

Authors Response to the Editor, and Reviewers Concern

Title: “Incidence and Predictors of Respiratory Distress Syndrome among Low Birth Weight Neonates in the first seven days in Northwest Ethiopia Comprehensive Specialized Hospitals, 2023; A retrospective follow-up study”.

Manuscript ID: bmjopen-2023-079063

Date: October,19, 2023.

Subject: Revision of the manuscript

Thank you very much dear editor and reviewers for your insightful and comprehensive comments. We found that the comments are very helpful and constructive to further improve the manuscript. This is a point-by-point response of authors to reviewers' concern about a manuscript entitled “Incidence and Predictors of Respiratory Distress Syndrome among Low Birth Weight Neonates in the First Seven Days in Northwest Ethiopia Comprehensive Specialized Hospitals, 2023; A retrospective follow-up study” which has a Submission identification of “bmjopen-2023-079063” given by the journal. It is known that the manuscript has been reviewed by reviewers and sent back to the authors for revision and resubmission. As authors of this manuscript, the comments and concerns raised by the reviewers and editor were highly insightful suggestions and enabled us to improve the quality and plausibility of the manuscript. To do so, we have addressed all of the reviewer's concerns point by point. Therefore, we are very much pleased to resubmit the revised version of the manuscript for further revision process and facilitation of its publication on BMJ Open.

We look forward to hear from you at your earliest convenience.

With best regards.

On behalf of Co-authors.

Wubet Tazeb Wondie (Corresponding Author)

On behalf of Co-authors

Editor(s)' Comments and Authors Response

Concern 1: Please work to improve the quality of the writing throughout your manuscript. We recommend asking a colleague who is proficient in written English to assist you; alternatively, you could enlist the help of a professional copy editing service.

Authors Response: Thank you very much dear editor for your Golden suggestion. We have accepted and tried to correct the revised version of the manuscript.

Concern 2: Please revise the 'Strengths and limitations of this study' section of your manuscript (after the abstract) by using bullet points.

Authors Response: Thank you for your suggestion. We have accepted and corrected in the revised version of the manuscript.

Concern 3: Please ensure that you have fully discussed the methodological limitations of the study in the Discussion section of the main text.

Authors Response: Thank you for your Constructive comment. We have accepted and corrected the revised version of the manuscript.

Concern 4: Please include a statement whether or not the data charts were de-identified.

Authors response: Thank you dear editor for your valuable concern. We already included the de-identification process in the method and Ethical approval section. To make it clear, Records have a re-identification code, but any personal identifier information were **not recorded (i.e. personal identifier information was removed)**. And recorded information does not identify an individual.

Dear Editor, thank you for your Golden suggestions. If something is unclear/wrong, please let me know again!

Point-by-point Response Letter

Dear editorial office of BMJ open we have presented our point-by-point response in a way that the reviewers' concern is depicted first, and the authors' response has been given immediately next to it.

Reviewer 1(Dr. Razieh Sangsari): Concerns and authors response

Concern 1: The date of your study in the method of abstract is wrong.

Authors Response: Thank you dear reviewer for your golden suggestions. We have accepted and corrected in the revised version of the manuscript.

Concern 2: The sentences in the text are very similar to the references please correct similarity.

Authors Response: Thank you for your concern. We have accepted, and corrected in the revised manuscript.

Concern 3: You wrote in Iran 76% (17) of Low birth weight neonates had RDS, but the reference of that describes the cause of mortality rate in LBW infant in Iran.

Authors Response: Thank you dear reviewer for your concern. But Reference 17 is about both mortality and morbidity of Neonates with birth weight 1500 or below with Gestation age of 30 weeks or below. "*Navaei F, Aliabady B, Moghtaderi J, Moghtaderi M, Kelishadi R. Early outcome of preterm infants with birth weight of 1500 g or less and gestational age of 30 weeks or less in Isfahan city, Iran. World Journal of Pediatrics. 2010;6(3):228-32.*"

Concern 4: Respiratory Distress Syndrome (RDS) manifests in early hours of birth not the first seven days of life.

Authors Response: Thank you for your concern: As you have said RDS occurs in the early hours of birth, But, in our country due to a lack of appropriate postnatal follow-up care, these neonates develop RDS in the first seven days of life. In addition, in our study there were several comorbidities like PNA, sepsis...., these comorbidities cause respiratory epithelial cell injury, and inactivation of surfactant in the context of immature lung which increases the risk of developing RDS in the first seven days of life.

Concern 5: You must also write the complete word the first time you write the abbreviation word.

Authors Response: Thank you dear reviewer for your concern. We have accepted, and corrected in the revised manuscript.

Concern 6: Congenital anomalies should be exclusion criteria not independent variables.

Authors Response: Thank you for your golden Concern. As you have said We exclude neonates with major respiratory and cardiovascular anomalies, but we include other congenital anomalies.

Concern 7: In 65 cases age of the neonate at admission were in days 4-7 days but RDS manifests in early hours of birth not 4-7 days maybe that's why the disease is more in your study.

Authors response: Thank you for your Concern. As we have mentioned above, in this study, there were several comorbidities, so these comorbidities like perinatal asphyxia could **cause inactivation of surfactant in the context of immature lung**. In addition to this, some comorbidities (mainly sepsis) induce respiratory epithelial cell injury. Therefore, all of these factors increase the occurrence and exacerbation of RDS in our study.

Dear reviewer, thank you for your constructive concerns. If something is unclear/wrong, please let me know again!

Reviewer 2 -Dr. Shuping Han: Concerns and Authors response

Concern 1: In Page 9 line 53, the number of median weight is far above normal level of birth weight.

