preterm infants as a measure of milk production. *Breastfeeding Medicine*. 2023;18(7):506-513.
13. Esquerra-Zwiers A, Vroom A, Geddes D, Lai CT. Use of a portable point-of-care instrumentation to measure human milk sodium and potassium concentrations. *Breastfeeding Medicine*. 2022:17(1), 46-51.
14. Tat Lai C, Gardner H, Geddes D. Comparison of inductively coupled plasma optical emission spectrometry with an ion selective electrode to determine sodium and potassium levels in human milk. *Nutrients*. 2018;10(9):1218.
15. R Core Team. R: A language and environment for statistical computing. R foundation for statistical computing, 2021.
16. Wei P & Connett JE. Selecting the correlation structure in generalized estimating equations with application to the lunch health study. *Statistica Sinica*. 2002;12:475-490.
17. Caliński T & Harabasz J. A dendrite method for cluster analysis. *Communication in Statistics*. 1974;3(1):1-27.
18. Jegier BJ, Johnson TJ, Engstrom JL, Patel AL, Loera F, Meier PP. The institutional cost of acquiring 100 mL of human milk for very low birth weight infants in the neonatal intensive care unit. *Journal of Human Lactation*. 2013;29(3):390-399.
19. Medina Poeliniz C, Engstrom JL, Hoban R, Patel AL, Meier PP. Measures of secretory activation for research and practice: An integrative review. 2020;15(4):191-212.
20. Neville MC, Keller R, Seacat J, Lutes V, Neifert M, Casey C. et al. Studies in human lactation: Milk volumes in lactating women during the onset of lactation and full lactation. *The American Journal of Clinical Nutrition*. 1988;48(6):1375-1386.
21. Casey CE, Neifert MR, Seacat JM, Neville MC. Nutrient intake by breast-fed infants during the first five days after birth. *American Journal of Diseases of Children*. 1986;140(9):933-936.
22. Saint L, Smith M, Hartmann PE. The yield and nutrient content of colostrum and milk of women from giving birth to 1 month post-partum. *British Journal of Nutrition*. 1984;52(1):87-95.
23. Santoro W, Martinez FE, Ricco GR, Jorge SM. Colostrum ingested during the first day of life by exclusively breastfed healthy newborn infants. *Journal of Pediatrics, The*. 2010;156(1):29-32.
24. Meier PP, Engstrom JL, Janes JE, Jegier BJ, Loera F. 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. *Journal of Perinatology*. 2012;32(2):103-110.
25. Mago-Shah DD, Athavale K, Fisher K et al. Early pumping frequency and coming to volume for mother's own milk feeding in hospitalized infants. *Journal of perinatology*. 2023;43(5):629-634.

26. Meier PP, Engstrom JL, Hurst NM, Ackerman B, Allen M, Motykowski JE, 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. *Breastfeeding Medicine*. 2008;3(3):141-150.
27. Parker LA, Sullivan S, Cacho N, Engelmann C, Krueger C, Mueller M. Indicators of secretory activation in mothers of preterm very low birth weight infants. *Journal of Human Lactation*. 2021;37(3):581-592.
28. Bendixen MM, Weaver MT, Parker LA. Milk volume outcomes in pump-dependent mothers of critically ill infants. *Advances in Neonatal Care*. 2022;22(3):253-260.
29. Meier PP. PROVIDE: A training compendium on providing mothers’ own milk in NICU settings the global health network: LactaHub. Accessed September 5, 2023. https://Lactahub.org/nicu-training.
30. Parker LA, Hoban R, Bendixen MM et al. Milk biomarkers of secretory activation in breast pump-dependent mothers of preterm infants: An integrative review. *Breastfeeding Medicine*. (in press).
31. Nommsen-Rivers LA, Wagner EA, Roznowski DM, Riddle SW, Ward LP, Thompson A. Measures of maternal metabolic health as predictors of severely low milk production. *Breastfeeding Medicine*. 2022;17(7):566-576.
32. Lee S & Kelleher SL. Biological underpinnings of breastfeeding challenges: The role of genetics, diet, and environment on lactation physiology. *American Journal of Physiology: Endocrinology and Metabolism*. 2016;311(2): E405-E422.
33. Ingram JC, Woolridge MW, Greenwood RJ, et al. Maternal predictors of early breast milk output. *Acta Paediatrica*. 1999;88(5):493-499.
34. Chen DC, Nommsen-Rivers LA, Dewey KG, Lonnerdal B. Stress during labor and delivery and early lactation performance. *The American Journal of Clinical Nutrition*. 1998;68(2):335-44.

