

Dear Editor,

Thank you for the opportunity to address the reviewer comments. We believe this has allowed us to significantly improve the manuscript. Below, we address each comment: our response is in italic font, with changes to the manuscript shown in bold font, with strikethrough for deleted parts.

Reviewer 1:

1. The authors present an interesting retrospective study evaluating risk factors in children <3years with liver transplantation within 10 years in 65 children mostly with biliary atresia. Overall, the manuscript is written well, and should be recommended for publication in World Journal of Hepatology after minor corrections.

Thank you for this comment.

2. The term surgeon should be explained better, including comments on the training and experience of the surgeons.

*We mention that all three surgeons were operating throughout the 10 year period. All three are fellows of the royal college of surgeons of Canada, and do all the adult and pediatric liver transplants at our center. We have added in the methods section the following: “All three surgeons **were Fellows of the Royal Society of Surgeons of Canada, ~~operating~~ performed all the adult and pediatric LTs** during the entire 10 year period, and transplant cases were done by whichever surgeon was on service at that time).”*

3. More detailed comments on anti-thrombin would be interesting.

*Thank you for this suggestion. We have added the following to the discussion: “First, the independent association of low anti-thrombin levels post-LT ~~transplant~~ with any thrombosis, **any** severe complication, graft loss, and ventilation days has not, to our knowledge, previously been examined or reported. **Anti-thrombin is an anticoagulant produced by the liver, with its effect mediated by irreversibly inhibiting plasma serine proteases (including activated factors X and thrombin); this effect is greatly accelerated by heparin.[34] In addition, anti-thrombin has anti-inflammatory properties.[34] Although anti-thrombin does not have beneficial effects in critically ill patients in general, it has not been studied in the setting of LT patients who are high risk for thrombosis.[34]”***

*Reference 34: Allingstrup M, Wetterslev J, Ravn FB, Moller AM, Afshari A. Antithrombin III for critically ill patients: a systematic review with meta-analysis and trial sequential analysis. *Intensive Care Med* 2016;**42**:505-520 [PMID:26862016; DOI:[10.1007/s00134-016-4225-7](https://doi.org/10.1007/s00134-016-4225-7)]*

4. Design of all figures should be optimized in a reader-friendly manner (letterings).

The figures are in the supplemental material. We have not been able to figure out how to improve the axes labelling. However, we believe that the labelling should be clear given the title provided for the figure.

Reviewer 2:

The manuscript needs major corrections regarding its all parts (Abstract, introduction, Patients and methods, results and discussion) see the revised manuscript.

We address each comment made on the manuscript in the below.

1. Abstract: use LT to abbreviate liver transplant; write 'aged' instead of 'age'; and several suggested corrected grammar and language to each section.

We have written it as "of age" for better reading, instead of the suggested "aged". We have so many abbreviations in the abstract that we decided not to abbreviate liver transplant "LT"; however, we agree that we should do this in the manuscript, and have done so.

We have made grammar and language changes as suggested to make the abstract easier to read. Thank you for this suggestion.

2. Core tip: use "less than" instead of "under" age 3 years.

We have made this change.

3. Introduction: "need correction regarding language grammar, references and scientific content."

We have made extensive changes to grammar and sentence structure. We are not sure what the concern is about references and scientific content, as we believe the information discussed in the introduction is accurate.

4. Methods: all paragraphs are said to "need correction regarding language, grammar, references and scientific content", to "need to be shortened" and to "need alignment".

We have made extensive changes to the methods section paragraphs to improve language, grammar, and to shorten the paragraphs. We are not sure about what the comment about references and scientific content is referring to, as here we describe the methods we used, and we use only few references, all of which we believe are scientifically accurate. We also do not understand the "need alignment" request. Of note, we did not correct the word "missingness" to read "missing ness" as the correct statistical term is indeed "missingness".

5. Results: first paragraphs "needs correction regarding language".

We have made many corrections to improve the language, as suggested.

The question about "any severe complication": was it according to any classification? This was also mentioned in the methods section as a suggestion to "put the complications according to clavien grading classification."

This is an interesting question. We did not use a formal classification system to determine the "any severe complication" definition used. We considered the complications that the co-authors agreed were most concerning after LT, in our clinical experience affecting graft and liver survival, and patient morbidity. We used the definition as "any one of HAT, PVT, bile leak, bowel perforation, intra-abdominal infection, death, or re-transplant". These would all fit at least Grade III [requiring surgical, radiologic, or endoscopic intervention] or Grade IV [life-threatening requiring ICU management], and sometimes Grade V [death]. We have added the following to the limitations paragraph of the discussion to make this clear:

“Second, the ‘any severe complication’ outcome was not based on the Clavien-Dindo classification of surgical complications; however, the definition we used would include only complications of Grade III-V, and mostly of Grade IV (life-threatening requiring ICU management).⁵²”

6. Discussion: most paragraphs have the comments “The previous paragraphs need correction regarding language, grammar, references and scientific content). The previous paragraphs need to be shortened. The previous paragraphs need alignment.”, or “Rewrite!”

We have made extensive revisions to improve the language and grammar, and to shorten the discussion. Again, we are not sure what the comment about references and scientific content is referring to, as we believe these are accurate. Also, we do not understand the request that the paragraphs “need alignment”.

In the limitations paragraph we write: some variables were missing for several patients (e.g., blood products given during the transplant surgery), and others were not available (e.g., size of hepatic artery, hepatic veins, or portal vein, and graft to recipient body-size ratio).” The reviewer asks: why??? How the center doesn't record the previous data or how cannot you obtain them???

*We have modified this sentence to be more clear as follows: “Some variables were missing **from the medical records** for several patients (e.g., blood products given during the transplant surgery); ~~and others were not available (e.g.,~~ size of hepatic artery, hepatic veins, or portal vein; and graft to recipient body-size ratio).” Since this information is missing from the medical records [i.e., was not recorded in the patient’s chart], we have no way to obtain data regarding the missing variables.*

Reviewer 3:

In this retrospective study, Alobaidi et al investigate potential predictor variables of complications post-operatively in the PICU after liver transplantation in children age <3 years. They found surgeon was associated with complications, and whole liver graft and lower AT postoperative were associated with more early complications. This study is another one study about this topic that has been analyzed by other groups with variable results. Although this study has some limitations described by authors, and sample size is small/modest, results suggest a new potential risk factor for early complications in young children.

Thank you for this comment.

Thank you again for all the reviewers’ comments, and the opportunity to respond to each.

Sincerely,

Ari Joffe, for the co-authors