Reviewer’s report

Title: Identifying risk factors for perinatal death at Tororo District Hospital, Uganda: a casecontrol study

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Reviewer: Jillian Pintye

Reviewer's report:

This is an interesting and well written article about an important topic, perinatal death in a rural Ugandan setting. The authors support that there are limited data on perinatal death from rural settings in Uganda, despite some previous studies from urban settings. The authors conducted a case-control study using maternity/birth registries to identify factors associated with stillbirth and perinatal death. The design is strong and the interpretation of results is sound. My primary recommendation is to tie the main findings to stronger implications supported with evidence-based recommendations cited with available literature. For example, the authors report that breech presentation is associated with perinatal death and suggest that stronger training on intrapartum management is needed to prevent such deaths. More information on what that may look like in Uganda and whether there are recommended interventions or implementation strategies for improving intrapartum management would enhance the discussion and strengthen how this work fills an important gap. My main critique is that the rationale for the analysis of macerated stillbirths vs fresh stillbirths and perinatal deaths is unclear. There were also no clear differences between the two groups. Combing fresh stillbirths and neonatal deaths could be obfuscating differences and I recommend comparing stillbirths (fresh and macerated) vs neonatal deaths or conducting separate analyses for each respective outcome vs controls to identify risk factors for each. Other specific comments are below:

Introduction

1. In the paragraph that starts with, "Uganda is among the top fifty countries with the highest burdens of perinatal deaths…", there are comparisons between Uganda and the U.S. It would be more informative to include targets for perinatal/neonatal deaths in Uganda. For example, does the government of Uganda have a goal of reducing perinatal mortality from its current rate of XX/1000 to XX/1000 by a specific year? What about progress on MDG/SDGs? This would be helpful to clarify the existing gap.
2. Is there a citation available for this: "There are also notable differences between rural and urban populations with estimated 52% of deliveries in rural Uganda occurring in hospital settings as compared to close to 90% in urban areas"? How does this suggest a high likelihood of "case mixes"? Do the authors mean that the populations of mothers in urban vs. rural settings are different because urban mothers are more likely to deliver in hospitals? This is not clear as it is currently written. Please describe more fully.

Methods

1. It is unclear if only data from birth registers were used or if the study team actually interacted with human subjects seeking delivery services. Can this aspect of the design please be clarified in the being paragraph of the methods section? It is mentioned in the limitation sections of the discussion, but it is not clear in the methods section.

2. It is also unclear why the women were presenting at the health facility and to which unit. For example, were all controls coming in for normal vaginal deliveries? Were all cases attending clinic for their obstetric issue? Adding more detail to the data collection procedures could clarify this (e.g., the entry before and after a stillbirth recorded in the maternity registry).

3. Information on data collection procedures should be specified. For example, how did the study team digitize the data? Did mobile data teams abstract the data on site and hand enter the data into an electronic system?

4. Is there any information available on approximate timing of death and the death-to-delivery interval for the stillbirths?

5. Please operationally define a "normal delivery outcome" in the methods. Was this just a live birth?

6. What happened if 2 cases were consecutively admitted? Was only one case included in your study?
7. How was gestational age determined? This is important both for staging the primary perinatal death outcomes but also the cofactor of prematurity. Was this information abstracted from maternal health cards? How is gestational age typically determined in this setting (e.g., LMP, fundal height, etc)?

8. It could be more clear to just say "≥4 births" instead of using "Grand multiparity", particularly in the abstract where grand multiparity is not defined.

9. Please operationally define how "perinatal mortality" was included in regression models (ie, any case defining outcome—stillbirth or neonatal death).

10. A lot of outcomes/variables included in the models are likely collinear or on the casual pathway to one another, rather than independent exposures/outcomes. This could also explain some of the unusual/imprecise estimates with wide confidence intervals. For example, preterm birth is on the casual pathway to perinatal and neonatal death. Twin birth and prematurity are collinear. There should be a rationale inserted for why the authors chose to assess this set of variables as independent predictors for their outcome(s) and how potential collinearity was handled.

Results

1. It would be helpful to know how many potential cases/controls were excluded due to missingness, incomplete entries, etc. Using routine data, it is hard to believe that every case was able to be used with no incomplete data out of the >5000 entries.

2. The analysis for comparing cases with fresh stillbirths and neonatal deaths to macerated stillbirths is confusing and not described in the methods. If you wanted to assess whether there are differenced in factors associated with fresh stillbirth/neonatal deaths vs macerated stillbirths, the appropriate analysis would be to run 2 separate models: one with controls vs macerated stillbirths (no other outcome included) and then a separate model with controls vs fresh still birth/neonatal deaths. One could also argue that the more appropriate comparison would be combing macerated/fresh still birth into one outcome (instead of fresh stillbirth/neonatal death) as the casual pathways are likely more similar.
Discussion

1. It would be more convention to report that prematurity, breech, and twin gestation had the "strongest association" rather than "most significant".

2. It would also be helpful to try and explicit state what gaps these data fill. It is already known that prematurity, breech presentation, and twin gestation are association with adverse perinatal outcomes. How will confirming this information in this rural setting fill any gap or advance programs?

3. It seems that "17/2019 12:29:00 PM" was added to the end of a paragraph in error?

4. The authors state, ".we are the first group to analyze risk factors based on the type of perinatal death: stillbirth (macerated or fresh) and neonatal death". Do you mean in the specific setting of Tororo? Other studies in African settings have looked at these outcomes separately with robust prospective designs. One example from a rural setting is Warr AJ et al Sexually transmitted infections during pregnancy and subsequent risk of stillbirth and infant mortality in Kenya: a prospective study. Sexually Transmitted Infections 2019 PMCID: PMC6525108. There are other examples too. Please clarify this statement and contextualize within the broader literature which has examined this research question (ie, predictors of stillbirth and neonatal death in similar populations).

5. Please cite studies that support, ".increased training on intrapartum management and vaginal delivery of breech presentation may improve outcomes" is an evidence-based intervention. For example, the PRONTO studies.

6. The authors note that HIV prevalence was low in their study population. What about info on other MCH indicators? For example, syphilis results from pregnancy?
7. A major strength of this paper is that routine programmatic data were used to answer a question linked the local context with potentially direct implications for practice. I think it would be beneficial to raise this, given the move in the field towards strategic use of programmatic data to answer implementation science questions tailored to the context. It sounds like the field team may not have encountered much missingness which is also a strength to be noted. Using routine registries for such surveillance studies is exactly the direction we should be going in and it would helpful to include a couple of sentence on this since it is a unique and important aspect of this paper.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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