Author’s response to reviews

Title: Proximate determinants of infant mortality in Ethiopia, 2016 Ethiopian Demographic and Health Surveys: Results of Survival Analysis

Authors:
Masrie Abate (masriegetnet16.biostat@gmail.com)
Dessie Angaw (dessieabebaw96@gmail.com)
Tamrat Shaweno (babiynos@gmail.com)

Version: 2 Date: 31 Aug 2019

Author’s response to reviews:

Author's response to a review

Proximate determinants of infant mortality in Ethiopia, 2016 Ethiopian Demographic and Health Surveys: Results of Survival Analysis

To: BMC archives of public health

Subject: Submitting a revised version of the manuscript

Object: Manuscript AOPH-D-19-00007 Proximate determinants of infant mortality in Ethiopia, 2016 Ethiopian Demographic and Health Surveys: Results of Survival Analysis

We would like to thank the reviewers and editor for sharing their view and novel scholarly experiences. The comments are very imperative which we strongly believe in improving the manuscript. The point-by-point responses for each of the comments, questions, and the revised manuscript is provided in the attached documents. Yellow color showed that there is some modification. We all authors are ready to reply again for those points not raised.

Reviewer #2: Major Comment##

1. There is a need to check the data very carefully as something is wrong with the analysis. Please check the outcome variable, whether it is chosen the setting variable or failure event in the Cox regression model and Kaplan-Meier survival function in figure 2 correctly. The given results are not promising as at least education, wealth index, ANC, etc. should be necessary for child survival apart from other findings. Also, the variable "size of the infant at birth"- don't know (DK) category seems minimal number in table 2, then how it comes highly significant in your results? Please check whether it is combined missing cases recode with DK variable?
Author response: Based on your constructive comments, we have revised the data and reanalyzed. The new results found that educational level of mother’s was a significant variable. Besides, we have used the categories as it is from EDHS. Thus, we did lots modifications on the results on table 1 (pages 7-8), table 2 (pages 10-11) and Kaplan-Meier on the figure 3.

2. Also, no theoretical framework of the analysis has discussed, and I would suggest adding the analytical framework given by the below reference and plan your analysis frame accordingly with the predictors. Mosley, W. H., & Chen, L. C. (1984). An analytical framework for the study of child survival in developing countries. Population and development review, 10(0), 25-45.

Author response: Thank you for your guidance to use this interesting theoretical framework, we have incorporated it as figure 2.

3. Overall, English write-up and interpretation of the results are poor and need to strengthen.

Author response: based on your constructive comment Fluent English speaker and authors revised the whole part of the manuscript accordingly.

Minor comment ##

4. In abstract, background needs to restructure, as it is not up to the mark and in method section line, no 20-21 is repeating the same content. In result part line no 33- "It was observed that 68% of the deaths occurred in the first month of life" - from where you have concluded these findings (similarly in discussion section line no 29, page no 13)?

Author response: Thank you once again, we have merged the repeating contents in the revised version based on your comments on page 2 of methods part first line; we have added also the sources as figure 4.

5. In background section-, the Starting line is inadequate as it is the definition of IMR, which is not required a reference. The literature review is not enough as per the recent, and some sentences are repeating in most of the places, for example, on page no 4 first paragraph. Last paragraph of the page no 4 is poorly written and can be modified with identifying the research gap and what is new through this research. It is written but needs to restructure the sentences with more information.
Author response: Based on your comments, we have removed the reference of the first line of the first paragraph under background section on page 3. Moreover, we have re-write the last paragraph of the background section on page 3 & 4 also.

6. In method section-, most of the information is already available in the DHS report, so there is no need to explain all again here and need to give relevant information regarding the analysis where necessary with reference. Also, I do not see the relevance of figure 1 as it can be present in the text itself. It will be helpful if it can separate the definition of the outcome variable, predictors, and statistical analysis- as the current form is not well presented.

Author response: Thank you so much, after your constructive and advanced comments all the method sections were re-write again on pages 4-6.

