

In response to reviewer

Round #1

#Reviewer 1

Specific Comments to Authors: The paper presents data on vaccinations and infections during the follow-up of children with liver transplantation. There are important data as in Asia there is little in the literature about that. It is important to know that immunization can prevent some of the infections in these patients. The findings of this study add to the data from other parts of the World and present that only a part of these patients was correctly vaccinated before, and even after liver transplantation some did not catch-up the schedule. Also, they present the severity of the infections and the etiology function to the time from transplantation.

1. Even that the title reflects the main subject of the manuscript, I would change it as " and the others" does not sound very professional...
 - We have corrected as your suggestion. The title was changed from "vaccine-preventable vaccine infections and others" to "vaccine-preventable and non-vaccine-preventable infections"
2. The abstract summarizes the work in this study but it must be improved: - the phrases should be corrected (infections ... and its morbidity and mortality were high... infections could not be high but could be more frequent probably).
 - Thank you very much for your kind comment. We changed "its morbidity and mortality were high" to "may be more frequent"
3. also, the methods could be presented more clearly, without repeating "in our hospital" or "VPIs and non-VPIs" - morbidity could be referred to as the severity of the infections probably
 - We changed "in our hospital" to "at King Chulalongkorn Memorial Hospital in Thailand" and omitted some repeated in our hospital and VPIs and non-VPIs. We also changed "morbidity" to "severity of infections," as a suggestion.

4. as the authors described the length of stay and ventilator support in ICU - the results also should be corrected: age probably should be mean age; time of the follow up should be " between" - do not put results in the conclusions
 - We changed age and the follow-up time to the mean age and the mean follow up duration.
5. The keywords reflect the focus of the manuscript but I would not include both immunization and vaccination as here it refers to the same idea.
 - We omitted vaccination in the keywords already and added "hospitalization, Thailand" to keep 6 keywords.
6. The Background (introduction) seems to be very short, describing the present status and importance of the study as there are very little data on this theme in Asia. Maybe the authors could add more data about that from the literature.
 - We added more data from the literature in the introduction part. Moreover, the recommendation about the accelerated vaccine by IDSA and AST was also mentioned in the introduction part.
7. In the Methods probably would be better to clearly define the inclusion and exclusion criteria. Again, try to not use repeatedly some words (in our hospital).
 - We added the inclusion and exclusion criteria into the materials and methods part.
8. Instead of citing from the IDSA guidelines, there is a need for reference to table 1.
 - We added the note under table 1 about the accelerated vaccines recommended by IDSA and also added table 1 into the manuscript.
9. Explain better what was done in the study (there is no word about the etiology of the infection - diagnosis and other details)

- We added "Infection etiology and source were investigated by the doctors in charge. Culture from specimens was available for all bacterial origins, and immunological and molecular techniques were available for the diagnosis of both viral and bacterial infections, including polymerase chain reaction panel analysis for respiratory tract infections and gastrointestinal infections, and antibody titers for hepatitis A/B/E, dengue, and measles" into the material and methods part

10. The Results presentation should be improved. Even that are interesting results the way the authors decided to present did not value them. Firstly, again there are repeated phrases (when presenting the number of patients with incomplete immunization).

- We deleted the repeated phrase with the same meaning of "There was a significant proportion of children who had incomplete vaccination following the Thai's EPI (n=25, 52%) and accelerated vaccine in accordance with the IDSA (n=43, 89.5%)", in our hospital, VPI and non-VPI in the result part already.

11. Secondly, again "mean age", follow-up of the patients " between". Also, there is again in the second paragraph the presentation of the follow-up period. Probably it would be better to present the mean duration of the follow-up for all patients.

- We presented the data as the mean age and mean follow-up time as your suggestion.

12. When presenting the data, there is no link with the tables. That should be mentioned in the text in the appropriate place. Table 3 could be separated into 3 different smaller tables as it contains 3 different aspects (the type of infection, the organs, and the severity and mortality); mortality could not be included in morbidity.

- We mentioned table 1-6 in the manuscript and divided table 3 into 3.1, 3.2, and 3.3.

13. Table 4 should be changed as it is very difficult to be understood in this way. You can list the pathogens on a column (grouped in bacteria, viruses) and the time on the first line. In this way, the numbers could be easily viewed by the readers.

- We edited the table 4 as a suggestion to bacterial and viral/fungus/unidentified origins.

