OPEN PEER REVIEW

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What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
- More motivations for all involved roles in the review process
- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
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You can find out more at:
https://sites.kowsarpub.com/kowsar/knowledgebase/category/tree.html#opr.html

Jundishapur Journal of Microbiology
Article DOI: 10.5812/jjm.102899
Published in: Jundishapur Journal of Microbiology: 13(4); e102899

Peer Review Report for "Is Coronavirus Disease 2019 (COVID-19) Associated with Renal Involvement? A Review of Century Infection"

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Review Timeline:

Submit Date:	19 Mar 2020
Revised Date:	1 Apr 2020
Accepted Date:	7 Apr 2020

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (0)

29 Mar 2020

Dear AE,
This paper has some language issues, which need to be addressed to improve readability. It seems that the study needs a full revision before it can be considered for possible publication in this journal. These corrections should begin with the introduction of the study which would need more information about COVID-19. There are some other points which have been reported as follow:
- Even if the topic is of interest, I believe that the manuscript is poorly scientifically sound and has to be improved to be accepted for publication.
- First of all, No considerations were raised regarding the mode of action of chloroquine. Because the authors pointed out this drug, I suggest that the mechanism of chloroquine should be included in the manuscript. The mechanism of chloroquine was discussed by the article with the title of “New insights on the antiviral effects of chloroquine against coronavirus: what to expect for COVID-19?” by Christian a. Devaux.
- The authors indicate the SARS Coronavirus-2 route of infection; I suggest that they can point out other ways of infections that have been discussed such as fecal-oral transmission.
- The authors in Page 7, indicate that “COVID-19 disease tends to involve multiple

organs…" Please describe the rate of SARS coronavirus detection in different organs which were detected COVID-19.
- Finally, the conclusion is short and the authors need to expand it. The authors should be compared more results of other and updated articles and extract more conclusions.
- Abstract reformat according to JJM instruction.
Thanks.

REFEREE: Associate Editor | **Revision** (0) 31 Mar 2020

Dear EIC,
The manuscript is studied, and there are some comments which should be addressed by the author. According to the comments, the document needs major revision.
Kind regards,

REFEREE: EIC | **Revision** (0) 31 Mar 2020

Dear Authors,
Thank you for submitting your manuscript to JJM. I have completed the review of your manuscript and a summary is appended below (Pleases find attached files). The reviewers recommend the reconsideration of your paper following major revision. I invite you to resubmit your manuscript after addressing all reviewer comments. Please answer point by point to reviewer's comments on a separate sheet under WORD format and write your modifications in the revised version (WORD format) in colored or highlighted letters. Your answers to reviewers' queries are not only for the Editorial Board but for the readers and should be included, when appropriate, in the manuscript for improvement and a better understanding.
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Thanks.

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Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Response to reviewers' comments in revised version

Dear editor and reviewers,

1: About the format of abstract according to the journal's guideline: The abstract with details was added and highlighted (We did not found the recently review published in your valuable journal then the format of this paper may be a little different).

Background: Novel coronavirus disease (COVID-19) is one of the most threatening pandemic in the history involving multiple organ, in which kidney is one of them. **Objective**: This study was aimed to review the association of the Coronavirus disease 2019 (COVID-19) with renal involvement.

Methods: This study was aimed to review the association of the Coronavirus disease 2019 (COVID-19) with renal involvement. International databases including Web of Science, PubMed, Scopus, Google scholar were reviewed for search of articles by 1 April 2020. Keywords were COVID-19, coronavirus disease, SARS-CoV-2, kidney, renal function, acute kidney injury, and acute renal failure, or a combination of them in the title/abstracts.

Results: There are few studies in light of COVID-19 and renal failure due to short time of its epidemic spread. The results showed that two signs of hematuria and proteinuria in the corona-positive patients were common in patients with COVID-19

Conclusion: Conclusion: Patients with elevated creatinine are at risk of mortality two times more than patients with normal creatinine. Also, elevated BUN, proteinuria and hematuria increase the risk of mortality in patients with COVID-19 up to four times compared to patient with normal tests. Therefore, it is important to check creatinine, BUN, proteinuria and hematuria in primary assessment. Generally, all routine measures for people affected with COVID-19 can be done for COVID-19 patients with acute renal failure by the time that the current knowledge is changed. Chloroquine phosphate may improve the likelihood of treatment.

2: For improved visibility of articles by search engines, we added some new key words accordingly.

