

ANSWERING REVIEWERS

Dear Editor,

Please find enclosed the edited manuscript in word format (file name: 22144-Review).

Title: Facility-based constraints to exchange transfusions for neonatal hyperbilirubinemia in resource-limited settings

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Name of Journal: *World Journal of Clinical Pediatrics*

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Firstly, the title has been revised for better clarity. Secondly, the manuscript has been revised to reflect the following observations/suggestions from the reviewers:

Reviewer No. 00742205

1. No good solution was provided by this review but intensive phototherapy can by some time when immediate solution is not available.
Reply: The review has highlighted potential delays that need to be promptly and appropriately addressed to minimize the duration between the decision to exchange and when the procedure is done. Intensive phototherapy seeks to optimize the window of opportunity provided by the unavoidable waiting period for ET.
2. Another important message provided by the authors is the fact that G-6-PD deficiency is one of the most common causes of hemolytic jaundice in the resource-limited countries which is a situation that O-negative blood is probably not necessary for the exchange transfusion. However, G-6-PD deficiency usually will not cause severe hemolysis unless the baby is exposed to free radicals generating drug or chemicals. How to avoid the chemicals or drugs that cause acute hemolysis should be addressed.
Reply: We agree with reviewer and wish report that this aspect has been comprehensively addressed elsewhere [References 8 & 15].
3. Although the authors did raise the concern that low blood count may delay the exchange transfusion but it should not be a concern since the risk of anemia is far less important than the severe jaundice.
Reply: We agree with the reviewer that the risk of anemia is far less important than the severe jaundice. However, blood Banks will not readily dispense blood with low packed cells unless it is absolutely impossible to get blood with normal packed cells. Consequently, some delay is inevitable.
4. With limited resource available we do hope experts in this field can come up with good idea such as the filtered sunlight phototherapy that can buy some time for the physicians.
Reply: This observation has been noted in the manuscript [see page 6, lines 189-192].
5. The paper is relatively well-written but not without grammatical errors and inadequate use to words. To point out a few:
 - 1. Page 3: The procedure is not risk-free as it is commonly associated with complications such as sepsis, electrolyte imbalance, air embolism, portal vein thrombosis, cardiac overload,

---. It is actually not very common if the performer is well-trained. The use of cardiac overload will be better change into fluid overload.

Reply: We have revised this statement appropriately [see page 3, line 84].

- 2. Page 5: --- the attending staff well trained to provide the best possible care for the affected infants preparatory to ET. The word attending should be taken out.

Reply: Done.

- 3. Page 5: Additionally, mother's blood may also not be available on-time because of critical illness or the mother is on admission in another hospital. Does it mean "in-time"? Also, the mother is admitted in another hospital.

Reply: Revised as suggested.

- 4. Page 5: Difficulties may also be encountered where the mother is unavailable due to premature death. Why describe the mother's death as "premature death"?

Reply: Child birth is a natural process that should ordinarily result in death. When such unexpected death occurs before the average life expectancy of around 63 years in LMICs, it is regarded premature.

Reviewer No. **00503689**

No comments for authors to address.

Reviewer No. **02446483**

1. There are repetitions and some parts, like metabolism of the bilirubin are not highlighted. This part should be more expanded with a schema.

Reply: A section on 'Bilirubin metabolism and neurotoxicity' has been introduced. See page 4.

2. Some words seem to be not correctly selected.

Reply: The entire manuscript has been critically edited to address this observation.

Reviewer No. **00069139**

1. May I suggest that the potential solutions of the problem that is a very important part of this paper be composed as Table - 2. - The paper seems to be a health system management or health economics.

Reply: We appreciate this observation and wish to state that having identified the potential sources of delay, we are of the view that different approaches and initiatives may be necessary across the heterogeneous settings in LMICs depending on the status of the health system. We have provided some suggestions on the way forward in the manuscript to guide policy intervention as most of the delays are systems-based requiring inputs outside the control of the clinicians (lines 341-355).

2. It might be good to show some figures about financial, investment cost or unit cost in this ET matter. - A couple of photo of typical ET facility in the LICs may interest some readers who are not able to imagine the hospital in Africa. Please do not worry about my suggestion. The paper is good as is and worth publishing. However, to the reader's point of view, it might be more interesting if you could add some points.

Reply: We thank the reviewer for this suggestion. We deliberately did not dwell of the various techniques for exchange transfusion as these are well covered in standard pediatric textbooks and reference 4 in the main text. We have, however, added a new figure (#1) for the benefit of the readership.