

Dear Editor and reviewers:

Thank you for opinions about our work. We have revised our manuscript and the responses are listed below.

Reviewer #1:

Specific Comments to Authors: It is an interesting manuscript. Authors succeed to present their data in a clear way adding information to the existing literature. Therefore, I have no corrections to do and the manuscript can be published unaltered.

Response: thank you very much for your review.

Reviewer #2:

Specific Comments to Authors: The paper deals with COVID-19 in diabetic patients. The theme must be an important issue for all the people all over the world. This is particularly because this report deals with patients in China, which is just the starting point of this pandemic, and it spans from February 13th to March 1st, which is the very period when this pandemic has just started to spread all over the world. In this sense, this paper is worthy of attention from all over the world. I have a few comments about this MS. #I admit that diabetes (DM) is an important determinant of the prognosis of patients with COVID-19, and is associated with the severity of COVID-19 (Tables 1, 2). This is ok. But according to this study (particularly Table 3) not only DM but also HT or hepatic dysfunction are closely associated with patients' severity. I think it ok to deal with DM with the biggest focus on it in this paper; but since I believe that to tackle this formidable disease, those factors addressed here (HT etc) should also count, which are worthy of attention as well in this study. Those factors may be independent risk factors for COVID-19. It is better to refine the MS (particularly the title, CONCLUSION of the abstract, or DISCUSSION) accordingly. # POPULATION AND METHODS>Study population: For the unit of BG, 'mmol/L' is used. This is ok. But there are a considerable number of counties, including that of this reviewer, where 'mg/dl' is more commonly used. Please indicate 'mg/dl' along with 'mmol/L'. #Please clarify the definitions of DM, HT, or hepatic dysfunction, etc, the authors used. They are just based on the history??? Simple ones are ok, but to show them clearly is very important. #Table 2 (also in the text): The normal values of Hb, CRP, or ESR, etc, used in this project, along with their units, need to be clearly shown. #Statistical analysis, line 1, 'Fisher's...in R 3.6.0': What does this 'Fisher's...in R 3.6.0' mean? #Generally, this MS is written well with a good command of English. And yet, there are a number of grammatical points that are questionable or mistaken. The following lists some of them. Please proofread it again carefully. - Abstract>RESULTS, line 3 & CONCLUSION, line 1, OR ELSEWHERE in the MS: 'invasive' >>> (Probably) 'intensive'. (I guess what is meant here is 'an intensive care using, for example, a ventilator', right?) -Abstract>RESULTS, last 6th to 8th line: 'the history of...were risk factors' >>> 'the history of...was a

risk factor' -Abstract>RESULTS, last line: 'inpatients' >>> 'patients' -Abstract, CONCLUSION, last line: 'lead to patients exacerbation' >>> 'lead to the exacerbation of patients' -INTRODUCTION, line 16: 'according to' >>> 'just as it is in'? -POPULATION AND METHODS>Study population, line 10: 'invasive treasures' >>> 'intensive treatments' -RESULTS, line 5-7: '43 cases (70.5%)... mostly demonstrating hepatic' >>> '43 cases (70.5%) showing abnormal laboratory findings including hepatic' -etc, etc, etc...

Response:

Thank you for your review. Here are our reply:

1. in Methods Line 93-110 we added detailed categories of our variables including the diagnoses of patients' history, lung involvement, hepatic dysfunction, and the treatment they received.
2. the unit of blood glucose has been indicated in mg/dl as in Line 116-119. The normal value of laboratory findings has already been added in Table 2.
3. the description and discussion of hepatic dysfunction have been added to the abstract(Line 41), discussion(Line 226-240) and conclusion(Line 257-259) as shown in our revised manuscript.
4. R language is the method we conducted our analysis. And we have changed the words we used to present the methods in Line 125-126.
5. the grammatical points with ambiguous meanings has been corrected as you reminded.

Reviewer #3:

Specific Comments to Authors: Comment #1: please provide evidence of Institutional Review Board (IRB) approval.

Response: thank you for your review. The IRB approval has been updated as attached files.

