

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 73759

Title: Incidence and clinical characteristics of hypertriglyceridemic acute pancreatitis: A retrospective single-center study

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05122737

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

Manuscript submission date: 2021-12-06

Reviewer chosen by: Jia-Qi Zhu

Reviewer accepted review: 2022-03-02 23:52

Reviewer performed review: 2022-03-13 03:20

Review time: 10 Days and 3 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 Grade E: Do not publish |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: [☐] Anonymous [☒] Onymous
Conflicts-of-Interest: [☐] Yes [☒] No

SPECIFIC COMMENTS TO AUTHORS

Reviewer's comments, Thank you for giving me the opportunity to review this interesting article. Lin XY et al. conducted a retrospective study regarding the clinical characteristics of HTG-AP. Because the treatment strategy for HTG-AP remains controversial, this study shows potentially significant results. However, there are several major issues to be addressed in this study. I attach the Reviewer's comments and recommend the authors to reconsider following issues. Major issues 1. Why was the incidence of HTG-AP increased recently, not only in your institution but also in other countries? For example, was it due to the improvement of disease recognition or availability of the detection of serum TG? 2. In this study, how did you decide or select lipid-lowering treatment such as intravenous insulin, HP or only anti-lipemic drugs? Please clarify the basic treatment strategy for HTG-AP in your institution. 3. In the 'Results section', the descriptions of 'Trends in Incidence of HTG-AP' are redundant. Each data is easily available in Figure 2, therefore please show and summarize important data in the main text. 4. In the section of 'Clinical Characteristics of HTG-AP', the descriptions of the symptoms of HTG-AP are also redundant. 5. The authors described that 54.7% of patients with HTG-AP were related to diet and/or drinking. I think identification of etiology in those patients is sometimes difficult. How did you distinguish between alcoholic AP and HTG-AP in patients with both drinking and high-level of TG? 6. Were eleven patients who died during hospitalization all categorized into SAP? I recommend clarifying the mortality rate according to disease severity. 7. The authors described that 90.6% of patients with HTG-AP had comorbidity with fatty liver disease. I recommend adding the body weight and/or body mass index to table 1. 8.

What was the dose of insulin in ING group? Were there any adverse events such as hypoglycemia? 9. Was there any difference in fluid resuscitation among MAP, MSAP, and SAP group? 10. In table 2, Why was the proportion of 'Intravenous insulin' extremely low (only 1.3%) in patients with SAP? 11. Of 219 patients, 84 and 32 patients were treated with intravenous insulin and HP, respectively. How did you treat HTG-AP in remnant 103 patients? Were there any patients treated with the combination of heparin and insulin? Some previous reports recommended the combination therapy as first-line therapy for severe HTG-AP. 12. Although the details of Table 2 and Table 3 were described in the discussion section of 'Comparisons of Different Grades of Severity of HTG-AP', these contents should be described in the 'Results' section. Also, I agreed high CRP, low calcium, and low albumin were risk factors of severe HTG-AP, as concluded from this study. However, these factors seemed not to be specific for HTG-AP. High CRP and low calcium are well known predictive factors for severe AP, caused by not only HTG-AP but also other etiologies including alcoholic and biliary AP. Therefore, these results only confirmed the usefulness of the revised Atlanta classification and did not indicate the novelty or strength of this study. I recommend changing 'Conclusion' and modifying the contents of 'Discussion'. 13. The 'Aim' of this study is confusing. Did the authors intent to clarify clinical characteristics of HTG-AP or to compare the treatment efficacy between ING and HP? I think the main finding in this study was the efficacy of intravenous insulin as a non-invasive and low-cost treatment for patients with mild or moderately severe HTG-AP. Therefore, I recommend describing the aim of this study more clearly. Minor issues 1. I think 'mg/dL' is more appropriate rather than 'mmol/L' as the unit of TG. 2. There are several misspellings in the section of 'ARTICLE HIGHLIGHTS', such as 'To compared', 'diffident' and 'sued'. Please check them carefully throughout the manuscript.

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03479389

Position: Associate Editor

Academic degree: MD, PhD

Professional title: Associate Professor, Director

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

Manuscript submission date: 2021-12-06

Reviewer chosen by: Jia-Qi Zhu

Reviewer accepted review: 2022-03-14 09:05

Reviewer performed review: 2022-03-14 10:29

Review time: 1 Hour

| | |
|---------------------------|---|
| 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 |



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

SPECIFIC COMMENTS TO AUTHORS

Aggressive initial fluid replacement is important for hypertriglyceridemic acute pancreatitis. Please investigate the initial fluid volume in this study. You should also state body mass index (BMI) in the patient background.

PEER-REVIEW REPORT

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03034605

Position: Editorial Board

Academic degree: MBBS, MCh, MD

Professional title: Assistant Professor, Attending Doctor, Chief Doctor, Consultant Physician-Scientist, Surgeon

Reviewer's Country/Territory: India

Author's Country/Territory: China

Manuscript submission date: 2021-12-06

Reviewer chosen by: Jia-Qi Zhu

Reviewer accepted review: 2022-03-14 10:50

Reviewer performed review: 2022-03-17 12:58

Review time: 3 Days and 2 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 |

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| Re-review | [<input type="checkbox"/>] Yes [<input checked="" 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 have conducted an interesting study to determine the incidence and clinical characteristics of patients with acute pancreatitis due to hyper triglyceridemia. I have following comments regarding the manuscript:

1. The first paragraph of the Methods section describing the number of patients should be mentioned in the Results section.
2. Some of the patients have multiple etiologies for acute pancreatitis such as gallstones with hypertriglyceridemia. Were such patients included in this study?
3. All patients were not given intravenous insulin therapy or hemoperfusion. So what were the indications of giving intravenous insulin therapy or hemoperfusion or CRRT in the study patients?
4. The role of intravenous insulin and hemoperfusion for hypertriglyceridemia is still evolving. So in order to determine their effectiveness, the authors should add a control group in the propensity score matching and compare the three groups.
5. Diet and drinking have been mentioned as the causes of hyper triglyceridemia. However, further details such as the type of diet and drinking should be mentioned. Also, if alcohol drinking causes hypertriglyceridemia, then it also causes acute pancreatitis. So, how was it determined whether acute pancreatitis was due to hypertriglyceridemia or alcohol? Whether such cases with dual etiologies included in this study?