Tables

Tables 1 to 2 are available in the Supplementary Files section

Figures

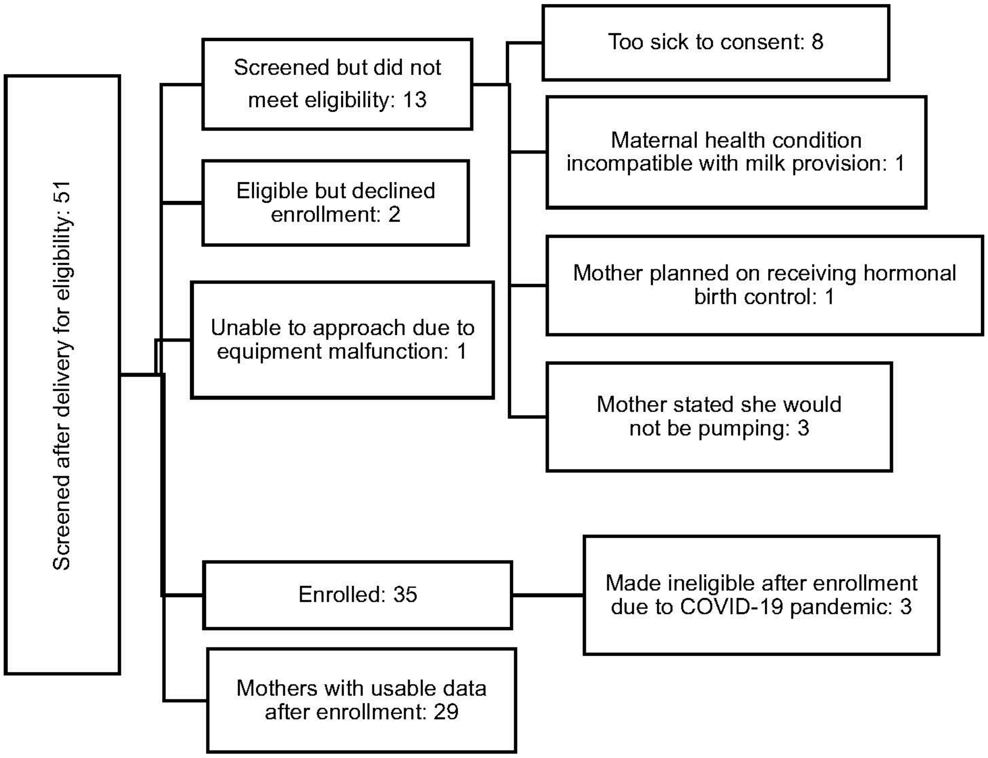


Figure 1: Study enrollment flowchart

Figure 1

See image above for figure legend.

