Author's responses to the reviewers' comments

We thank the editors and the reviewers for their insightful comments and helping in improving the quality of the manuscript.

Reviewer #1:

Specific Comments to Authors: no specific comments

Reviewer #2:

Specific Comments to Authors: The title of this article is"Diabetes mellitus as a consequence of acute severe pancreatitis: unraveling the mystery". However, in the second paragraph of the "Pathophysiology", the author mentions that since >10% of patients with non-necrotizing acute pancreatitis develop diabetes mellitus during short term follow-up, there is a slight inconsistency between the two.

Response

- To avoid the confusion to the readers, we have modified the above sentence in the revised manuscript.

Reviewer #3:

Specific Comments to Authors:

1. You should differentiate hyperglycaemia of acute pancreatic and T3cDM, as the former is transient and not considered to be T3cDM.

2. Be clear - is the article focusing on hyperglycaemia due to acute severe pancreatitis or T3CDM which includes all the conditions of exocrine pancreas including pancreatic malignancy and the mechanism of DM development is different in malignancy and majority of T3cDM patients are chronic pancreatitis rather than acute pancreatitis. The definition mentioned in the article includes chronic pancreatitis in criteria.

3. T3cDM is usually a consequence of acute pancreatitis or recurrent acute pancreatitis leading to chronic pancreatitis. Once the fibrosis occurs it is chronic pancreatitis which results in destruction of beta cells.

4. In acute necrotising pancreatitis there is insulin deficiency whereas in chronic pancreatitis early in the disease there is decreased pancreatic polypeptide response when leading to diabetes when insulin production is sufficient and can be managed by OHA's.

5. There is a role of Gut microbiota in T3cDM which is altered and different from those with T1Dm and T2DM and also CP patients without DM.

6. Role of inflammation in development of T3cDM.

7. Also add Indian studies on T3cDM prevalence, mechanism, role of Gut microbiome, and risk factors.

Response

- We thank the reviewer for pointing out the relevant point. Since, American Diabetes Association has now abandoned the use of term Type 3c DM, we have not used the same in the revised manuscript.
- In the revised manuscript, we have described the spectrum of dysglycemia in pancreatitis patients and have defined the individual terms.
- In the revised manuscript, we have removed the terminology T3cDM. We have used the term 'post-pancreatitis diabetes mellitus (PPDM)' to describe the diabetes in pancreatitis patients. This is further subdivided into, post-acute pancreatitis diabetes mellitus (PPDM-A) and post-chronic pancreatitis diabetes mellitus (PPDM-C). Since the review is about the diabetes in acute pancreatitis, we have focused on the PPDM-A only.
- In the revised manuscript, we have elaborated the pathophysiological aspects of development of PPDM-A.
- Only limited data is available on the PPDM-A from India. We have included the two papers from India (Gupta et al. and Chandrasekaren et al.) which have looked at the development of diabetes after acute pancreatitis.