

Reviewer #1:

The manuscript is well written describing each characteristics of metabolic disease separately which contains brief summary of the disease, treatment, LTx and future possible therapies.

1. I suggest that to make the manuscript better to understand easier for the readers, the authors may provide a table contains these separately described info together. Then, the manuscript will be ready for the publication.

Thank you for this comment. With the amount of information, it is difficult to condense this into a table format. We illustrate Figure 1 to set an outline of our manuscript for the conditions we describe in more detail in the text.

Reviewer #2:

This was a nice review on paediatric liver transplantation for inherited metabolic liver diseases. Although rare, these conditions represent increasing indications for liver transplantation in Centers with a Paediatric Liver Transplant Program. References are appropriate. The paper is not redundant and is void of typos.

1. Figures 1 and 3 are good, I would reconsider figure 2, explaining different types of available organ transplants (domino, deceased donor, living donor, auxiliary). Figure 1 is good; I would suggest to modify Figure 2 adding different types of liver transplantation (domino, split, auxiliary, living-donor). Figure 3: I suggest to add also graft survival.

Thank you for this comment. We have kept Figure 2 mainly to demonstrate auxiliary transplantation as described in the text, as opposed to the other common transplantation techniques.

2. Allogenic hepatocyte transplantations: are there available data on animal models or humans?

Thank you for this comment. Yes there are both animal and human studies on allogenic hepatocyte transplantation. We have included this in our references (Ref 10,11,35, 42, 43). We have not gone in to too much detail, as it is beyond the scope of this manuscript.

3. What medications can be used to increase nitrogen excretion in UCD?

Thank you for this comment. We have added examples of medications to increase nitrogen excretion in UCD.

4. Do patients with UCD improve their neurological damage after LT?

Thank you for this comment. We have now included a statement on cognitive outcomes and liver transplantation.

5. LT for WD: unfortunately, neurological improvement is not universal after transplant. This point may be added.

Thank you for this comment. We have stated that extra-hepatic symptoms generally improve after transplantation, particularly neurological signs.

6. Patients with MMA: is simultaneous LKT encouraged ? are there available data about the long-term outcome of these patients?

Thank you for this comment. There is no good long term data on outcomes of children who have received LKT transplantation. Selection of LKT has to be based on highly individualised criteria as stated on pg21.

7. GSD: the Authors said that adenomas can be considered indication to liver transplantation. Are there definite criteria (i.e., number, size, etc?)

Thank you for this comment. We have included the following “increase in size or appearance of new lesions” as indication for liver transplantation.

8. Is chronic rejection more prevalent in LBMD than other paediatric indications?

Thank you for this comment. We have alluded to the fact that chronic rejection is a common problem in liver transplantation for LBMD on pg21. However, with current immunosuppression regimes, we have not seen increased rates of chronic rejection in LBMD compared to other paediatric transplant indications.

9. Minor comments: - typos: orlistat instead of orlistate; figure 1 haemochromatosis

Thank you for these comments. This has been amended.

6 EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) *Science editor:*

5 Issues raised:

(1) All the author's institution information needs to provide a postcode. The corresponding author needs to provide more detailed address information, such as street information

Thank you for this comment. This has now been updated.

(2) I found the authors did not provide the original figures. Please provide the Figures cited in the original manuscript in the form of PPT. All text can be edited, including A, B, arrows, etc. With respect to the reference to the Figure, determine if it is the original Figure, if not, please provide the source of the picture and the proof that the Figure has been authorized by the previous publisher or copyright owner to allow it to be redistributed;

Thank you for this comment. We have now provided all figures in PPT. Figure 1, 2 and 3 (data from our centre) are original figures.

(3) I found the authors did not add the PMID and DOI in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout; and

Thank you for this. We have included DOI and PMID for the reference list.

(4) the author should number the references in Arabic numerals according to the citation order in the text. The reference numbers will be superscripted in square brackets at the end of the sentence with the citation content or after the cited author's name, with no spaces.

Thank you for this comment. References are now superscripted in square brackets.