**Reviewer's report**

**Title:** Mechanistic Study of the Cause of Decreased Blood 1,25-Dihydroxyvitamin D in Sepsis

**Version:** 0  **Date:** 13 Jul 2019

**Reviewer:** Kursad Unluhizarci

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1,25 (OH)2D level of 20 healthy subjects were compared with 79 patients with sepsis (either survivors or non-survivors) whose samples were obtained from stored plasma samples of a previous study. Additionally, C57BL/6 mice model has been used for experimental sepsis and the results of both studies were compared (regarding mechanistic similarities). Overall, experimental study results support this partially retrospective clinical study. In general, this is a well-written manuscript, however, I have some comments:

1- GH has pulsatile secretion and in healthy subjects, very low levels of GH exist during the day without indicating GH deficiency. Thus GH measurement during any time does not give adequate message regarding GH dynamics. Serum IGF-1 level is more informative on the GH axis.

2- Serum PTH level should be evaluated simultaneously with actual serum calcium level. The authors should give simultaneous serum calcium levels during the measurement of serum PTH level (may be given as an additional figure in Figure 1)

3- The numeric data are presented as figures. It would be better to give the data also as tables.

4- Figure 1E: Control subjects are healthy people !!. Why their serum creatinine level is also increased?

5- What was the serum 25 (OH)D levels? Were they replaced in case of deficiency?

6- Six patients have chronic renal failure (CRF) as a co-morbidity. As the authors suggest, 1-alpha hydroxylase activity is necessary for active vitamin D synthesis which is mediated by several factors such as FGF-23, PTH, etc. Presence of CRF will affect 1,25 (OH)2D activity/level irrespective of sepsis. Thus, the authors should also give data without including those patients with CRF. By this way, we will see the sole/real effect of sepsis on the mentioned parameters.

7- Conclusion: This paragraph should not be the repeat of summary of the presented data. Instead, it should provide clinical significance of the study and guidance for future studies.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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