7. In predictors, why wealth index is categories in three categories? In DHS, it is available for five categories, and it is good to have all the categories to see the variation among them.

Author response: In the new results, we have used the categories as EDHS categorized in to five on table 1 (pages 7-8).

8. Cox model is not present well. You can present the used model; define clearly the terminology, why cox model used for this analysis, what is the benefit for the use of it can be mention? Also, why variable with p-value < 0.25 sent to Cox regression model? P-value of what? Why considering this?

Author response: After your constructive comments, we have tried to present the used model by citing two references and also why variables with p-values included in the final model (on page 5-6 under Statistical analysis line 5-8).

9. In the result section- Descriptive results part, I do not see any table support for the explanation of child characteristics. Where from explaining these results? Also, interpretation is not clear and need to modify as lots of grammatical and structural issues in the interpretation.

Author response: dear reviewer thank you for your concern. After considering your constructive comments in the new analysis, we have incorporated the child characteristic (sex of the child) in the second paragraph of the descriptive results part on page 6 first paragraph of first line.

Author response: really I thank you very much. Based on your direction and guidance I have used this material to write the interpretations of Kaplan-Meier estimates for overall infant’s survival on page 9 of the first paragraph.

11. In Figure 2, X-axis is wrongly given up to 60 months, which will be applicable for under-five mortality. Please check. Also, the graph needs to modify for better presentation.

Author response: Thank you so much, we have corrected this as figure 3.

12. In discussion sections, the first paragraph is not written carefully, and it should strengthen with more information beginning with the objective of the study. In line 22 (page no 13) from where 5.1% value comes? The second para in the discussion is not clear what want to explain with the findings.

Author response: Dear reviewer thank you for your concern. Since the main objective of this study was explained on page 11 of discussions part, first paragraph of line numbers 1-3. Besides, in the new analysis the value 5.1% was reduced to 4.8%. It is from table 1 on pages 7-8.

13. The overall flow of the discussion is not clear, and need to arrange the order and restructure the sentences with arguments. The limitation is very poorly written, and it might mention other possible limitation for the data as well.

Author response: We have tried to restructure the sentences with arguments of the discussion pages 11-13. The limitation is also incorporated after your and third reviewer constructive comments received. (see page 13, discussion part, paragraph 2 line 8-9)

14. In conclusion, sections-, how it can be said that the high rate of death among infants was observed? Which analysis supports the results? You need to mention all these in a clear way.

Author response: thank you for your concern. This is based on the result observed from figure 4.
Reviewer #3:

1. I suggest to modify the title of the study to: "Results of survival analysis" as opposed to "Application of survival analysis"

   Author response: Done accordingly on the title.

In the abstract

2. There is some redundant information in the methods section "the study used data from the 2016 Ethiopian Demographic Health Survey" is mentioned twice. In the Results section of the abstract, and throughout the authors may want to refer to multiples only (which by definition include twins) as opposed to "multiple births or twins". Therefore, line 38 this should read the "results were higher for multiple births versus singletons".

   Authors response: Thank you for your nice view, we have merged the redundant information of the first three lines of the methods as one line on page 2.

3. In the conclusion of the abstract, the correct terminology is "infants low birth weight" (defined as birth before 2500g) as opposed to "infants below the normal weight".

   Authors response: Done accordingly on page 2 line number 3 of the abstract

Main manuscript/

4. In the background section, "the infant mortality rate" is not really a probability - it is defined by the number of infant deaths per 1000 live births.

   Line 29-33, p3 references are missing.

   Authors response: Thanks a lot, we have changed the first line of the background based on the comments from you and the second reviewer on page 3 of the first paragraph first line number.

5. In Methods, please define the "EA" abbreviation in the text. I would also specify the exact years when mentioning "the period of five years preceding the date of the survey" (line 56 p5)
Authors response: Dear reviewer, the second reviewer also gave comments on the methods part and we have re-write again this part on pages 4-6 by considering all comments from both reviewers.

