PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Associations between use of expressed human milk at two weeks postpartum and human milk feeding practices to six months: a prospective cohort study with vulnerable women in Toronto, Canada
AUTHORS	Mildon, Alison; Francis, Jane; Stewart, Stacia; Underhill, Bronwyn; Ng, Yi Man; Rousseau, Christina; Di Ruggiero, Erica; Dennis, CindyLee; Kiss, Alex; O'Connor, Deborah L; Sellen, Daniel

VERSION 1 – REVIEW

REVIEWER	Agakidou, Eleni Ippokration General Hospital, 1st Dept of Neonatology and NICU
REVIEW RETURNED	15-Oct-2021

GENERAL COMMENTS	REVIEWER's COMMENTS In this study the potential association between the use of expressed mother's milk at 2 weeks postpartum for feeding term (or near term infants?) with cessation of human milk (HM) feeding and non-exclusive HM feeding up to six months was examined. It was found that any use of expressed HM feeding at 2 weeks of age was associated with cessation of HM feeding before the age six months and with non-exclusive HM feeding at four and six months of age. Several previous studies with the same or similar subject have reached to similar conclusions. The results are well presented and support the discussion and conclusions. English is good as is the statistical analysis. There are certain limitations of the study, which have been addressed and adequately commented by the authors in the limitation section. However, there are concerns regarding the study population, as commented below. Major comments 1. There are certain problems with the population recruited. a. The population recruited must be clearly defined. Specifically, regarding the population of the study B, I wonder whether the pre-intervention mothers were actually eligible for the study. On page 5 (or 8/29), lines 3-5, it is stated "Study B was a pre/post intervention study designed to examine the effectiveness of implementing similar lactation support services in two other CPNP sites.[19]", while on page 5 (or 8/29) lines 28-30 it is stated that "All participants in Study A and those recruited to the post-intervention group in Study B had access to two free, in-home visits …." These data leads to the assumption that the population included in the part 2 was not the whole population of Study B (including pre- and post-intervention mothers) but only the post-intervention population of study B. This issue must be clarified.

	b. Although the authors stated, page 4 (or 7/29) line 10, that "mothers with term-born infants were recruited", the description of study participants in the method section implies recruitment of mothers giving birth to preterm infants as well. Specifically, for Study A, it is stated that "Study A was a prospective cohort study of infant feeding practices among clients of a CPNP site offering skilled postnatal lactation support …". This statement implies that all mothers registered to the CPNP were eligible regardless of the gestational age at birth. In addition, for Study B, it is stated that "Exclusion criteria for Study B were preterm birth (<34 weeks gestation), …" showing that, apart from term infants, late preterm infants were included as well. Given that prematurity is an important factor associated with feeding difficulties, thereby affecting the way of feeding, the gestational age should be presented and should be included in the regression analysis models as an exposure variable (confounding factor). Moreover, the statement in the introduction "mothers with term-born infants were recruited" must be modified appropriately. 2. Calculation of the sample size is not presented in the submitted manuscript. Although the sample size calculation is presented in a previous publication regarding the study protocol (see reference #19), it should be mentioned in the current study as well.

REVIEWER	Giannì, Maria Lorella Fondazione IRCCS Cà Granda, Study University of Milan, Department of Clinical Sciences and Community Health
REVIEW RETURNED	24-Oct-2021

GENERAL COMMENTS	The Authors aimed to investigate wether the early use of expressed milk is associated with early breastfeeding cessation. The paper is interesting. However, It is not clear to me which criteria the women were supposed to meet in order to be enrolled in the studies and be defined "vulnerable". Please, clarify this very important point. Moreover, I would suggest to discuss how the present results compare with those relating to non vulnerable women. How do the breastfeeding rates at six months and the use of expressed milk compare with other countries or different social contexts? In my opinion, this would strengthens the results of the study and the potential clinical implication in terms of optimization of breastfeeding suppor.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Dr. Eleni Agakidou, Ippokration General Hospital
Comments to the Author:
REVIEWER's COMMENTS

In this study the potential association between the use of expressed mother's milk at 2 weeks postpartum for feeding term (or near term infants?) with cessation of human milk (HM) feeding and non-exclusive HM feeding up to six months was examined. It was found that any use of expressed HM feeding at 2 weeks of age was associated with cessation of HM feeding before the age six months and with non-exclusive HM feeding at four and six months of age. Several previous studies

with the same or similar subject have reached to similar conclusions.
The results are well presented and support the discussion and conclusions. English is good as is the statistical analysis. There are certain limitations of the study, which have been addressed and adequately commented by the authors in the limitation section. However, there are concerns regarding the study population, as commented below.
Major comments
1. There are certain problems with the population recruited.
a. The population recruited must be clearly defined. Specifically, regarding the population of the study B, I wonder whether the pre-intervention mothers were actually eligible for the study. On page 5 (or 8/29), lines 3-5, it is stated "Study B was a pre/post intervention study designed to examine the effectiveness of implementing similar lactation support services in two other CPNP sites.[19]", while on page 5 (or 8/29) lines 28-30 it is stated that "All participants in Study A and those recruited to the post-intervention group in Study B had access to two free, in-home visits …." These data leads to the assumption that the population included in the part 2 was not the whole population of Study B (including pre- and post-intervention mothers) but only the post-intervention population of study B. This issue must be clarified.

Response: Thank you for this comment. The analysis included all participants recruited to Study B, including both the pre- and post-intervention groups. This has been clarified in the "Study Setting and Participants' section (page 5). The information about some participants having access to lactation support (page 5) is provided for context and is the reason we conducted the exploratory analysis with this subsample (page 9).

b. Although the authors stated, page 4 (or 7/29) line 10, that "mothers with term-born infants were recruited", the description of study participants in the method section implies recruitment of mothers giving birth to preterm infants as well. Specifically, for Study A, it is stated that "Study A was a prospective cohort study of infant feeding practices among clients of a CPNP site offering skilled postnatal lactation support …". This statement implies that all mothers registered to the CPNP were eligible regardless of the gestational age at birth. In addition, for Study B, it is stated that "Exclusion criteria for Study B were preterm birth (<34 weeks gestation), …" showing that, apart from term infants, late preterm infants were included as well. Given that prematurity is an important factor associated with feeding difficulties, thereby affecting the way of feeding, the gestational age should be presented and should be included in the regression analysis models as an exposure variable (confounding factor). Moreover, the statement in the introduction "mothers with term-born infants were recruited" must be modified appropriately.

Response: Thank you for highlighting this important area for clarification. It is correct that Study A did not exclude participants based on gestational age, and that Study B allowed for late preterm infants. We have added a statement about gestational age calculation in the Methods/Data Collection section (page 7) and included the rate of preterm birth (<37 weeks) in Table 1 of the Results section (page 11). Given the low frequency count (3.4%), we were not able to include preterm birth in the logistic regression models so we conducted a sensitivity analysis including only participants with term-born infants (page 9). This showed consistent findings with the regression results for the full sample (page 14). We have modified the statement in the introduction to remove the reference to term-born infants (page 3) but noted in the opening paragraph of the Discussion (page 14) that study participants primarily had term-born infants.

2. Calculation of the sample size is not presented in the submitted manuscript. Although the sample size calculation is presented in a previous publication regarding the study protocol (see reference #19), it should be mentioned in the current study as well.

Response: Thank you for this comment. The current study used the available dataset from Studies A

and B without a sample size calculation. The sample size calculation for Study B was published in the study protocol as noted, and has been added to the “Study setting and participants” section of the revised manuscript (page 4).

Reviewer: 2
Dr. Maria Lorella Giannì, Fondazione IRCCS Cà Granda, Study University of Milan
Comments to the Author:
The Authors aimed to investigate wether the early use of expressed milk is associated with early breastfeeding cessation. The paper is interesting. However, It is not clear to me which criteria the women were supposed to meet in order to be enrolled in the studies and be defined "vulnerable". Please, clarify this very important point.

Response: Thank you for this comment. The Canada Prenatal Nutrition Program uses broad criteria for social and economic vulnerability to describe its target participants. We have added this information in the Study Setting section of the Methods (page 4). There were no specific vulnerability criteria for enrollment in the studies, but Table 1 (pages 10-11) indicates the main vulnerabilities of the participants (newcomers, food insecurity, low income).

Moreover, I would suggest to discuss how the present results compare with those relating to non vulnerable women. How do the breastfeeding rates at six months and the use of expressed milk compare with other countries or different social contexts? In my opinion, this would strengthens the results of the study and the potential clinical implication in terms of optimization of breastfeeding support.

Response: Thank you for this comment. This study was conducted with a specific cohort of participants enrolled in three CPNP sites and is not representative of vulnerable women in the broader population. However, the literature presented for comparison with our findings on expressed human milk use is drawn from a few different countries. We have added the prevalence of breastfeeding to six months (or earlier endpoint) where available for these studies (page 15). Although most expressed HM data are from non-vulnerable women a few studies report comparisons by participant characteristics, and we have added a comment that there is limited evidence that expressed milk use may be lower among vulnerable women (page 15). We have also added a comparison of expressed HM use and breastfeeding to six months in our study with the other available Canadian study (page 15).

VERSION 2 – REVIEW

REVIEWER	Agakidou, Eleni Ippokration General Hospital, 1st Dept of Neonatology and NICU
REVIEW RETURNED	26-Jan-2022

GENERAL COMMENTS	No further comments

REVIEWER	Giannì, Maria Lorella Fondazione IRCCS Cà Granda, Study University of Milan, Department of Clinical Sciences and Community Health
REVIEW RETURNED	12-Feb-2022

GENERAL COMMENTS	I thank the Authors for addressing my previous concerns