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PEER-REVIEW REPORT

Name of journal: *World Journal of Hepatology*

Manuscript NO: 74526

Title: Natural history and management of liver dysfunction in lysosomal storage disorders

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05230413
Position: Peer Reviewer
Academic degree: MD
Professional title: Doctor
Reviewer's Country/Territory: South Korea
Author's Country/Territory: India

Manuscript submission date: 2021-12-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-01-01 12:28

Reviewer performed review: 2022-01-01 12:45

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

With interest, I read the manuscript entitled "Lysosomal storage disorders: Liver dysfunction and its outcome". The manuscript was well-written and the references were correct. I would like to recommend the authors to provide 1) schematic diagram of pathogenesis 2) photos of clinical presentation and pathology.

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Peer-review model: Single blind

Reviewer's code: 00722050

Position: Peer Reviewer

Academic degree: FRCP (C), MD, PhD

Professional title: Professor

Reviewer's Country/Territory: Canada

Author's Country/Territory: India

Manuscript submission date: 2021-12-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-02-05 01:35

Reviewer performed review: 2022-02-05 11:35

Review time: 10 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Thank you for the opportunity to review this manuscript. The manuscript is well written, but it is not comprehensive and numerous disorders have not been correctly included. An example is mucolipidosis type II or sialidosis, which has been indicated as a potential liver failure. There are reports in American Journal of Perinatology and Human Genetics about major liver dysfunction. The statement of the authors "Lysosomal storage disorders that cause liver dysfunction are Gaucher disease, Niemann-Pick disease and lysosomal acid lipase deficiency. Those that have neonatal-onset, predominant extrahepatic and multisystemic presentations have a poor prognosis. For the rest of the conditions, the options are enzyme replacement therapy (variable response) and liver transplantation." is unfortunately not correct, but there is a lot of potential in this manuscript. The authors should also liaise with NORD and other US based LSD databases for more information.

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Manuscript NO: 74526

Title: Natural history and management of liver dysfunction in lysosomal storage disorders

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05088164
Position: Associate Editor
Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Romania

Author's Country/Territory: India

Manuscript submission date: 2021-12-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-01-22 13:10

Reviewer performed review: 2022-02-08 08:47

Review time: 16 Days and 19 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors of this manuscript intended to review the liver involvement in lysosomal storage diseases. The abstract should be improved to present the essential aspects of the review, and it should also be clarified in the abstract the forms of LAL deficiency for a better understanding. The introduction brings important info in this field. There should be an explicit aim of the review presented at the end of this section. What this review brings new to the literature? The presentation of all three disorders is not uniform. The manuscript should be reorganized. For example, the pathology/histology of the liver is presented before clinical manifestations. The biochemical liver tests are presented in-depth in one disease, not in others. For example, in 1.3.1, hepatomegaly is presented in a separate section entitled biochemical liver dysfunction. There is only one sentence about the liver test and then again about the liver biopsy. The sections for GD should be rearranged and put in a logical order. Also, the section on Nieman Pick disease must be reorganized, and some info can be shortened (as liver function 2.3.2 is too in-depth compared to other similar sections). The three types of NP disease presentation did not follow the same structure, and it would probably be better to separate all aspects in 3 sections, not some to be together and some separated. Why for NPD-C did authors choose to have also extrahepatic manifestations discussed? Again for LAL-D the structure of this section should be changed. Some aspects are presented together, then an extensive section on CESD and a small one on WD. The conclusions should be improved. The tables are well designed and very explicit regarding the main aspects of the LSDs. Editing: - All the punctuation marks should be verified - The abbreviated words should be defined at first use and then used correctly in the

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manuscript - The numbering of the section should not overlap with the list of types (for example – at Gaucher disease types – no need for numbering here) The English language can also be verified again for some sentences that could be better written.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Hepatology*

Manuscript NO: 74526

Title: Natural history and management of liver dysfunction in lysosomal storage disorders

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05088164
Position: Associate Editor
Academic degree: MD, PhD
Professional title: Associate Professor
Reviewer's Country/Territory: Romania
Author's Country/Territory: India

Manuscript submission date: 2021-12-27

Reviewer chosen by: Han Zhang

Reviewer accepted review: 2022-05-01 16:29

Reviewer performed review: 2022-05-01 17:27

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Based on the authors answer to reviewers comments, I intended to verify the changes. Probably there is a problem with the system as I did not see the changes in the manuscript (no blue markings). Still, there are editing problems, English language corrections to be made, punctuation to be corrected. The structure of the chapters should be simplified. There are no number for 1, 2, 3, 4, just for the sub-chapters. It seems that are too many. Hepatomegaly is part of the clinical features in all diseases. Why a separate chapter? I would organize all the diseases in Clinical aspects, Laboratory/paraclinical or histology characteristics, Treatment and Outcome. Also, I would improve the title. In figure 6, better to use hepatosplenomegaly instead of splenohepatomegaly, Why there is a title "Main manuscript" after the Introduction?