6. Regarding the included variables, there needs to be a better explanation of the inclusion of the variable "size of child at birth" also in relation to the reference used for "average". Typically this variable should be collected and/or reported with respect to gestational age and/or birth weight in order for readers to understand how results from one population could be compared to another. What is considered average for a preterm baby vs. a baby born at 40 or 41 weeks will differ. There will also be sex differences, and the mother who just delivered will not necessarily be knowledgeable enough/or in a state to discriminate between GA:BW/ and or the increments of size…in particular for first time or younger mothers, or if there were complications during delivery. There needs to be more information in order for readers to understand how to interpret the results for this determinant.

Authors response: really I wonder your concern. Specifically mothers who are not knowledgeable enough to estimate the size in particular for first time or younger mothers. With its limitation we authors agree that instead of taking the reference very small or very large, average is preferable.

7. I would also reconsider the variable "when child put to breast". I would encourage the authors to better explain what is the underlying hypothesis for using this variable with respect to infant mortality? As a side note this variable is most likely confounded by mode of delivery (Cesarean section deliveries often times having a later onset of breastfeeding vs "immediately"). This variable also does not speak to the "duration of breastfeeding" which is more clearly associated with overall infant health.

Author response: Really I appreciate your concern. Of course immediately breastfeeding upon birth doesn't directly speak duration of breastfeeding. But, a child who feed colostrum (first milk) for the first hour has better immunity in which it has directly associated with overall infant health.
Forexample:

According to WHO report, Provision of mother’s breast milk to infants within one hour of birth ensures that the infant receives the colostrum, or “first milk”, which is rich in protective factors. Current evidence indicates that skin-to-skin contact between mother and infant shortly after birth helps to initiate early breastfeeding and increases the likelihood of exclusive breastfeeding for one to four months of life as well as the overall duration of breastfeeding. Infants placed in early skin-to-skin contact with their mother also appear to interact more with their mothers and cry less (https://www.who.int/elena/titles/early_breastfeeding/en/)

8. For the variable "smokes cigarette", it would be useful to have a bit more detail also as to how this variable was measured. (i.e. do authors have number of cigarettes smoked/day, did the mothers smoke during pregnancy?)

Author response: Done accordingly on table 1 page 8.

9. Finally, what is the underlying assumption also for looking at the link between " sex of household head" and infant mortality. For the analysis, I would check inclusions against known risk factors in the literature and have a better justification of other included variables that have not previously been explored in the literature.

Author response: Dear reviewer, as we have mentioned under statistical analysis on page 5, we have excluded variables with $p$-value≥0. 25. Thus, this variable (sex of household head) was excluded from the final model.

10. In the results section, perhaps the information in paragraph 1 could be included in table format or added as columns to current Table 1. In the current Table 1, the denominator should appear (whether women or babies in the table headers).

Author response: Table one is for infants. Hence, we have done it on page 8 table 1.

11. Line 51 p 8, replace ' the lowest deaths of infants" with the " lowest infant mortality rate".

Author response: After your valuable comments we have changed “the lowest deaths of infants” by “lowest infant mortality rate” on page 6 of the last paragraph of line number 3.
12. In the reporting of the Kaplan Meier estimates, the authors should provide more detail (i.e. exact time points) in the text and/or change the scale of the figure (fig 2). As it stands now, the reporting is not precise enough.

Author response: Thank you, the second reviewer gave comments also on this, hence based on comments from both reviewers, we have tried to re-write the Kaplan-Meier estimates again on page 9 of the first paragraph. Moreover, the figure of Kaplan-Meier estimates is on figure 3.

13. In the reporting of the Cox proportional Hazards, I would again add the N(denominator) in the table, and specify if there was any missing information on some of the variables? If so, this should be mentioned in the methods section ( proportion of missing or analysis done on complete cases only?)