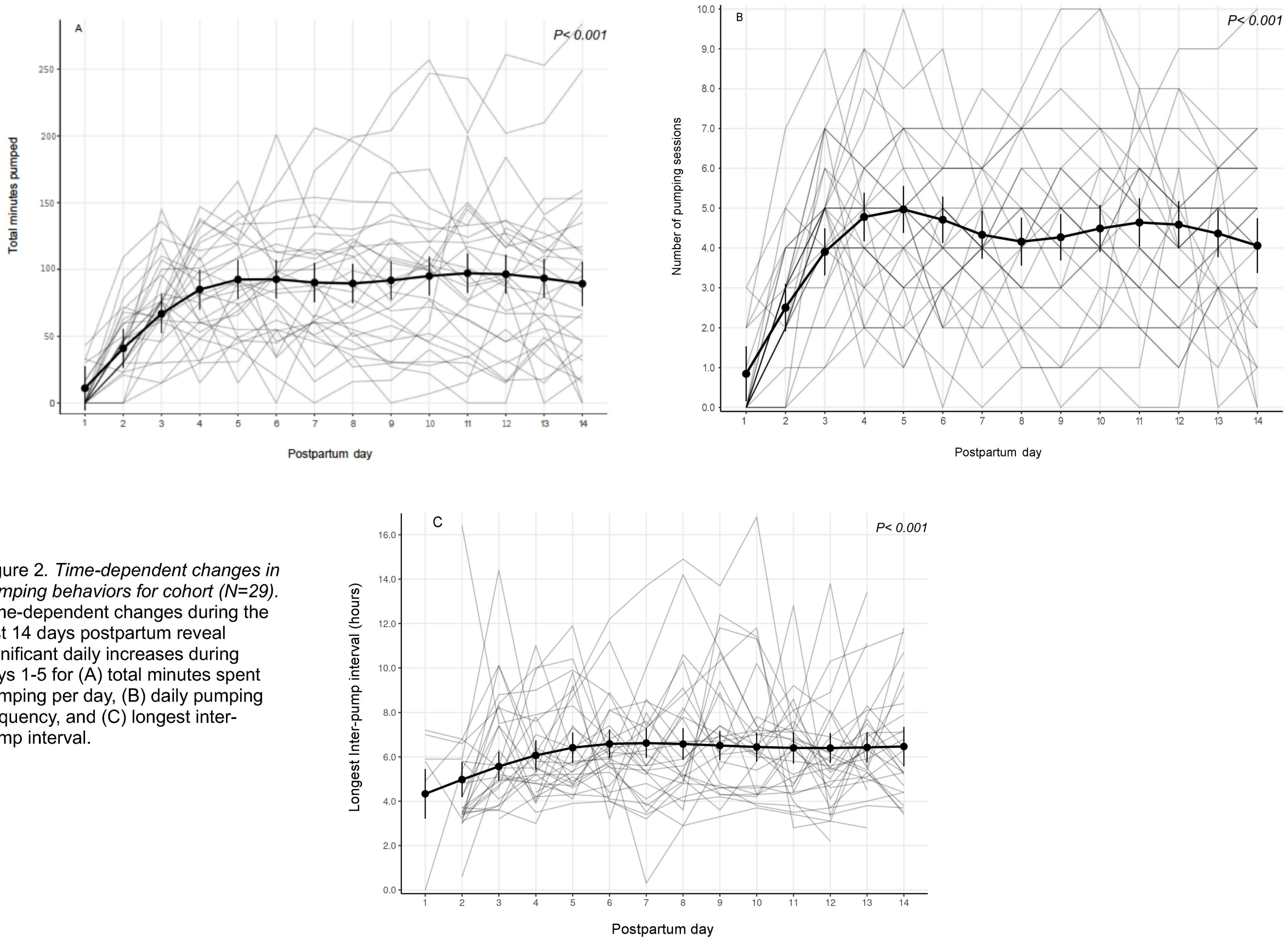
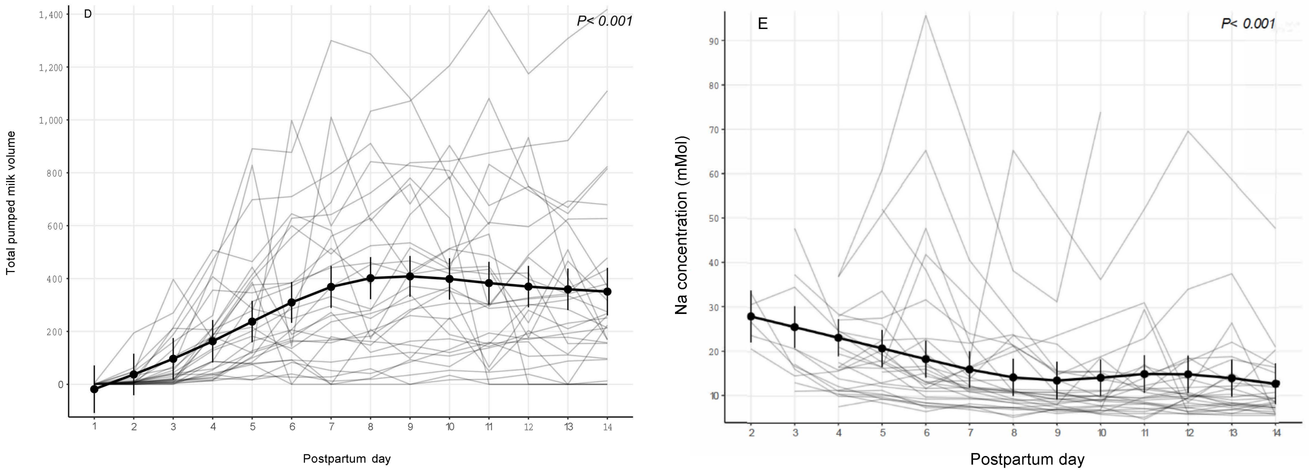


Figure 2*. Time-dependent changes in pumping behaviors for cohort (N=29).* Time-dependent changes during the first 14 days postpartum reveal significant daily increases during days 1-5 for (A) total minutes spent pumping per day, (B) daily pumping frequency, and (C) longest inter-pump interval.

Figure 2

See image above for figure legend.



