Round-1:

Dear Na Ma,

We do appreciate your decision letter and advice on our manuscript entitled "Comparison of clinical features and outcomes in peritoneal dialysis-associated peritonitis patients with and without diabetes: a multicenter retrospective cohort study". We are also grateful to the reviewers for the constructive and valuable comments and suggestions. We have revised the manuscript according to the comments and suggestions, and responded, point by point to the comments as listed below. The paper has been revised significantly throughout the text and we highlighted the amendments in the revised manuscript.

The revised manuscript has been edited and proofread by Medjaden Bioscience Limited. We hope that the revised manuscript is now acceptable for publication in your journal.

We are looking forward to your reply.

Sincerely yours,

Wenpeng Cui

Response Letter

For the issues raised by Reviewer:

1) Remove abbreviations from the Core Tip.

Reply: Thanks for your suggestion. We have removed abbreviations from the Core Tip in the manuscript.

2) Based on their Introduction, what is the authors' hypothesis?

Reply: Thanks for your comment. We have put forward the hypothesis in introduction.

3) Potential reasons for differences in the types of bacteria being cultured are not insightful. "Impaired vision" is not a sufficient potential origin. Please consider: i.) bacterial colonization in individuals undergoing peritoneal dialysis with and without diabetes mellitus; and ii.) the potential role of control of patients' diabetes; there are studies of impairment of neutrophil oxidative burst in individuals with elevated blood levels of glycosylated hemoglobin and/or blood glucose.

Reply: Thanks for your suggestion. We've added the relevant discussions.

Staphylococcus epidermidis is the most common CNS which can cause disease under certain circumstances. A study showed that the Staphylococcus epidermidis causing PDAP had low immunogenicity, which makes it more easily establish an infection since it can't be immediately recognized by the immune system[1]. Meanwhile, DM is related to impaired immunity[2]. We consequently infer that CNS inclined to colonize in PD patients with DM.

Moreover, DM patients are more susceptible to infection especially in poorly controlled diabetics[3]. The impairment of neutrophil oxidative burst in individuals with poorly controlled diabetics may explain this phenomenon. A negative correlation was observed between neutrophil oxidative burst and HbA1c levels in Osar' study[4]. And reduced neutrophil respiratory burst activity in diabetic patients could be restored to almost normal by blood glucose control[5].

4) With regards to "nutritional status of patients" (in authors' Discussion), the difference in blood albumin levels summarized in Table 1 and in Table 3 are not likely to be of clinical significance. Blood albumin is a better marker of an ongoing inflammatory response. There are published scoring

criteria for a diagnosis of protein malnutrition (Harvinder GS, et al. Dialysis Malnutrition and Malnutrition Inflammation Scores: screening tools for prediction of dialysis-related protein-energy wasting in Malaysia. Asia Pac J Clin Nutr. 2016; 25(1):26-33).

Reply: Thanks for your comment. We have carefully read the above reference.

Blood albumin is a marker of both ongoing inflammatory response and malnutrition, which is contained in the Malnutrition Inflammation Score (MIS). High MIS indicates malnourished status in patients undergoing PD[6], which further leads to bad clinical outcomes[7]. Clinicians need to pay more attention to the serum albumin status of patients with diabetes to improve prognosis of PDAP.

1 Jung K, Lüthje P, Lundahl J, Brauner A. Low Immunogenicity Allows Staphylococcus Epidermidis to Cause Pd Peritonitis. *Perit. Dial. Int.* 2020; **31**(6): 672-678 [DOI: 10.3747/pdi.2009.00150]

2 L. M. A. J. Muller KJG, E. Hak, W. L. Goudzwaard, F. G. Schellevis, A. I. M., Hoepelman GEHMR. Increased risk of common infections in patients with type 1 and type 2 diabetes mellitus. *Clin. Infect. Dis.* 2005; **41**: 281-288

3 ELLIOT J. RAYFIELD MJA, GERALD T. KEUSCH, MILTON J. BROTHERS, CHARLES NECHEMIAS, HARRY SMITH. Infection and Diabetes The Case for Glucose Control. *The American Journal of Medicine* 1982; **72**: 439-450