Keywords: COVID-19, Renal involvement, Kidney, Infection, Novel coronavirus, Chloroquine

3: About the COVID-19 in the first part

Coronavirus is one of the major pathogens that mainly target the human respiratory tract. Previous outbreaks of coronaviruses including Acute Severe Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) were previously known to be highly threatening factors for public health. In late December 2019, a number of patients were admitted to hospitals whose initial diagnosis was pneumonia of unknown etiology. These patients were linked to a seafood wholesale market in Wuhan, Hubei Province, China (1, 2). Indeed, coronaviruses are a large family of viruses and a subset of coronaviruses vary from the common cold up to the more severe infections including SARS, MERS, and COVID-19. The latest type of these spread to humans is COVID-19 (3). Initial reports predicted the start of a potential coronavirus epidemic with estimates of the basic reproduction number (R0) for the new coronavirus 2019 (COVID-19, designated by world health organization on 11 February 2020), and significantly higher than 1 (ranging from 2.24 to 3.58) (4).

4: About the details of Chloroquine

Starting antiviral medications is suggested to maintain vital organs function; hence it can reduce the morbidity and mortality of critical patients (43, 44). Chloroquine is a quinine with amine acidotropic form, in such a way that first synthesised in Germany by approximately 85 years ago (45). Chloroquine inhibits the completion of the viral cycle with binding of viral particles to cellular cell receptors (46, 47). Chloroquine phosphate is widely used as a medication to treat malaria for several years, however it shows apparent efficacy with enough safety in patients with COVID-19, in which multicenter trials approved the effect of Chloroquine in China. Als, Chloroquine may be included in the next version of the Guidelines to treat COVID-19 issued by the National Health Commission in China (48).

The benefits of Chloroquine can be summarized in some characteristic including "chloroquine prevents SARS Cov-2 replication", "in vitro, chloroquine *slow the* activity of lots of viruses", " acute viral diseases in humans were treated using Chloroquine for several years", and "big data in China show the effective role of Chloroquine in the treatment of COVID-19" (49). Also, Chloroquine is used to treat the chronic viral diseases such as HIV-infection (50). Additionally, Hydroxychloroquine is used in systematic immunodeficiency diseases like rheumatoid arthritis and systemic lupus erythematosus (51). In spite of wide use of Chloroquine in different viral infections, the treatment of patients with COVID-19 infected by SARS-CoV-2 was observed (49).

5: About multiple organ failure and the percent of affected patients.

Acute kidney injury reported in 5.1% of patients. Patients with renal failure have a higher risk to be expired (33-36). Various studies report multiple organ failure. Regarding lung, about half patients involve with moderate pneumonia and 20% have acute upper respiratory symptoms. Chu et al showed that 6.7% developed acute renal impairment at a median

duration of 20 days after the onset of disease (33, 37). Liver impairment reported in about 60% with elevation of the aspartate aminotransferase (38).

5: About transmission

Transmission is the fundamental issue in epidemic diseases, in which the passengers are the main transporter of the virus to other countries, and more than 30% of transmission happens by nosocomial rout as the main route of transmission for coronaviruses infections in adults. It should be noted that the possibility of virus transmission from children to other people has been approved. Since children developed mild symptoms without the need for hospitalization, then the rate of contact and infection transmission to health care workers from children is low (18-22). One third of infected case of COVID-19 had exposure to the epidemic area; and about 90% of children had a close contact with their family (23). Figure 1 and 2 shows the sharp increasing trend of epidemiologic curve by 1 April 2020.

6: About conclusion

It is important to check creatinine, blood urea nitrogen (BUN), proteinuria and hematuria on admission because patients with elevated creatinine are at risk of mortality two times more than patients with normal creatinine. Also, elevated BUN about four times, proteinuria up to four times, and hematuria up to five times increase the risk of mortality in patients with COVID-19. Considering that about five percent of patients referring to hospitals are developed renal failure, it is important to check creatinine, BUN, proteinuria and hematuria in primary assessment. Taking the ACE inhibitors can be useful and its stoppage is not recommended. Chloroquine phosphate may improve the likelihood of treatment. Due to the probability of recurrence of COVID-19 after recovery, follow-up should be considered in these patients and regularly checked by telephone or email. Generally, all routine measures for people affected with COVID-19 can be done for COVID-19 patients with acute renal failure by the time that the current knowledge is changed. It is suggested to perform

longitudinal studies to assess the renal function and development of kidney disease to provide strong documents in favor of decision-making.

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Revision (1)

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REFEREE: EIC | **Revision (1)** 7 Apr 2020

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