

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 75606

Title: Trends in Hospitalizations for Alcoholic Hepatitis from 2011 to 2017: A Nationwide Study.

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 01436308

Position: Editorial Board

Academic degree: MD

Professional title: Chief Physician

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2022-02-07

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-02-07 10:58

Reviewer performed review: 2022-02-12 07:04

Review time: 4 Days and 20 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No
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SPECIFIC COMMENTS TO AUTHORS

The authors analyzed the trends in hospitalizations for alcoholic hepatitis from 2011 to 2017 by analyzing the National Inpatient Sample (NIS) database. They found that the number of alcoholic hepatitis inpatient hospitalizations significant increased from 2011 to 2017. The topic is interesting and the manuscript is well-written. My comments are listed below:

1. ICD-9 and ICD-10 codes in Table 1 include not only alcoholic hepatitis, but also alcoholic fatty liver and alcoholic cirrhosis.

Response: The description of the method was corrected. We included these ICD codes in the analysis due to overlap of the alcoholic fatty liver changes, alcoholic hepatitis and cirrhosis in a lot of these patients. At the time of discharge if AH diagnosis was the first on the list then the admission would be considered primary AH admission.

2. It would be interesting to analysis the comorbidities of the alcoholic hepatitis patients.

Response: Yes, we produced more information from the database that has some comorbidities and their effects on these patients. This was added to the main results section.

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Peer-review model: Single blind

Reviewer's code: 03208726

Position: Peer Reviewer

Academic degree:

Professional title:

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2022-02-07

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-02-07 15:25

Reviewer performed review: 2022-02-16 05:56

Review time: 8 Days and 14 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This manuscript studies the changes in the hospitalization rate of ah in the NIS database from 2011 to 2017. Analyzing the hospitalization rate and mortality of ah has certain significance for public health. However, I think there are still areas for improvement in the analysis. If the author can improve or supplement these details, the content of the manuscript will be more substantial.

(1) Since the author mentioned hospitalization expenses, can we analyze the influencing factors of hospitalization expenses?

Response: This part might be hard to analyze from the current NIS database we have, because we need to take inflation into consideration, and we need to differentiate the primary diagnosis and secondary diagnosis.

(2) If the data in the database allows, can authors add the relationship between age, sex, liver function, metabolic indexes and AH mortality and incidence of complications?

Response: Yes. We produced some more information as requested by fitting a model. Liver function is not a variable recorded in the NIS database but we were able to perform regression analysis for risk factors associated with mortality and included in table 5.

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Peer-review model: Single blind

Reviewer's code: 06245556

Position: Peer Reviewer

Academic degree:

Professional title:

Reviewer's Country/Territory: Reviewer_Country

Author's Country/Territory: United States

Manuscript submission date: 2022-02-07

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Reviewer accepted review: 2022-02-10 08:08

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Review time: 7 Days and 6 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous
	Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No

SPECIFIC COMMENTS TO AUTHORS

The authors present an investigation into the number of alcoholic hepatitis-related hospitalisations between 2011 and 2017. It was not clear what the hypothesis was; however, the authors have identified a rise in the number of AH-related hospitalisations during this period. This manuscript provides an update on AH-related admissions and associated mortality risk factors. The significance lies in the substantial healthcare costs and overall prevalence of AH-related admissions, in parallel with figures of alcohol abuse in the US. The authors aim to "provide an up-to-date descriptive analysis of trends in AH hospitalizations within the United States" however the data are from between 5 and 11 years ago. Is more recent data available, and could this be incorporated into the analysis?

Answer: NIS database published data are usually lagging behind in few years, at this moment we have the database until 2017. We changed the wording of "Up-to-date" to a "relatively recent data" to fit the context.

The conclusions drawn from the study could be more insightful regarding the impact of the results generally, and for clinical practice. For example, "prevention of alcohol use" (last sentence of conclusion) is not informative, whereas "prevention of alcohol abuse" would be more relevant. In the discussion, which is currently a recapitulation of the results, a discussion around the impact of the major results could be provided.

Answer: The conclusion wording was updated.

Specific comments:

1. The title reflects the aims of the manuscript. The title should specify which nation the

data pertains to - ie. the United States. Similarly in the abstract the country under investigation should be made much more explicit, and also earlier in the introduction rather than in the last sentence of the introduction.

Answer: **Added United states to the tittle and abstract.**

2. The abstract summarises the work done. As above, the authors should make the nation of study more explicit.

Answer: **Added the country as above**

3. The keywords are appropriate.

4. Background: The introduction establishes the context of the study and its significance. A sentence describing the timeframe(s) over which severe ALD develops would be useful.