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Title: Incidence and clinical characteristics of hypertriglyceridemic acute pancreatitis: A retrospective single-center study

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05722857

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Czech Republic

Author's Country/Territory: China

Manuscript submission date: 2021-12-06

Reviewer chosen by: Jia-Qi Zhu

Reviewer accepted review: 2022-03-18 19:17

Reviewer performed review: 2022-03-18 19:34

Review time: 1 Hour

| | |
|---------------------------|---|
| Scientific quality | <input checked="" type="checkbox"/> Grade A: Excellent <input 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 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 checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection |
| Re-review | <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No |



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**Peer-reviewer
statements**

Peer-Review: [☐] Anonymous [☒] Onymous

Conflicts-of-Interest: [☐] Yes [☒] No

SPECIFIC COMMENTS TO AUTHORS

Excellent work with important message for clinical practice. Only one comment - I miss a comment that it is hard to tell sometimes if the AP is alcoholic or primarily caused only by TG, since alcoholics have high TG quite often. And people lie about alcohol consumption. How did you exclude alcohol as a cause of AP?

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Title: Incidence and clinical characteristics of hypertriglyceridemic acute pancreatitis: A retrospective single-center study

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05077679

Position: Peer Reviewer

Academic degree: MD

Professional title: Associate Professor

Reviewer's Country/Territory: South Korea

Author's Country/Territory: China

Manuscript submission date: 2021-12-06

Reviewer chosen by: Jia-Qi Zhu

Reviewer accepted review: 2022-03-17 05:24

Reviewer performed review: 2022-03-29 04:41

Review time: 11 Days and 23 Hours

| | |
|---------------------------|---|
| Scientific quality | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" 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: [☒] Anonymous [☐] Onymous

Conflicts-of-Interest: [☐] Yes [☒] No

SPECIFIC COMMENTS TO AUTHORS

The authors reported a retrospective single-center study on the incidence, clinical characteristics, and treatment of hypertriglyceridemic acute pancreatitis. The authors evaluated the effect of intravenous insulin and hemoperfusion in hypertriglyceridemic acute pancreatitis using propensity-score matching. However, I have some concerns which need to be addressed.

1. What was the reason that hemoperfusion was used instead of plasmapheresis or continuous renal replacement therapy? How was hemoperfusion started and stopped? Please describe in detail how hemoperfusion was performed.
2. All patients included in this study received proton-pump inhibitor and low molecular weight heparin. Why?
3. Did all patients receive somatostatin/octreotide inhibitor? Or somatostatin/octreotide? Why?
2. Was serum lipase level checked in the patients of this study?
3. Was there any difference in the severity of patients with DM or fatty liver?

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 73759

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03479389

Position: Associate Editor

Academic degree: MD, PhD

Professional title: Associate Professor, Director

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

Manuscript submission date: 2021-12-06

Reviewer chosen by: Han Zhang

Reviewer accepted review: 2022-05-01 03:41

Reviewer performed review: 2022-05-01 04:22

Review time: 1 Hour

| | |
|---------------------------|---|
| 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 |
| Peer-reviewer | Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous |



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statements

Conflicts-of-Interest: [☐] Yes [☒] No

SPECIFIC COMMENTS TO AUTHORS

Initial fluid replacement is important for the treatment of hyperlipidemic acute pancreatitis. This study does not mention the type or amount of initial fluid replacement. Please also investigate the relationship between fluid volume and pancreatitis severity.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastroenterology*

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Academic degree: MBBS, MCh, MD

Professional title: Assistant Professor, Attending Doctor, Chief Doctor, Consultant Physician-Scientist, Surgeon

Reviewer's Country/Territory: India

Author's Country/Territory: China

Manuscript submission date: 2021-12-06

Reviewer chosen by: Han Zhang

Reviewer accepted review: 2022-05-01 06:44

Reviewer performed review: 2022-05-02 07:29

Review time: 1 Day

| | |
|---------------------------|---|
| 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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection |



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**Peer-reviewer
statements**

Peer-Review: [☒] Anonymous [☐] Onymous

Conflicts-of-Interest: [☐] Yes [☒] No

SPECIFIC COMMENTS TO AUTHORS

The authors have made appropriate changes in the manuscript as per the reviewers' comments.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastroenterology*

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Reviewer's code: 05722857

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Czech Republic

Author's Country/Territory: China

Manuscript submission date: 2021-12-06

Reviewer chosen by: Han Zhang

Reviewer accepted review: 2022-05-02 10:20

Reviewer performed review: 2022-05-02 10:23

Review time: 1 Hour

| | |
|---------------------------|---|
| 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 |
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| Peer-reviewer | Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous |



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statements

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

SPECIFIC COMMENTS TO AUTHORS

Accept

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

Manuscript submission date: 2021-12-06

Reviewer chosen by: Han Zhang

Reviewer accepted review: 2022-05-01 10:26

Reviewer performed review: 2022-05-03 03:01

Review time: 1 Day and 16 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 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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection |
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statements

Conflicts-of-Interest: [☐] Yes [☒] No

SPECIFIC COMMENTS TO AUTHORS

The authors have responded appropriately to almost all comments of the reviewer. So, I have no additional comments.