Authors Response: Thank you dear reviewer for your valuable concerns. It was an editorial problem and We have accepted and corrected in the revised version of the manuscript.

Concern 2: In Page 9 line 55, it is suggested to uniform the writing style of IQ.

Authors Response: Thank you for your concern. It was an editorial problem, and We have accepted and corrected in the revised version of the manuscript.

Concern 3: In Page 12 line 40, the author should provide the detail of the calculation of neonate day observation, how to get the number of 1771?

Authors response: Thank you for your golden suggestion. We have accepted, and corrected in the revised manuscript.

Concern 4: Why the author selected the first 7 days of life in this study? Whether this caused the missing of Clinical and other characteristics of LBW neonates, including the mortality of LBW neonates?

Authors response: Thank you dear reviewer for your concern. Due to organ immaturity, RDS occurs in the early hours of life. But in the presence of different comorbidities like PNA, Sepsisit occurs after a certain hours of life (Up to seven days of life), because these

comorbidities contribute to surfactant inactivation and respiratory epithelial cell injury after a certain hours/days of birth, probably up to seven days of life. So, we emphasis on the first seven days of life.

Regarding the missing of clinical and other characteristics of LBW neonates, including mortality, as we have mentioned above RDS occurs in the early age of life, most of the clinical characteristics and other contributing factors for RDS occurrence were available, and we assessed during the data collection, and consider them as a predictor.

Concern 5: It is suggested to supplement the relevant weakness of this study in Discussion.

Authors response: Thank you for your concern. We have accepted and included the relevant weakness of the study in the discussion section.

Dear reviewer, thank you for your valuable suggestions. If something is unclear/wrong, please let me know again!

Reviewer 3: Dr. Jackson Maina- Concerns and Authors response

Concern 1: Under the study setting the authors would need to provide some more background on who provides the care in these units e.g., is it neonatologists, or trainee doctors; this may have a bearing on the diagnosis and documentation in the clinical records. Also, information about the clinical records were these are paper-based or electronic medical records? has a bearing on the level of missing data.

Authors response: Thank you dear reviewer for your valuable concern. We have accepted and tried to include it in the revised manuscript. But to make it clear, the neonatal care in these hospitals were provided in team including Neonatologists, General practitioners, Comprehensive Nurse, , Pediatrics Nurses and Neonatal Nurses etc. Regarding the diagnosis, it is mainly done by Neonatologists and General practitioners, and the documentation were paper-based and made by the team.

Concern 2: I propose the authors write the abbreviations used in the report in full when first used e.g., the abbreviations on page 7 of the report need to be written in full.

Authors Response: Thank you dear reviewer for your suggestions. We have accepted and corrected in the revised version of our manuscript.

Concern 3: I suggest the data collection tool described on page 6 be added as supplementary material in this manuscript. Also describe more on how maternal data were collected, seeing presumably the charts we primarily neonatal data.

Authors response: Thank you for your dear reviewer for your concern. We have added it as supplementary material.

Regarding maternal data, in neonatal history the maternal profile and comorbid conditions were taken from the mother and were well documented in the neonate's chart (medical record). So important variables are available in the neonate's Chart and taken from it.

Concern 4: Under the results sections, I propose the authors edit tables 1 and 2. For example, binary outcomes "Yes" or "No" may be worth stating one instead of both. Also please explain all the abbreviations in the footnotes e.g., on page 10 the abbreviation PNA is not described.

Authors Response: Thank you dear reviewer for your concern. We have accepted and tried to correct it, but it is the nature of the variable's response.

Regarding the Abbreviation, we have accepted and corrected it in the revised manuscript.

Concern 5: In the diagnoses, I presume one baby may have had several disease conditions which may mimic the signs of RDS, perhaps worth presenting the diagnoses in a Venn diagram to help the readers understand the disease patterns better.

Authors response: Thank you for your valuable concern. As you have said, some neonates had several disease conditions. But When the neonates have two or more signs of respiratory distress syndrome it is diagnosed as RDS and if other comorbid conditions present, it is considered as additional comorbidity. So, the presence of other comorbid conditions is common, and Known, and it doesn't confuse readers.

Concern 6: For the diagnosis, I suggest the authors describe if these were admission diagnoses or any diagnoses during the babies' stay in the unit.

Authors response: Thank you dear reviewer for your suggestion. Regarding the diagnosis, we follow the neonates from the date of admission up to the seventh day of life. Starting from the admission date at any time they may develop RDS. So the diagnosis can be made at any time during the follow-up, not only admission date diagnosis.

Concern 6: On page 11, lines 44-53, this is very crucial information that can be better displayed as a table to allow the readers to better understand the outcome of interest in the study.

Authors Response: Thank you for your Golden suggestion. We have accepted and corrected it in the revised version of the manuscript.

Concern 7: For Table 3, I propose the authors look at the denominators again for some of the variables e.g., the numbers on mode or delivery differ slightly from what was described in the baseline data table.

Author Response: Thank you for your Golden suggestion. We have accepted and corrected in the revised manuscript.

Concern 8: In the results section, these are data from hospitals in different regions in Ethiopia, I wonder if there are any significant differences between these regions worth mentioning in this paper?

Author Response: Thank you dear reviewer your Suggestions. We have accepted and corrected in the revised manuscript.

Concern 9: The discussion section is clear and well written.

Authors Response: Thank you, dear reviewer.

Dear reviewer, thank you for your Golden suggestions. If something is unclear/wrong, please let me know again!

We thank the Editor and reviewers for their constructive suggestions.