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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 71356

Title: In-Hospital Mortality of Hepatorenal Syndrome in the United States: Nationwide Inpatient Sample

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05022758
Position: Peer Reviewer
Academic degree: MD, PhD
Professional title: Surgeon
Reviewer's Country/Territory: Poland
Author's Country/Territory: United States

Manuscript submission date: 2021-09-04

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-09-06 09:18

Reviewer performed review: 2021-09-16 13:51

Review time: 10 Days and 4 Hours

Scientific quality	[Y] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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

Kaewput et al. present the result of a nationwide, retrospective cohort study evaluating in-hospital mortality of hepatorenal syndrome in the United States. They found that in-hospital mortality among patients admitted for hepatorenal syndrome significantly improved during the analyzed period. Moreover, they identified several predictors for hospital mortality. The overall scientific quality of the manuscript is excellent and the authors must be praised for their extensive work on the subject. I have only a few comments regarding the manuscript. • In the results section, the length of hospital stay and hospitalization cost are presented as median values whereas in table no 1 they appear as mean +/- SD. • In table no 1 an asterisk appearing after SE does not have an explanation below the table. • The definition of the hepatorenal syndrome has changed over the years. I understand that the national registry may not provide all the necessary answers but can authors elaborate on the diagnostic criteria of hepatorenal syndrome and whether it was uniform in the studied population? • I do agree that there are no clear indications on the use of TIPS in patients with HRS. Since mortality in patients with HRS undergoing TIPS is driven mainly by poor liver function it may be possible that there was a population selection bias and these patients had initially better liver function resulting in better survival.

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Reviewer's code: 05121717

Position: Editorial Board

Academic degree: MBBS, MD

Professional title: Consultant Physician-Scientist

Reviewer's Country/Territory: India

Author's Country/Territory: United States

Manuscript submission date: 2021-09-04

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-09-18 03:22

Reviewer performed review: 2021-09-18 03:51

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) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

Why is paracentesis associated with reduced mortality-please discuss. Add the definitions of neurological disorders and coagulopathy considered for the current study.

Hepatic encephalopathy (HE) is known to be associated with mortality (PMID: 30076614 DOI: 10.1002/hep.30208). Is it HE or other neurological disorders as well? Discuss the reason for pulmonary failure in these patients (PMID: 33065772 DOI: 10.1111/liv.14703 can be useful.) The treatment of HRS is not assessed in the study. If there is any data on vasoconstrictors should be added. As non-response to vasoconstrictors can also predict mortality. Please elaborate this major limitation-Maiwall R, Sarin SK, Moreau R. Acute kidney injury in acute on chronic liver failure. Hepatology international. 2016 Mar 1;10(2):245-57. Kulkarni A, Sowmya T, Sharma M, et alIDDF2020-ABS-0192 Terlipressin non-response predicts mortality in acute-on-chronic liver failure-a prospective cohort study Gut 2020;69:A87-A88. Was the MELD data not captured? MELD is considered as a predictor of mortality in patients with AKI-HRS (PMID: 30076614 DOI: 10.1002/hep.30208)

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Peer-review model: Single blind

Reviewer's code: 04737476
Position: Peer Reviewer
Academic degree: MBBS, MD, MSc
Professional title: Senior Lecturer
Reviewer's Country/Territory: Egypt
Author's Country/Territory: United States

Manuscript submission date: 2021-09-04

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-09-18 15:57

Reviewer performed review: 2021-09-20 08:14

Review time: 1 Day and 16 Hours

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

I would like to thank the authors for their efforts searching National Inpatient Sample database for evaluation of in hospital mortality of patients with hepatorenal syndrome that is a major complication for patients with liver cirrhosis and grave outcomes. The use of weighting is advantageous in sampling of patients, the authors used discharge weight provided by the Healthcare Cost and Utilization (HCUP) to estimate the total number of hospital admissions for hepatorenal syndrome. In the results section they mentioned that there were 4,938 hospital admissions with hepatorenal syndrome as the primary diagnosis in the unweighted sample and 23,973 admissions in the weighted sample. The difference is very big as we are talking about hospital admissions not individual patients with multiple admissions throughout their disease course. I hope the authors could clarify the cause of this difference to the readers. Also in table 1 the numbers in the second column are for unweighted sample while the third column is the percentage of the weighted sample. The authors should separate weighted from unweighted as performed in table 2. Kindly provide footnote for tables and figures with the abbreviation used. There are few writing mistakes probably typos errors for example; the repetition of the word "and" in the introduction, second paragraph, line 8; "male" in the first paragraph of the results section should be (males) and "coverted " at the end of data collection should be (converted). Minor polish is needed. The documentation and reporting of in the patient mortality of hepatorenal syndrome is crucial but, I have another inquiry for the authors about the time frame (Why exactly the time frame chosen for this study was from 2005 to 2014 and not just the 10 years before the pandemic for example?)

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Peer-review model: Single blind

Reviewer's code: 05226494
Position: Editorial Board
Academic degree: MBBS, MD
Professional title: Additional Professor
Reviewer's Country/Territory: India
Author's Country/Territory: United States

Manuscript submission date: 2021-09-04

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-09-23 11:37

Reviewer performed review: 2021-10-04 08:36

Review time: 10 Days and 20 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

It's a well written paper.