

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Risk Factors for Mortality in a Hospitalized Neonatal Cohort in Botswana
AUTHORS	Kitt, Eimear; Hayes, Molly; Congdon, Morgan; Ballester, Lance; Sewawa, Kgotlaetsile; Mulale, Unami; Mazhani, Loeto; Arscott-Mills, Tonya; Steenhoff, Andrew; Coffin, Susan

VERSION 1 – REVIEW

REVIEWER	Sujata Sujata National Institute of Nursing Education Post Graduate Institute of Medical Education and Research, National Institute of Nursing Education
REVIEW RETURNED	13-Apr-2022

GENERAL COMMENTS	This is a relevant and interesting submission offering good knowledge regarding risk factors for neonatal mortality. The main challenges in reading the submission are (for a generic audience) : The literature referred to is appropriate and well referenced.
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REVIEWER	Tapas Banerjee Dr Ram Manohar Lohia Hospital and Post Graduate Institute of Medical Education and Research, Department of Neonatology
REVIEW RETURNED	10-May-2022

GENERAL COMMENTS	Overall 1. The manuscript is not written well. There are lots of grammatical mistakes throughout the manuscript. Write up def needs improvement Title Title is not clear as which cohort the author was studying i.e. neonates in a community or in hospital set up Introduction This part needs to be rewritten again highlighting 1. Why it is important to focus on neonatal as compared to post-neonatal mortality 2. distribution of timing of neonatal death 3. What is the national figure of neonatal mortality in Botswana 4. Why this study is important and what will it add to the literature 5. The 2nd para in introduction section needs to be deleted as it is irrelevant to discuss only neonatal sepsis as a cause of neonatal mortality Methods 1. what are premature unit, full term unit, overflow unit and nutritional support unit. Explain in detail as there is no such standard nomenclature
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	<p>2. Sepsis is usually entertained as one of the differentials for all those cases with new onset clinical symptoms. It is usually either ruled in or ruled out based on analysis of clinical symptoms along with the lab results. So, how author pinpointed the diagnosis of sepsis in the present study?</p> <p>3. What is code event</p> <p>4. why 2 softwares were used for analysis</p> <p>Result</p> <p>1. why babies with HIV exposure were admitted to the unit??</p> <p>2. Mention the graphical representation of the morbidities (include numbers) with which the babies were admitted in the NNU</p> <p>3. What was the reason for such a discrepant mortality rates between NBW and LBW</p> <p>4. There is gross mistake in data representation in table 1</p> <p>References</p> <p>reference 24,27and 28 are >10 yrs old</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Comments to the Author:

This is a relevant and interesting submission offering good knowledge regarding risk factors for neonatal mortality. The main challenges in reading the submission are (for a generic audience) :
The literature referred to is appropriate and well referenced.

We appreciate the review of our manuscript and thank the reviewer for their comments.

Reviewer: 1

Competing interests of Reviewer: NO

Reviewer: 2

Comments to the Author:

Overall

1. The manuscript is not written well. There are lots of grammatical mistakes throughout the manuscript. Write up def needs improvement

We have reviewed the manuscript for grammatical errors and are unable to find any spelling errors. We do note that this manuscript used American English and so, should it be preferred, we are happy to convert this to British English. If errors are found by the editorial staff, we are more than happy to fix them.

Title is not clear as which cohort the author was studying i.e. neonates in a community or in hospital set up

We have included the word 'hospitalized' to clarify that this study was of hospitalized neonates only.

Introduction

This part needs to be rewritten again highlighting

1. Why it is important to focus on neonatal as compared to post-neonatal mortality
2. distribution of timing of neonatal death
3. What is the national figure of neonatal mortality in Botswana
4. Why this study is important and what will it add to the literature
5. The 2nd para in introduction section needs to be deleted as it is irrelevant to discuss only neonatal sepsis as a cause of neonatal mortality

We appreciate these suggestions and have expanded our introduction to address the above points. Specifically, we have outlined the significant mortality risk associated with the neonatal period in particular, the timing of neonatal deaths in low resources settings, the national statistics specific to Botswana and the reason for our performing this study; namely to identify modifiable risk factors where efforts can be focused to reduce mortality rates in Southern African NICUs. We did leave in the section on neonatal sepsis as our paper focuses both on (1) risk factors for mortality in neonates in general in addition to (2) a sub-analysis of risk factors for mortality in neonates with sepsis, given the high burden of infection in the population.

