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Title: Association between newborn hypoglycemia screening and breastfeeding success in an Ottawa, Ontario, hospital: a retrospective cohort study
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Reviewer 1: Dr. Russell Kirby
Institution: University of South Florida
General comments (author response in bold)

In this manuscript the authors examine the association between breastfeeding in the first 24 hours after birth and outcomes of screening for asymptomatic hypoglycemia in the newborn. The study is single hospital over about 4 years, the hospital delivering about 1/3 of births in Ottawa, Ontario.

From about 14000 singleton live births, exclusions were made for NICU care, early discharge, pregnancy risk, maternal complications, congenital conditions, and death prior to discharge, leaving a study population of 10965. Among these 1952 had 3 or more screens for hypoglycemia in the first 24 hours.

1. Table 2 contains no statistical inferences, which might be helpful to readers seeking to assess how those screened differed from those not screened. Given known factors associated with breastfeeding, its interesting that maternal race/ethnicity was not assessed, nor maternal age or some proxy measure of socio-economic status.
Hôpital Montfort, like most hospitals in Ontario, does not systematically record race/ethnicity of patients. In Ottawa, there's not a clear association between establishing breastfeeding and age of mothers who are 20 years old and above (https://www.ottawapublichealth.ca/en/reports-research-and-statistics/resources/Documents/infant_feeding_2015_en.pdf). We could not directly access data on families' socioeconomic status (SES). What is specifically tricky about the study hospital's catchment area is which includes both an area called Vanier (which is on the low end of SES) and Rockcliffe (which is at the high end of SES).

2. In statistical tables, results and abstract, ORs and CIs should be rounded to two decimal places, and 3 implies a greater precision than warranted in this largely exploratory study.
Thank you this was adjusted for tables 4-6.

3. Did the authors assess missingness of study variables, and consider multiple imputation? A propensity score matching analysis might also be warranted, given the small number of study subjects screened.
1256 (11.5%) data were omitted due to missing data for the primary and tertiary logistic regressions, with a final sample of 9709. For the secondary logistic regression, 2668 (24.3%) data were omitted with a final sample of 8297. We added this information on the sample size for Table 4, 5 and 6. The data was missing completely at random and was not considerable, therefore we it was deemed safe to omit them.

4. The authors should also consider potential bias given that many members of the research team are located at the study hospital and may have been involved in care processes for the study subjects. Decisions as to whom to screen may have biased the study.
Newborn screening involves nurses applying the hospital's protocol on newborn hypoglycemia. Roughly once a year, nurses asked the study investigator Dr. Michael Saginur, a pediatrician, whether a baby should be screened for hypoglycemia, based on the hospital protocol (typically not based on Dr. Saginur's full assessment of the baby). Other investigators were not involved in the care of newborns. It was fair to question the extent of this involvement in clinical care potentially biasing the study, however, its effect could only have been negligible.

5. Also, as the authors note, study generalizability is limited- at minimum the authors might compare data from BORN Ontario to determine the characteristics of all births in Ottawa during the study period and how the study sample compares.
That is true, though BORN lacked important clinical data, including data on which babies underwent screening for hypoglycemia, as well as data on exclusive breastfeeding to 24 hours.

6. In beginning the discussion, consider editing line 30 on p 4 to read 'This study addresses whether . . .'. Making a statement of primacy for this study is unwarranted.
Modifications have been made to the manuscript. Please see p. 5.

Reviewer 2: Dr. Nancy Wight
General comments (author response in bold)

Canada is usually thought of as much more breastfeeding supportive than the USA. I am appalled at the amount of supplementation in this hospital 2014-2018 and the lack of use of dextrose gel in the same time period.

1. Your title is misleading and implies that the screening itself causes decreased breastfeeding - more likely is the indiscriminate use of formula.
The title of the manuscript has been modified from:
"Effect of newborn hypoglycemia screening on breastfeeding success: a population-based retrospective cohort study"
To:
"Association between newborn hypoglycemia screening and breastfeeding success in an Ottawa, Ontario, hospital: a retrospective cohort study" (p.1)

2. Was this study approved or waived by the hospital Institutional Review Board?
The study was approved by the Montfort Hospital Research Ethics Board on April 12, 2021 (file number: 17-18-03-029). This was added at the end of the Methods section.

