31381-Response Letter

Reviewer 1 (Reviewer's code: 02861252)

Comment to Authors- Good Work

Response to reviewer- We thank the reviewer for the assessment of our article.

Reviewer -2 (Reviewer's code: 00006258)

Comments to Authors - The manuscript is well written and covers an area of current clinical interest. The data is presented and described well and comes from a reasonably sized cohort of patients. My main concern relates to the interpretation and title of the manuscript. The authors report no significant change in mortality, survival or longevity, following VD supplementation. Modest effects are only seen in the multivariate analysis where confidence is low– thus the title of the article is misleading. Similarly within the study groups, 84% of patients were described as being vit D deficient. However VD deficiency is relatively common in many poropulations . In India prevelance can be as high as 70%. Thus it would be very important to incorporate an age and sex matched control population without cirrhosis. Otherwise it is very hard to confer causality. Table 5 is very useful but does highlight the lack of originality in the current study. Similarly the studies reviewed do suggest that one might have expected a response to treatment in the current study. Would be helpful to have a discussion of routes and details of administration strategies in the reviewed articles to contract to the current study where Vit D administered IM and orally. Was the dose and route used here appropriate? Also I wonder whether this Table could be preented in a clearer / more impactful way as a schematic figure perhaps? It certainly needs a better title. The manuscript text describes the information in this table 'We also performed systemic review of prevalence

and the role of VDD in patients with CLD. ' Presenting this section as a 'systematic review' in this way is misleading and full details of review protocol and exclusions should be given if it is badged thus. Currently no is detail given in the methods section to outline the review strategy– better to brand as a ‘review’ of the literature. Minor comments- Although aetiologies of CLD within the control and VD treated groups are supplied in the results text it would be important to highlight these in the demographic tables. The Tables should be accompanied by descriptive legends and titles for clarity.

Response to reviewer-

Thank you for your valuable comments and review of our manuscript.

1. We changed the title of the manuscript- ‘’Effect of replenishment of vitamin D on survival in patients with decompensated liver cirrhosis: A prospective study’’.

2. We agree with the reviewer regarding the enrolment of an age and sex matched control population without cirrhosis. Unfortunately, we did not assessed vitamin D level of control population without cirrhosis. We have mentioned this in study limitation.

3. We reviewed and included all relevant studies regarding the vitamin D deficiency in noncholestatic liver disease and summarized in Table 5 and 6. We revised the tables 5 and 6 to make it clearer and impactful. We also changed the legends/titles of table 5 and 6.

4. We added a paragraph in discussion section regarding the routes and details of administration strategies.

The dose of VD and mode of administration in VD deficient/insufficient patient of CLD is not clear. Lim et al suggested periodic monitoring of VD in patients with CLD. Therapy is required in those with VD levels <30 ng/mL, which includes administration of 5000 IU of vitamin D3 daily or 50000 IU of vitamin D2 or D3 weekly for 3 months, followed by 1000 IU/day indefinitely [40]. In a systemic review authors have recommended that vitamin D3 be used for supplementation over vitamin D2. A single VD doses ≥300,000 IU are most effective at increasing VD levels [41]. Although both oral and intramuscular administration routes are effective and safe, intramuscular administration is more effective in increasing VD levels [42,43].In our study, we used intramuscular cholecalciferol 300,000 IU as loading dose and 800 IU /day oral as maintenance dose along with 1000 mg oral calcium supplementation.

5. We agree with the reviewer's concern for use of word **'systematic review'**. We have changed those words in the revised manuscript.

   We also reviewed the data on the prevalence and the role of VDD in patients with liver disease. A concise literature review of VDD in patients with noncholestatic liver disease is summarized in Table 5 and 6.

6. We added/highlighted the etiologies of CLD in Table 1.