**Author’s response to reviews**

**Title:** Epidemiology of neonatal infections in hospitals of Nepal: Evidence from a large-scale study

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Archives of Public Health

Reference-Submission of manuscript “Epidemiology of neonatal infections in hospitals of Nepal: Evidence from a large-scale study”

Dear Dr. Herman and Professor Olivier

Thank you for the review. Please find the point to point response to the reviewer’s comment.

Response to First reviewer’s comment

Reviewer #1: Technical concept: Academic Pair, article publication.

Comment 1# Study: Epidemiology of neonatal infections in hospitals in Nepal: Study of large-scale evidence. The study mentioned, used a considerable number of births registered in public hospitals in Nepal, which can be a very good universe for decision-making in the management of neonatal infections in public hospitals in Nepal. They have a clear methodology, which is explained and which
apparently was used in a technical way. However, from my technical concept, the fact of not having taken into account the comorbidities, or "as a previous medical history" as the authors mention in the limitations may constitute a bias that can vary significantly the results, given a systemic commitment of the mother. Situation that is clarified, and that is very valid, but that perhaps a decision maker would omit it for such bias. The article gives many lights to intervene and, in addition, it provides the opportunity for further studies in the deepening of details that can help improve the understanding of neonatal infection in Nepal, perhaps expanding it from the purely epidemiological field and going more to the community and social. Therefore, according to my concept, the article would be suitable for publication, with the limitation mentioned by the author.

Response: Thank you for your comment and review.

Response to second reviewer’s comment

Comment 2# Abstract. P2/line21 : "babies who were born to first time mothers were at 59% higher risk of having infection (aOR-1.64, 95%CI1.3-2.06, p<&lt;0.001)." Could the authors explain how this percentage was calculated?

Response : This was a typo. It is corrected as 64%. Thank you for pointing out. (Page no : 2, line 21)

Comment 3# Methods. Overall, I have one major question on the set-up of the study. The regional distribution of the hospitals has been well explained in the protocol paper (Bergstrom et al., 2017) and as said I am not familiar with the Nepalese Health Care System, but what is the role of primary health care units in deliveries? Often these local health posts have little or no equipment in case of neonatal complications and transportation to hospitals is often not existing or very slow and rudimentary due to geographical remoteness. I wonder, are Nepalese women always delivering at a (regional) hospital? Some women, particularly the most vulnerable, might not have easy access to these regional hospitals? Could this lead to a selection bias? Would it theoretically be possible to compare the results with the prevalence of neonatal infections in hospitals which did not participate in the study and what would be the expected result? Could it be that neonatal morbidity and mortality mainly happens outside these 12 hospitals where hygiene and equipment are inferior and qualified care givers are less available than in these regional hospitals?

Response: The prevalence of institutional delivery is about 54 % in Nepal. The study sites were 12 hospitals ranging from district level, zonal to regional which are located in densely populated areas in Nepal. These hospitals also serve as referral centers. There is no established referral health care system in Nepal, as result women can access care from these centers without consultation to the Primary Health Care facilities. Extrapolating the findings from this cohort study may not be a selection bias because these are the government owned hospitals where the delivery charge is free and government also provides incentives for ANC visits and institutional deliveries in Nepal. It is a matter of concern that because of various other factors including transportation there are women who are not able to reach health facilities. However, our study aims to find out the risks of neonatal infection among those institutional deliveries. For this purpose we did take a large sample of 60,062 newborns and 12 hospitals of different geographical locations. The following figure is added for illustration. Thank you.
Comment 4# Inclusion criteria were defined as 'babies with a birth weight 1500 gram or more and/or gestational age 32 weeks or more'. Could the authors clarify why these cut-offs were used?

Response: We chose these cut-offs considering the fact that babies born with very low birth weight and preterm babies have their own risks and complications. In general, all babies with birth weight less than 1500 gram and 32 weeks of gestation are routinely admitted in NICU and treated with antibiotics considering the risk of hospital acquired infections and sepsis.

Comment 5# What is meant by 'no formal education'? Does it mean that more than 15% of the women is illiterate (table 1)? Or did they not finish primary school? Could it be that women with little or no formal education are underrepresented in the sample and that this might be the result of the aforementioned potential selection bias due to geographical remoteness?

Response: Explanation to 'no formal education' has been added in page 7, lines 16-19. Mothers who are illiterate or have received education through informal trainings other than in schools were categorised as having 'no formal education' while those who had gone to school for education were considered as having 'formal education'.

Yes, it is possible that in our sample, there were more number of literate women (85 %) because we studied on a topic engaging younger age-group. Other reason might be that literate ones might have more access or preference for institutional delivery. Thank you.