Reviewer #4:

Specific Comments to Authors: Unfortunately this is not worthy of publication. 1) This study has a very small sample size which does not add any significant new findings to the literature when compared to larger national and international datasets. 2) Furthermore, markers of disease severity are used as a endpoint, but there is no endpoint data about mortality, length of hospital stay, costs of hospital admission etc. 3) The implications (in the title, abstract, and conclusions) that poor glycaemic control is associated with worse COVID-19 severity are overly ambitious and not borne out by the study data. The authors of this study did not statistically analyse for COVID-19 severity according to markers of glycaemic control such as HbA1c% or pre and post-prandial blood sugar levels. 4) There are far too many terms that are not defined. - in the abstract, the "severe status" of COVID-19 should be defined (according to what criteria?) - throughout the manuscript, "invasive treatments" are never defined. - throughout the manuscript, "venous

treatments" are never defined. - "Lung involvement recovery trend" in table 1 is never mentioned in the manuscript and is never defined. - "Large lung involvement" is never defined. - "hepatic dysfunction" is never defined. Furthermore, if the authors consider abnormal albumin to be a marker of hepatic dysfunction, as suggested in table 2, this is incorrect as albumin is a non-specific serum marker of inflammatory response and an acute phase reactant. Low albumin alone in patients with COVID-19 does not reflect hepatic dysfunction. 5) The authors incorrectly analyse numerous continuous variables as categorical variables. ESR, CRP, haemoglobin, neutrophils, lymphocytes, platelets, ALT, bilirubin, albumin, age and pre-prandial/ post-prandial BSL levels are continuous variables and are analysed as such in most scientific literature and severity scoring systems. It is clinically meaningless to analyse them as binary categorical variables: by doing so, a patient with a CRP of 20 may be placed in the same category as a patient with a CRP of 200, when it is clear that they have different level of inflammation. Similarly, a patient with a pre-prandial BSL of 9 mmol/L may be placed in the same category as a patient with a pre-prandial BSL of 25 mmol/L, when it is clear that they have different level of glycaemic control. These variables should be statistically summarised with mean +/- standard deviation, or median + interquartile range depending on the normality of distribution; compared between diabetic and non-diabetic groups with Student's t-testing or Mann-Whitney testing; and entered into logistic regression as such. 5) Variables such as Complement, IgE, K+ and High-sensitive cardiac troponin I are included in Table 2 but are never explained or mentioned in the manuscript. With extremely meaningless low numbers (n=1 for most variables), these variables should be deleted from the table.

Response:

Thank you for your review. Here are our reply:

1).we are afraid that we are able to collect more samples to present our data and conclusion because of the limited time we have during the research. We are aware that this is the limitation of our study.

2) our ward is designed for mild patients and patients in severe conditions will be transferred either to other ward or ICU, which makes it harder for us to trace the final outcomes including mortality, length of hospital stay, costs of hospital admission. We are aware that this is the limitation of our study.

3) we are writing this manuscript to alert the situation that diabetic patients are facing challenges in this pandemic disease. Therefore, we only used the categorical data for our analysis. We are aware that this is the limitation of our study.

4) in Methods Line 93-110 we added detailed categories of our variables including the diagnoses of patients' history, lung involvement, hepatic dysfunction, and the treatment they received.

5) because of the limited resources, we are not able to analyze the laboratory findings as numeric variables. Thus, we only used non-parametric Chi-square

test for our analysis. Even though this method is not the best here, but we think the results are still indicating the relationship between diabetes and COVID-19.

6) we have removed the redundant data in Table 2 as you advised.

Reviewer #5:

Specific Comments to Authors: This is an important report which deserves publication. However, the definition of hepatic dysfunction should be clarified. Also, the authors should discuss the link between diabetes, hepatic dysfunction, and COVID-19 severity. Is hepatic dysfunction a cause or consequence of diabetes and COVID-19 infection?

Response:

Thank you for your review. Here are our reply:

1) we have presented detailed definition of variables we used in this work in Method in Line 93-106.

2) we have discussed the prevalence, importance and potential cause of hepatic dysfunction in Discussion in Line 226-240.