Author response: Dear reviewer, As you have mentioned some variables are not complete. Hence, we considered the variables for the final models based on Hosmer and Lemishow variable selections recommended procedures on page 5-6 statistical analysis part.

14. In the discussion, the results are well explained. There are some additions that could bring out more the importance of this study. For example, the discussion on the size of the child at birth is missing important information on Gestational age/birthweight/sex and the associations between these underlying determinants. Also how was the size of the child at birth collected in the study? I m not sure I understand the inclusion of the "don't know" category…is this missing GA information? Or poor maternal recall?

Author response: The second reviewer also raised the points on this, thus, we have tried to address all the comments given from both reviewers on table 1 page 7. Actually, the size of child had five categories from EDHS: larger, larger than average, medium, smaller than average and very small( table 1 page 7).

15. I would suggest to add more in the limitations section based on the reviewers' comments, and in relation to sample size or other methodological limitations.

Other minor comments relate to rewording:

Author response: thank you very much. Based on your constructive comment it is incorporated in the main document (discussion part, page 14, paragraph 2, line 8-9).
16. I would specify which "other setting"s the authors refer to in line 22 p13

Author response: Thank you so much, this is corrected on page 12, discussions part of the second paragraph of line numbers 1-2.

17. Lines31-32 are not very clear. I am not sure I understand what the authors mean by "all infant deaths occurred at the end of the observation period"? The observation period from what I understood was N-5 years, so it would make sense that all infant deaths would occur before then…As suggested earlier, perhaps adding the dates of the study would help clarify.

Author response: dear reviewer thank you very much .Based on your comment ; I have written this in clear way on page 12, discussions part of the second paragraph of line number 3.

18. Line 37 p 13, not just "due to poor monitoring and short follow up time" but poor antenatal care in general or lack of access to care also.

Author response: I have done accordingly on page 12, discussions part of the second paragraph of last line number.

19. Reword "showed that the better birth space of infants had a better survival". i.e. infants born after longer interpregnancy intervals had better odds of survival. When referencing the literature on interpregnancy interval, please add the number of months used in the other studies and/or identified as the optimal interpregnancy interval (also 24 months. This may vary by studied birth outcome).

Author response: Done accordingly on page 13, third paragraph line number five.

20. Reword line 25 p 15 "being male sex of the infant had a statistically significant impact on infant mortality" with for i.e. "male sex was significantly associated with infant mortality".

Author response: Done accordingly on page 14, second paragraphs of conclusions and recommendations of last line numbers.
21. Overall, this is an interesting study with valuable population based results for Ethiopia. However before publication, variables included in the study need to better detailed/justified, and the reporting of the survival analysis in the figures and tables also needs to be more precise with some further language edits. I would encourage the authors to strengthen the discussion with broader public health arguments and recommendations that will help bring the study results in context. This would require more emphasis on what are the implications of this study specifically for Ethiopia either with respect to antenatal/perinatal care policies in urban vs rural, or for mother with higher risk pregnancies. Perhaps authors may want to consider infant mortality/perinatal health trends in Ethiopia also and previous survey results in other years. Moreover, although some variables were not statistically significant (i.e level of education or (maternal age), I would also discuss these inconclusive findings as these determinants are those typically associated with poorer birth outcomes in the literature (this could be relevant for the limitation section also).

Author response: dear reviewer, we really thank you for your constructive comments. We learn a lot from the comments. Based on your and second reviewer comments we tried to address many of the concerns.

1. $ Titles of tables and figures should not include abbreviations
   Author response: done accordingly

2. $ Figure 2: * Title should also refer to place, period and study (similarly as the other titles of figures and tables)
   Author response: done accordingly (see fig 1-4)

3. $ Figure 2: * * Given the values have a small range compared to the scale 0-1 of the Y-axe, please rescale the Y-axe in order to be more informative
   Author response: we tried it to be more visible (see fig 3)

Thank you very much indeed!!!

Yours sincerely

Dessie Abebaw (BSc in OHS, BSc in PHO and MPH in Epidemiology and Biostatistics)