

Review of: "Tocilizumab Plus Corticosteroid in Elderly Patients Hospitalized With COVID-19 Pneumonia: A Retrospective Cohort Study"

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Potential competing interests: No potential competing interests to declare.

Dear authors,

about the manuscript entitled "Tocilizumab Plus Corticosteroid in Elderly Patients Hospitalized With COVID-19 Pneumonia: A Retrospective Cohort Study " enclosed my suggestions:

-please introduce and fully describe the population at higher risk of infection, worse prognosis, such as reduced response to vaccination, as patients with diabetes mellitus (DM) and hypertension. In this context, we have to say that higher risk/worse prognosis patients could be also the hypertensive patients and those with diabetes. Indeed, the hypertensive are higher risk patients for COVID19, ICU admission and deaths (J Am Heart Assoc. 2020 Jul 7:e016948. doi: 10.1161/JAHA.120.016948; BMC Cardiovasc Disord. 2020 Aug 14;20(1):373. doi: 10.1186/s12872-020-01658-z). Notably, this study did not evidence any effect of particular classes of anti-hypertensive therapies in COVID-19 prognosis for hypertensive patients. Indeed, it was the first study to evaluate clinical outcomes in hypertensive COVID-19 patients as ACEi vs. ARBs vs. CCBs. Conversely, if possible give to us information about pro-thrombotic status and AB0 group of study cohorts. Notably, this study has not been evaluated in your submission. Please explain this point and the suggested reference.

-According to your suggestions, I would remark that the chronic hyperglycemic condition (and insulin resistance), as in the case of DM , but also the acute hyperglycemia at hospital admission could both increases the risk of mortality (Diabetes Care. 2020 Jul;43(7):1408-1415. doi: 10.2337/dc20-0723; Cardiovasc Diabetol. 2020 Jun 11;19(1):76. doi: 10.1186/s12933-020-01047-y). However, as you could see in the current international literature, the role of diabetes , and of hyperglycemia in worse prognosis in COVID-19 has just been previously discussed and published. However, please describe in detail this point. This could improve the quality of the present article.

-Please stress the concept of hyperglycemia as negative trigger and negative prognostic factor for COVID-19 infection (Diabetologia. 2020 Nov;63(11):2486-2487. doi: 10.1007/s00125-020-05216-2), and cause of refractoriness to tolicizumab therapy: Diabetes Metab. 2020 Oct;46(5):403-405. doi: 10.1016/j.diabet.2020.05.005. Please discuss this information and this reference.

-Do not forget to indicate the refractoriness to anti-SARS-CoV-2 vaccination in diabetics (Nat Commun. 2022 Apr

28;13(1):2318. doi: 10.1038/s41467-022-30068-2.), and hyperglycemic patients. Please describe and discuss this point.

METHODS:

- How did you collect clinical data? Did you use electronic systems? Who did perform data collection?
- Who did perform data analysis?
- How did you calculate sample size of study population?
- How did you diagnose the diabetes status? Please introduce the full diagnostic criteria according to international guidelines for diagnosis and management of diabetes mellitus (DM).

RESULTS:

-I would see the study results as:

1. Inflammatory/immune response study results;
2. Human study results (clinical data and outcomes). As example, in humans' transplanted hearts authors showed the over-expression and glycation of ACE2 receptors in diabetics vs. non-diabetics patients, and this could be an evidence of worse prognosis in COVID-19 patients (Cardiovasc Diabetol. 2021 May 7;20(1):99. doi: 10.1186/s12933-021-01286-7). Please fully describe this point.

-In the tables there are relevant problems:

1. there are not data about systolic/diastolic blood pressure, and body mass index of study cohorts.
2. there are not data about medical therapies as anti-diabetic (really frustrating this) and anti-viral (not acceptable). Please correct the table and show the data for further revision process. The antidiabetics medications and much more the drugs with lowering effects on hyperglycemia could influence clinical outcomes, as suggested before (Diabetes Care. 2020 Jul;43(7):1408-1415. Doi: 10.2337/dc20-0723; Diabetologia. 2020 Jul 6:1-2. doi: 10.1007/s00125-020-05216-2; Diabetes and Metabolism 2020; doi: 10.1016/j.diabet.2020.05.005). You have to clarify and discuss these points.

DISCUSSION:

It is too long and not well focused on main study results. Please short it and focus it on main study news. Please re-write it as "what is new and what is known".

In addition, Improve English quality of the text.

Include a study flow chart figure.