4 Osar Z, Samanci T, Demirel GY, Damci T, Ilkova H. Nicotinamide Effects Oxidative Burst Activity of Neutrophils in Patients with Poorly Controlled Type 2 Diabetes Mellitus. *Experimental Diabesity Research* 2004; **5**(2): 155-162 [DOI: 10.1080/15438600490424244]

5 Sung-Hee Ihm HJY, Sung Woo Park, and Chan Jeoung Park. Effect of Tolrestat, an Aldose Reductase Inhibitor, on Neutrophil Respiratory Burst Activity in Diabetic Patients. *Metabolism* 1997; **46**: 634-638

6 Harvinder GS, Swee WC, Karupaiah T, Sahathevan S, Chinna K, Ahmad G, Bavanandan S, Goh BL. Dialysis Malnutrition and Malnutrition Inflammation Scores: screening tools for prediction of dialysis-related protein-energy wasting in Malaysia. *Asia Pac. J. Clin. Nutr.* 2016; **25**(1): 26-33 [PMID: 26965758 DOI: 10.6133/apjcn.2016.25.1.01]

7 Choi HY, Lee JE, Han SH, Yoo TH, Kim BS, Park HC, Kang SW, Choi KH, Ha SK, Lee HY, Han DS. Association of inflammation and protein-energy wasting with endothelial dysfunction in peritoneal dialysis patients. *Nephrol. Dial. Transplant.* 2010; **25**(4): 1266-1271 [PMID: 19926717 DOI: 10.1093/ndt/gfp598]

For the issues raised by Science Editor:

1) The "Author Contributions" section is missing. Please provide the author contributions;

Reply: Thank you for your suggestion. Meng LF analyzed the data and wrote this manuscript; Li XY, Zhao J, Liu SC and Zhuang XH collected the data; Yang LM, Zhu XY and Zhang XX provided the data; Luo P organized the study; Cui WP designed this study and reviewed this manuscript.

2) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

Reply: Thank you for your advice, we will upload the funding agency copy of the approval document.

3) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

Reply: Thank you for your reminder. We have prepared and arranged the figures using PowerPoint.

4) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text.

Reply: Thank you for your comment. We have added the "Article Highlights" section at the end of the main text.

5) The STROBE Statement lacks of the page number.

Reply: Thanks for your comment. We have added the page number.

Round-2:

SPECIFIC COMMENTS TO AUTHORS

Do the authors have a hypothesis? A hypothesis should be stated in their introduction; the results of their study, in reference to the authors' hypothesis, should be mentioned in their Discussion.

Reply: Dear Prof. Ma, We would like to express our sincere appreciation for your letter and advice on our manuscript entitled "Comparison of clinical features and outcomes in peritoneal dialysis-associated peritonitis patients with and without diabetes: a multicenter retrospective cohort study". We are also grateful to the reviewers for the careful reading and valuable comments and suggestions to improve this paper. We have addressed all issues raised by the reviewer, and responded as listed below. The paper has been revised significantly throughout the text and we highlighted the amendments in the revised manuscript. The revised manuscript has been edited and proofread by Medjaden Bioscience Limited. We hope that the revised manuscript is now acceptable for publication in your journal. Once again, thank you very much for your comments. We are looking forward to your reply. Sincerely yours, Wenpeng Cui Response Letter For the issues raised by Reviewer: Do the authors have a hypothesis? A hypothesis should be stated in their introduction; the results of their study, in reference to the authors' hypothesis, should be mentioned in their Discussion. Reply: Thanks for your comment. We have put forward the hypothesis in introduction. Meanwhile, we have discussed the results in reference to our hypothesis in the part of discussion of our manuscript. The specific sentences relevant to the hypothesis in Discussion were highlighted in the manuscript. Introduction (Page 5): We hypothesize that there may be some differences in clinical features (symptoms and pathogens) and prognosis of PDAP between DM and non-DM patients. Discussion (Page 10): The present study aimed to explore differences in the clinical features and outcomes in PDAP patients with and without diabetes as

we hypothesized. We found that the symptoms of PDAP between DM group and non-DM group were similar; DM group had more infections with CNS and less infections with E. coli as compared to the non-DM group; the therapeutic outcomes of PDAP including complete cure, catheter removal, PDAP-related death and relapse were comparable between DM group and non-DM group; DM was an independent risk factor of all-cause mortality but not technique failure in PDAP patients.