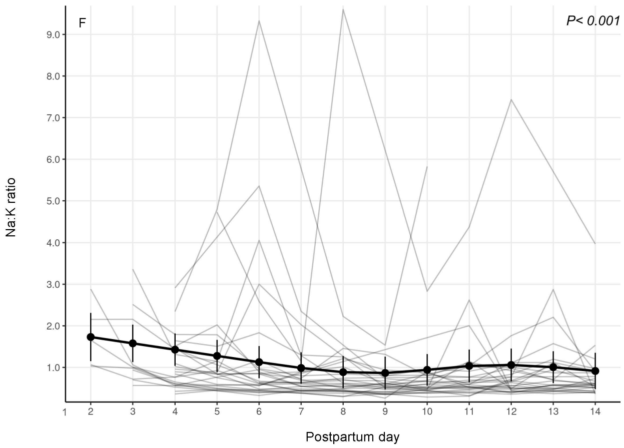


Figure 3. *Time-dependent changes in pumped milk volume, Na, and Na:K ratio for cohort (N=29).* Time-dependent changes during the first 14 days postpartum reveal significant change between days 1-8 and minimal change days 9-14 for (D) total pumped milk volume; (E) Na concentration, and (F) Na:K ratio.

Figure 3

See image above for figure legend.

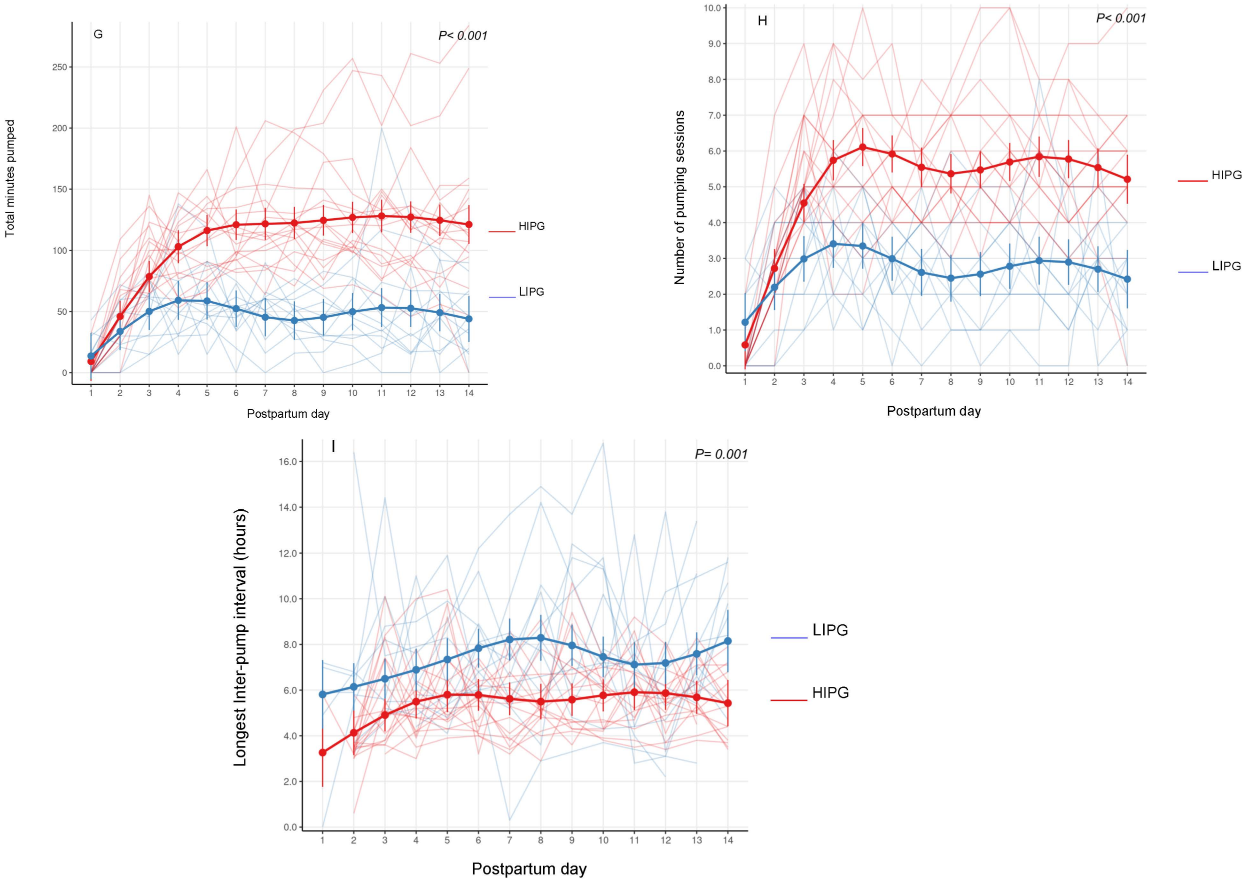


Figure 4. *Time-dependent differences in pumping behaviors for HIPG (N=17) and LIPG (N-12).* HIPG cluster (in red) had significantly G) greater total minutes pumped and H) greater number of pumping sessions than LIPG cluster (in blue). LIPG cluster had significantly longer inter-pump intervals than HIPG cluster.

