

Revision: Manuscript "Clinical management of acute liver failure: Results of an international multi-center Survey" (number 23730)

Dear Editor

We thank the editor and reviewers for allowing us to re-submit our manuscript entitled "Clinical management of acute liver failure: Results of an international multi-center Survey" (number 23730).

We carefully read the reviewer's comments and thank them for their concise and helpful remarks. We have now revised the manuscript in accordance with the reviewer's and editor every comment.

Below find a point-by point response to the reviewer's comments.

We hope that you now find the manuscript acceptable for publication.

Yours

Oren Shibolet

Director of the Liver Unit

Tel-Aviv Medical center

on behalf of all authors

Point-by point response:

Reviewer 02860874

1. **Comment:** Would be reasonable to presume that high-volume centers are the most expert, then I want to ask the authors if they have information about significant differences in transplant free survival and in survival after LT compared with low-volume centers?

Response: Our study is a survey addressing the clinical practice and management of ALF patients that was sent to 22 EUROALF consortium members. As a survey, the results represent the perceived views of the participants in regard to current practices in their centers. As a survey our study did not include the clinical data collected by centers over time. However, following the reviewer comment we were able to include clinical data (including clinical presentation, management and outcome) collected in our pilot run of the clinical database from 85 ALF patients admitted over a 3 months period in 13 centers. Since we could not include all centers in this analysis we were not able statistically to address the issue of "low volume" versus "high volume" centers.

Reviewer 02860540

1. **Comment:** I found this survey very interesting because it gave me an idea about the clinical management of acute liver failure. This survey involves 22 transplantation centers in 11 countries, treating between 300 and 500 ALF cases and performing over 100 liver transplants for ALF annually. This study could be of interest for the readers especially for the physicians involved in the management of the acute liver failure. This paper could stimulate a consensus about this topic. In my opinion this manuscript is suitable of publication.

Response: We thank the reviewer for the kind remarks.

Reviewer 02462179

1. **Comment:** The authors divide all centers into low volume and high volume centers. Are there any differences between two centers besides antibiotics and antifungals?

Response: Indeed the main areas of divergence between "low volume" and "high volume" centers were the use of antibiotics and antifungals. In all other aspects of care mentioned in the paper there was no statistically significant difference between "low" and "high" volume centers, with the exception of **greater** use of hypertonic saline as ICP lowering medication ($p=0.05$), this was not included in the paper due to editorial preference.

2. **Comment:** The deaths and survivals should be discussed, such as the mortality rate, the differences between two groups, and so on.

Response: We thank the reviewer for the comment. We included "real life" data as requested. See comment to reviewer 02860874.

3. **Comment:** The labels of Figure 2A and 2C have spelling mistakes.

Response: We thank the reviewer for pointing this out, figure labels were corrected.

Reviewer 02860590

1. **Comment:** The authors should show the mortality data and the survival rate. This data should be analyzed, especially the comparison between "high volume" and "low volume" centers.

Response: We thank the reviewer for the comment. We included "real life" data as requested. See comment to reviewer 02860874 and reviewer [02462179](#).