3. Your reference list is inappropriate:

a. You cannot refer to conclusions of an unpublished reference (1) that cannot be checked.
The article has since been published and updated in the reference list (see reference number 4 on p. 8).

b. references 2-6 are tangential at best
Reference 2 was the Canadian Pediatric Society Guideline that prescribed appropriate management of postnatal hypoglycemia during the study period. References 3 and 4 described rates of maternal diabetes and late preterm birth, which informed the estimate of the proportion of babies for whom hypoglycemia screening would be recommended. References 5 and 6 demonstrated a lack of adherence to screening guidelines.

c. You did not include the most recent international review, which summarizes a few key international recommendations: Wight NE & ABM Protocol Committee: ABM Clinical Protocol #1: Guidelines for Glucose Monitoring and Treatment of Hypoglycemia in Term and Late Preterm Neonates. Breastfeeding Medicine 2021; 16(5): 353-365. DOI 10.1089/bfm.2021.29178.new
It has now been cited, both in acknowledging the ongoing controversy about the definition of hypoglycemia and its management, and as a source which validates the practice of checking the glucose levels of babies felt to be jittery (while acknowledging the lack of specificity of that sign) (see reference number 3 on p. 8).

d. Several of your references are > 10 years old.
Please see below comments related to a number of the older references:
The CPS guideline that was in effect during the study period was published in 2004.
The studies informing power calculations with estimates of the frequency of diabetes in pregnancy and late prematurity were the ones that were cited: uncertainty around the exact, current percentages did not change the study interpretation.
The systematic literature search in the cited scoping review found only one primary study published in 1993 on effects of hypoglycemia screening on breastfeeding, therefore the cited commentary published in 2001 based mostly on professional experience in the context of an active discussion the literature from around that time did not appear to be dated by the nature of the available evidence (for newborn hypoglycemia screening, blood gas analysers and continuous glucose monitoring still are not widespread … the technology and our information remain quite similar: 'significant' hypoglycemia can cause long-term neurodevelopmental harm).
Finally, the publications that found associations between shorter-term breastfeeding and longer-term breastfeeding were older, however, the biology and the technologies involved have remained the same. As such, the studies were deemed valid.

4. Although you went to great lengths to exclude possible confounders, you did not define "prematurity". You excluded infants < 36 weeks but did not define "prematurity" in your text or tables.
There is no variability in the definition of prematurity: it is defined as a baby born before 37 completed weeks (eg, WHO https://www.who.int/news-room/fact-sheets/detail/preterm-birth; To be explicit, however, this was specified under exposure. 'Small for GA and premature (<37 week GA) babies are screened every 3 to 6 hours in the initial 24 hours (see p.3).

At the studied hospital (Montfort), babies under 36 weeks were routinely admitted in the 1st 24 hours to the NICU for monitoring of cardiorespiratory stability and feeds … separated from their parents. These babies were excluded from the study because of their NICU admissions.

5. What is EG and EMB?
They were 2 authors. We wanted to express how two authors versed in the databases generated a long list of potential variables, and two authors with an appropriate background reviewed the long list of variables.

6. Overall, the paper would require significant shortening.
This was done.

7. Are you suggesting that screening of at-risk infants should be discontinued? or that it should be modified? If so, how?
We are suggesting that there is evidence of potential harm of screening for hypoglycemia, and that this needs to be considered in defining 'at risk' populations who warrant screening.
It is likely that certain risk factors predispose to hypoglycemia to varying degrees. The cited scoping review found that it was more common for guidelines to recommend screening infants of diabetic mothers and premature babies than to recommend screening large for gestational age babies. Even if some large for gestational-age babies should be screened, maybe only babies in the top 5th centile of birthweight for gestational age need to be screened at 40 weeks gestation.
Recognizing that screening isn't entirely benign would support a judicious approach to defining which babies are at risk of hypoglycemia, and warrant screening.

8. Was donor human milk used as a treatment, or just formula?
No, donor milk was not used as treatment since the supply is limited. Only formula is used as a treatment.

Overall, I applaud your quality improvement efforts by reviewing your hospital's available data, but I recommend a closer look at current references and a more appropriate (and obvious) conclusion: over-screening is associated with overuse of formula supplementation.
We appreciate your kind words, as well as the provided interpretation. We have added this information in the discussion of future research (see p. 7). It is difficult to say what is over-screening when guidelines vary and the data is lacking, however, it seems as though screening is associated with more use of formula, and potentially more judicious postnatal hypoglycemia-screening criteria would reduce the amount of formula administered to babies (recognizing that some populations of babies likely benefit from screening ... it is just difficult to specify exactly who), as well as avoiding pain for new babies and stress for their parents.