Methods

1. what are premature unit, full term unit, overflow unit and nutritional support unit. Explain in detail as there is no such standard nomenclature

The Princess Marina Hospital Neonatal Unit (NNU) contains 39 beds in which there are “units” including a 6-bed neonatal intensive care unit (NICU) for critically ill infants, a premature unit for infants less than 32 weeks admitted for reasons related to preterm status, a unit for late preterm infants between 32-37 weeks requiring nutritional support, a full-term unit for infants admitted above 37 weeks, an overflow unit to manage additional neonates when census is high, and an isolation unit for infants with known colonization or infection with multidrug resistant organisms. We have clarified this in the manuscript as follows:

Line 89-96: “The NNU contains 39 beds including a 6-bed neonatal intensive care unit (NICU) for critically ill infants, a premature unit for infants less than 32 weeks admitted for reasons related to preterm status, a unit for late preterm infants between 32-37 weeks requiring nutritional support, a full-term unit for infants admitted above 37 weeks, an overflow unit to manage additional neonates when census is high, and an isolation unit for infants with known colonization or infection with multidrug resistant organisms. The neonatal unit also cares for infants on the maternity floor that required intervention at birth and ongoing management in the newborn nursery setting.”

2. Sepsis is usually entertained as one of the differentials for all those cases with new onset clinical symptoms. It is usually either ruled in or ruled out based on analysis of clinical symptoms along with the lab results. So, how author pinpointed the diagnosis of sepsis in the present study?

Sepsis was defined as described in lines 123-126:

“A diagnosis of sepsis was defined as documentation of an episode of clinical sepsis by the lead clinician at least once in the medical record throughout the hospitalization. Sepsis was classified as early onset sepsis (EOS) if sepsis was documented within the first 3 days of birth, and late onset sepsis (LOS) if sepsis was diagnosed after 3 days of birth.”

3. What is code event

We defined critical illness as patients who were admitted to the Neonatal Intensive Care Unit (NICU) section of the NNU, or if they required an intubation and/or had a code event requiring neonatal resuscitation in the first 24 hours after admission to the NNU. A code event was defined as requiring neonatal resuscitation (specifically requiring vasoactive medications) in this 24 hour period.

4. why 2 softwares were used for analysis

The analysis was done by 2 study team members who each specialize in separate software platforms. Descriptive statistics were completed by E.K. using Stata, cox proportional hazard models were run by L.B. using SAS and confirmed by E.K using Stata.

Result

1. why babies with HIV exposure were admitted to the unit??

The finding of HIV exposure was one of a demographic nature; in that the baby was not admitted solely for this reason but instead HIV exposure status was documented for all neonates in the study.

2. Mention the graphical representation of the morbidities (include numbers) with which the babies were admitted in the NNU

Table 1 outlines the full cohort (n=229) of patients and the sepsis sub-cohort (n=140) with associated comorbidities including: birthweight and gestational age, HIE, HIV exposure status and congenital abnormalities.

3. What was the reason for such a discrepant mortality rates between NBW and LBW

This was a somewhat unexpected finding and our theory for this is discussed in detail in lines 215-232. We hypothesize that LBW infants are admitted primarily for nutritional support and typically of low acuity. However, infants born at extremes of birthweight (i.e., either NBW or ELBW) are typically of higher acuity. For example, of the NBW neonates who died, 12/21 (57%) occurred in the first 48 hours. Additionally, Princess Marina Hospital (PMH) is a referral hospital for Southern Botswana. Hence many high risk deliveries (including those where the baby may be at significant risk for hypoxic ischemic encephalopathy) are delivered at PMH.

4. There is gross mistake in data representation in table 1

We have rechecked our data results and are unable to find any gross mistakes. We would like to point out that, as highlighted below the table, there were some missing data thus not all fields add up to the total cohort.

References

reference 24,27 and 28 are >10 yrs old

While these references are indeed over 10 years old, we feel they are relevant to include in our paper, particularly given the sparse nature of literature in this area, to which we hope our study adds.