Response: **Added in the background**

5. Methods: The methods describe the cohort and the statistics in adequate detail.

6. Results: - The authors have shown that AH-related admissions in US hospitals increased between 2011 and 2017. - Is the p-value quoted in the first sentence of the results relating to the total number of hospitalisations for AH or for the percentage of total hospitalisations? If the former, have the authors adjusted for total population increase over that period?

Answer: **The p-value tests the percentages of the AH among all hospitalization over time.**

NIS HCUP database uses data that are weighted sample data to reflect the national estimates and no adjustment is needed for population change. The annual total admission was adjusted in the chi-squared test. We also conducted a trend test to test the increasing trend of the AH-related admissions in percentages

- The comment on a stable level of mortality should be moved to the discussion.

Done

Given there is a significant difference, the authors should consider commenting on the effect size similarly, the median length of stay increased from 5.98 to 6.14 days which is significant statistically though perhaps not clinically.

Answer: **Addressed in discussion**

- It seems improbably that sepsis could go from making up 7.4% of mortality risk factors in 2014 to 46.7% in 2016 and 48.3% in 2017 - can the authors provide a putative explanation for this in the discussion?

Answer: **The ICD codes used to generate sepsis flag are as below. The reason why there's a jump between 2015 to 2016 is because the conversion of ICD9 to ICD10 in hcup. We added this to the discussion now.**

Comorbidity	ICD-10
995.91 Sepsis	A02.1 Salmonella sepsis A22.7 Anthrax sepsis A26.7 Erysipelothrix sepsis A32.7 Listerial sepsis A40.0 Sepsis due to streptococcus, group A A40.1 Sepsis due to streptococcus, group B A40.3 Sepsis due to Streptococcus pneumoniae A40.8 Other streptococcal sepsis A40.9 Streptococcal sepsis, unspecified A41.01 Sepsis due to Methicillin susceptible Staphylococcus aureus A41.02 Sepsis due to Methicillin resistant Staphylococcus aureus A41.1 Sepsis due to other specified staphylococcus A41.2 Sepsis due to unspecified staphylococcus A41.3 Sepsis due to Hemophilus influenzae A41.4 Sepsis due to anaerobes A41.50 Gram-negative sepsis, unspecified

	<p>A41.51 Sepsis due to Escherichia coli [E. coli]</p> <p>A41.52 Sepsis due to Pseudomonas</p> <p>A41.53 Sepsis due to Serratia</p> <p>A41.59 Other Gram-negative sepsis</p> <p>A41.81 Sepsis due to Enterococcus</p> <p>A41.89 Other specified sepsis</p> <p>A42.7 Actinomycotic sepsis</p> <p>A54.86 Gonococcal sepsis</p> <p>B37.7 Candidal sepsis</p> <p>A41.9 Sepsis, unspecified organism</p>
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- What was the sample number used to calculate the statistics? Throughout the manuscript the authors have extrapolated the data to "produce an accurate estimate of the patient population nationwide" - but was the original smaller sample number used in the statistical analysis? This for example would not be clear from Tables 2-3.

Reponse: The LOS listed in this paragraph is the mean length of stay. The HCUP conclusion can be weighted to approximate the national estimate. All the summary statistics presented are weighted.

7. Discussion: - 71,290 is not double of 47,140, it is 1.5x

Reponse: Corrected in the discussion

- Over how many years was the 5% mortality of AH determined? Or was this just determined by those who died in hospital? This would not be an accurate determination of mortality rate.

Response: This was determined by those who died in the hospital and that is why it is not an accurate estimate of mortality. This was also addressed in the discussion part as one of the limitation of the study.

8. - Chart 1: This chart is poorly designed. Where are the axis labels? Where is the figure legend providing information on the analysis? The statistical result (p-value) should be provided for the graph, so that it can prove information when standing alone from the results main text. The y-axis should be percentage of total admissions which is a more meaningful demonstration of year-by-year changes in the number of admissions relative to total population changes.

Reponse: Chart is edited and changed as requested.

9. Why was a chi-squared test used instead of a mixed effects model? Time/Year is not a categorial variable.

Response: Chi-squared was used to compare the distribution (independence) of categorical variables (e.g., race) among all groups.

10. SI units are fine.

11. References are fine, however a reference #31 has been included in the reference list but has not been cited in-text.

Response: The Reference numbers were checked and made in order now.

12. The manuscript is concise.