Comment 6# Antenatal care: it might be interesting to the reader not familiar with the Nepalese health care system to understand how this is organized. For instance, what is meant by a 'skilled provider'? And do women go to the same hospitals for their ANC as for the delivery?

Response: By 'skilled provider' we mean the health care provider (Doctors or Nurses or Paramedical staffs) who have received formal trainings on 'maternal and child health' (Skilled Birth Attendant training). Women may not go to same hospital for their ANC as for their delivery.

Comment 7# Severe anaemia during pregnancy: since data sources/measurement refers to data collected at the hospital during and after delivery and through semi-structured interviews, how was this information collected?

Response We have mentioned in the data sources heading in page 6, lines 12-16 'a data retrieval form was used to extract clinical information on mothers and newborn from the patient records and register'.

Comment 8# Could it be possible to add the test which was used to calculate the incidence rates and p-values?

Response: The incidence rates were calculated by dividing the number of neonatal infection by total number of neonates in the respective group. The P-values were calculated by using Chi-square test and fisher-exact test.

Comment 9# Did the authors consider using for instance t-test or chi square for comparison of groups?

Response: We used chi-square test for comparison of the groups.

Comment 10# Please introduce the use of crude and adjusted odds ratios as they are used in the results section.

Response: They have been explained in page 9, line 19-21 as “Crude odds ratios were calculated from
bi-variate analysis and adjusted odds ratio were calculated from multi-variate analysis.”

Comment 11# We suggest to reduce the results section and not to copy the entire tables 1, 2, 3 in words. It might be sufficient to focus on the most remarkable findings.

Response: The result section has been revised.

Comment 12# For each paragraph it might be good to add some more explanation for readers unfamiliar with the Nepalese health care system. What are the practical implications derived from the results?

Response: The necessary explanation has been added in the background in page 5, lines 6-10 as “In Nepal, maternal and newborn health service is delivered through three tier approach. Primary health care center provides routine antenatal care service, normal vaginal delivery and basic newborn care. District or secondary level hospital provide basic emergency obstetric services and in-patient management of sick newborns. Regional or tertiary level hospital provide comprehensive emergency obstetric services and specialized newborn care to sick newborns.”

Comment 13#: For example, infections can happen when the newborn is transferred to the sick newborn care units, but what is needed for a reduction of infections during this transfer? Are sick newborn care units in a worse state than general neonatal care units?

Response: One of the possible source of infection is sick newborn care units as they cannot be considered sterile enough. This can be said on the basis of our study findings. However, we are not comparing the condition of general neonatal care units to sick newborn care units. (page no- 12, line 11—13 as “Hospital acquired infections may occur when babies born with asphyxia are transferred to sick newborn care units for further management where the units are not in a sterile condition”

Comment 14# When young mothers have poor hygienic practices, does that mean that they should be better informed on how to handle their babies just after delivery? Is this part of the ANC?

Response: Yes, the young mothers should be made aware and informed about hygiene practices just after delivery. Though hygiene practices and information on other measures of health promotion are part of ANC, handling of baby after delivery is a part of Post-natal Care (PNC).

Comment 15# Intuitively it seems unusual that advantageous ethnic groups have more restrictions in the hygiene practices than disadvantage groups. Could it be briefly explained? The very last sentence in the conclusion (which is missing a verb) would suggest that there is no reason to state that in Nepal advantageous ethnic groups have more restrictions in the hygiene practices than disadvantage groups.

Response : We have made the explanation in page 12, line 22 and page 13 lines 1-3 as “Many cultural practices of advantageous groups like wrapping newborn with old clothes, applying oil to umbilical cord and poor breast feeding practices can result in neonatal infection. A study in a rural Nepal showed that the level of awareness among disadvantageous group is better than advantageous ethnic group.”
Comment 16# The authors claim that the study is likely to be representative for the incidence of neonatal infections in Nepal. Either they should argue why they think this is the case or drop the statement. For example, the set-up of the study, as questioned above in the methods section, might support the idea of a selection bias.

Response: This is a cohort study conducted in 12 hospitals ranging from district, zonal, sub-regional and regional level on the basis of service coverage area. These hospitals are located in densely populated areas of Nepal. These are government run institutions and services on maternal and child health are mostly free of cost. We agree that the neonatal infection incidence can represent the hospital based incidence rate rather than nation-wide

Comment 17# Table 3 Comment: Please add the reference category.

Response : Reference categories has been added.

Comment 18# Comments: Non-exhaustive typo issues: P3/line4: &lt;-value: missing '1': p-value&lt;0.001 not 0.00. P6/line18: 'open-ended questionS'. P7/line10: 'MotherS who…' P8/line1: 'at least.one', dot between least and one. P9/line11: 'The variables… was included' should be '…were included.' P10/line 13 'aN infection'

Response : All typos mentioned were corrected. Thank you for your review.