Figure 4

See image above for figure legend.

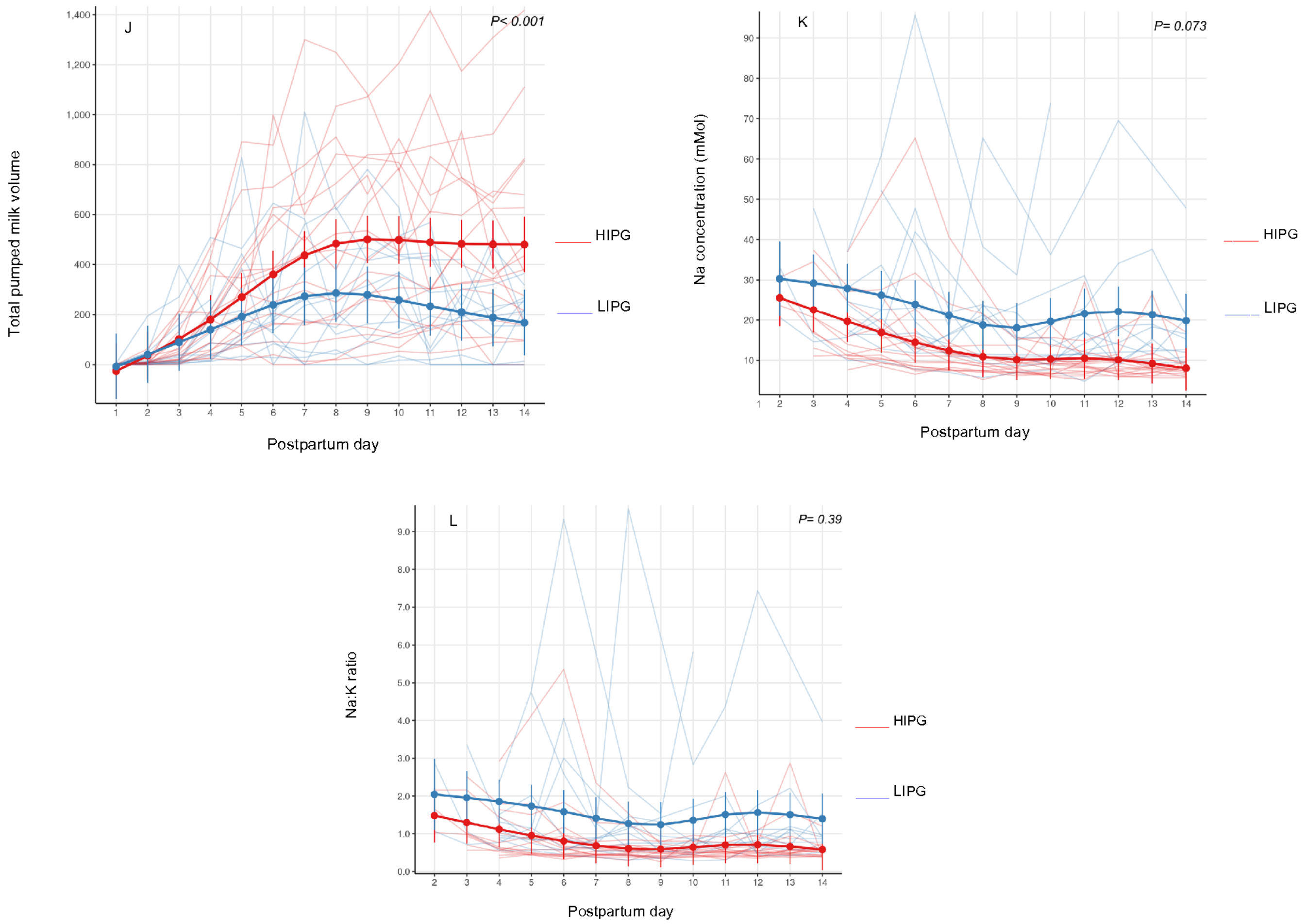


Figure 5

Time-dependent differences in pumped milk volume, Na concentration, and Na:K ratio for HIPG and LIPG. HIPG cluster (in red) had significantly G) greater total minutes pumped and H) greater number of pumping sessions than LIPG cluster (in blue). LIPG cluster had significantly longer inter-pump intervals than HIPG cluster.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementalFigure112292023.pdf
- Finaltable11229.jpg
- Finaltable21229.jpg