14. The authors interpret the results appropriately, highlighting the important aspects, but they should not repeat the presentation of the results.

- We deleted the repeated words and sentences in the result part.

15. In Discussions, all the data from the study should be discussed in correlation with other data from the literature. Maybe it would be better to compare with studies from other important centers from other continents.

- We added the correlation with other data from the literature in the discussion part as a suggestion. "To the best of our knowledge the current study is the first to investigate immunization status and infections requiring hospitalization in Asian children who underwent a liver transplant. Compared to previous studies in Europe^[9,10] and the United States^[4], in the present study there was a higher rate of incomplete age-appropriate immunization before liver transplantation, particularly with respect to the accelerated MMR and varicella vaccination. However, the number of hospitalizations with VPIs (13.1%) was comparable to that in a study conducted in the United States by Feldman et al.^[4] (11.3%). Moreover, the VPIs in that study were more severe and required longer hospital stays than those in the current study. Genetic risk factors may explain this phenomenon, as with the more contagious and severe coronavirus disease 2019 infections in Europe and the United States than in Thailand."

16. Biostatistics. There is very few statistic analysis presented in the paper. That should be improved.

- We added more statistic analysis and p value in table 2-5.

17. The authors cited appropriately important references, less in the introduction, and more in the discussion sections.

- We cited the important references more in the introduction part as suggestions.

18. The manuscript needs to improve the presentation, both in some aspects of the language and style of writing. The study was reviewed and approved by the local ethical review committee even that is mostly a retrospective study and there are no interventions. The authors tried to present also the limitation as they have data from a single-center, with not many patients included.

- We have already sent the edited manuscript to native English, polishing again at the final step.

19. The conclusions paragraph should be added at the end of the text of the manuscript, before ARTICLE HIGHLIGHTS (without presenting the results).

- We added the conclusion part "Incomplete immunization was common in children pre-liver transplant and post-liver transplant. Almost all of the children in the study required hospitalization due to VPIs or non-VPIs within 5 years post-liver transplant. The severity of infections was highest in the first year post-liver transplant." As the journal requirement.

Again, we would like to express our sincere gratitude for your time and constructive suggestions for our manuscript. Thank you very much, indeed, for your devotion.

#Reviewer 2

Specific Comments to Authors: This manuscript addresses an informative issue associated with infections after liver transplantation including vaccine preventable

diseases in Thailand. Pathogens causing hospitalization after the transplantation has been described in detail. 1) The focus of the manuscript is not very clear. The authors tell about incomplete immunization, and the number of cases with vaccine preventable and unpreventable diseases, but the relationship between them is not clear. 2) The authors do not show how important the immunization before the transplantation is. Among 48 children, the authors should show 2 x 2 table with some adjustments; (the number of children who developed vaccine PREVENTABLE or UNPREVENTABLE diseases) x (the number of children with COMPLETE or INCOMPLETE immunization before transplantation). Did the children with INCOMPLETE immunization tend to develop vaccine-preventable diseases? Reviewed, until July 4, 2020.

- Thank you very much for your intellectual aspect to improve our manuscript. We appreciate your kind suggestion. We added 2x2 table analysis using Chi-square test between the number of children who developed vaccine-preventable or unpreventable diseases and the number of children complete or incomplete immunizations and presented this analysis in the manuscript and table 4.

Other revision

- We would like to change the authors, funding as a highlight in red characters, and the attached documents (Copyright Licence Agreement Form, funding document) also be changed as well.

Round #2

#Reviewer 1

The paper was improved based on the recommendations. Still, some small corrections need to be done: - typo corrections; - I would not add the number of cases in discussions chapter when VPI hospitalizations are presented

- Thank you very much for your suggestion. We deleted the numbers of cases in discussions chapter when VPI hospitalizations are presented from "The VPIs requiring hospitalization in the current study were due to rotavirus (n = 8), influenza (n = 6), varicella (n = 5), dengue fever (n = 4), measles (n = 3), S. pneumoniae (n = 2), hepatitis B/E, and Vibrio cholerae (n = 1)." to "The VPIs requiring hospitalization in the current study were due to rotavirus, influenza, varicella, dengue fever, measles, S. pneumoniae, hepatitis B/E, and Vibrio cholerae." Enclosed is the

manuscript file that we have edited. Thank you very much indeed for your time and kind suggestion.