Reviewer's report

Title: Relationship between chronic hepatitis C and serum 25-hydroxyvitamin D3 levels in Japan

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Reviewer: Jennifer Lai

Reviewer's report:

Thank you for the opportunity to review this manuscript entitled: “Relationship between chronic hepatitis C and serum 25-hydroxyvitamin D3 levels in Japan”. In this original article, Atsukawa et al aimed to evaluate 25OHD levels in Japanese patients with chronic hepatitis C and factors associated with 25OH deficiency.

The strength of this paper is its large cohort, which is impressive in size at 619 subjects. The main conclusions from these analyses are: 1) deficiency in total 25OHD is common among individuals with chronic hepatitis C infection, 2) total 25OHD levels did not vary significantly with fibrosis score (by FIB-4), and 3) cold weather, female gender, older age, and low hemoglobin are associated with vitamin D deficiency (<20 ng/mL) in adjusted analyses.

- It is well established in the literature that total 25OHD deficiency is common among individuals with chronic hepatitis C. This has been shown in Asian cohorts as well. The investigators need to provide a stronger justification for their largely descriptive study. This should not be the stated objective of the study.

- The lack of association between total 25OHD levels and FIB-4 is interesting. Many studies have reported high rates of 25OHD deficiency among patients with cirrhosis and suggested a linkage between 25OHD levels and fibrosis progression/cirrhosis. This large study is an opportunity to suggest otherwise – that possibly low 25OHD levels are due to the fact that decompensated cirrhotics simply do not go outside as much. I think that this point should be highlighted more, and perhaps even an explicit aim of the study.

- Information regarding sun exposure and vitamin D supplementation should be included. If this information was not collected, then it needs to be discussed as a limitation.

- What are potential explanations for the associations between low hemoglobin levels and vitamin D deficiency? One might speculate that low hemoglobin is a surrogate marker for chronic illness, and patients who are chronically ill go outside in the sun less frequently. This makes collecting information regarding sun exposure all the more important – otherwise this association between low hemoglobin and 25OHD deficiency seems a bit spurious. The investigators should consider whether including it in the model at all is clinically relevant. If the investigators do wish to include it in their model, then it needs to be discussed.

- Please explain the clinical relevance of evaluating factors predictive of 25OHD
sufficiency after evaluating factors predictive of deficiency. If not relevant, then the authors should consider taking it out.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests