**Reviewer’s report**

**Title:** Number of cholangitis episodes as a prognostic marker to predict timing of liver transplantation in biliary atresia patients after Kasai portoenterostomy

**Version: 0 Date: 02 Apr 2017**

**Reviewer:** Jaime Chu

**Reviewer's report:**

Chen et al. present a study to examine whether cholangitis post-Kasai portoenterostomy (KP) is a prognostic marker for liver transplant (LT) in biliary atresia. While this question has been looked at before, a strength of this paper is the use of this national database, NHIRD, over a 14-year period, and, as the authors point out, in Taiwan where there is universal stool card screening. The methods used were well-defined (i.e. use of discharge diagnosis to improve accuracy of cholangitis diagnosis). However, the major limitation inherent in the use of this database is the lack of biochemical data, namely bilirubin and ALT levels. The authors do address this limitation in the Discussion section, but this is a major factor that precludes the ability to make comprehensive conclusions. That being said, this appears to be a well-designed study that would merit publication with the following revisions:

**Major Points:**

One of the major take home points of this study is that episodes of early cholangitis did not make a difference, and that cumulative incidence of cholangitis was not related to LT in the first 2 years of KP (Lines 160-161) - more discussion needs to be provided as to why the authors believe this is the case.

A major weakness is the lack of data presented after age 2. It would be a stronger study if the authors could query cholangitis episodes past 2 yrs of age. It would be helpful to see the age at last episode of cholangitis, the total number of cholangitis episodes per child. It would be helpful if the LT patients were evaluated more closely to help determine number of episodes of cholangitis which best prognosticates risk for LT, not just the number in comparison to non-LT.
The group of BA patients that had cholangitis but avoided early LT is an interesting group to analyze - how are they avoiding early LT? This again brings up the need to look at biochemical data to help determine how cholestatic these patients are.

Table 1: liver biochemistry is lacking and very pertinent; a potential solution to this would be to query a large center within Taiwan to obtain a sample of BA patients with known biochemical correlates, and pair this with the current NHIRD analysis.

What is the p-value for age at Kasai > 60 days?

Line 105- "mortality rate did not significantly differ..." but what were the causes of mortality? These are likely different between those with or without LT. This should be addressed in the results.

The authors should provide a p-value for their statement in Lines 110-111 - the difference in rate of cholangitis within 2 years between LT and non-LT groups. These numbers differ from the "Cholangitis Rate" in Table 1 (presumably includes cholangitis episodes > 2 years).

Figure 2: Again, it would be nice to see the cumulative incidence tracked out past 2 years (ideally within the 11 year follow up period).

Minor Points:

Line 102: "More patients who underwent KP within 60 days of age survived with their native liver..." However, "more patients" who underwent KP after 60 days of age also survived with their native liver (51 patients versus 31 patients with KP>60 days and needed LT). This should be more precisely stated in the text.

Should define "late-presenting" liver failure.

Should label Y axis in Figure 3.

Should be consistent with terminology. Many different terms used ie incidence, cumulative incidence, cumulative duration vs episodes, occurrences, rate...

Hypothesis should be more clear in background- is it "time of first cholangitis episode affecting risk for LT" or number cholangitis episodes.

In Discussion, the paragraph starting "repeated cholangitis is also a consideration..." they seem to repeat the finding that repeated cholangitis episodes was significantly higher in pts with LT than in those without LT.

There are some minor grammatical errors throughout the paper.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:
Needs some language corrections before being published

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?
2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?
3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?
4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?
5. Do you have any other financial competing interests?
6. Do you have any non-financial competing interests in relation to this paper?
If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal