Reviewer’s report

Title: Geographic Patterns of Hepatocellular Carcinoma Mortality with Exposure to Iron in Groundwater in Taiwanese Population: an Ecological Study

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Reviewer: How-Ran Guo

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This study described the geographical distribution of mortality rates due to hepatocellular carcinoma (HCC) in Taiwan at the township level and evaluated their association with land subsidence and iron in groundwater. As a result, the authors found positive associations between concentrations of iron in groundwater and HCC mortality rates in both genders, and correlation coefficient for men (0.286) reached statistical significance \( p = 0.0043 \), while that for women did not (coefficient = 0.192, \( p = 0.0577 \)). The topic is a relevant public health issue, and the finding is interesting.

Major Compulsory Revisions

1. The authors claimed that the correlation coefficient between concentrations of iron in groundwater and HCC mortality rates was significant in both genders, but the \( p \) value was 0.0577 for women, which was above the 0.05 cut-off. On the other hand, the correlation coefficient between concentrations of iron in groundwater and HCC incidence rates was significant in both genders, and it is not clear why the authors choose the mortality rate as their focus of discussion.

2. The authors stated “the exposure to iron in groundwater may play a decisive role for HCC mortality rates” in the Conclusion of the Abstract and “the exposure to iron in groundwater may play an important role for HCC mortality rates” in the Conclusion of the text. The absolute value of a correlation coefficient is more informative in terms of the strength of correlation than the \( p \) value. In general, correlation coefficients less than 0.4 are considered as small, and the correlation coefficients in this study were small for both genders. Therefore, the authors should be more conservative in interpreting their results.

3. It is not clear why the authors included the data on lung cancer in the first place. If this was what they had planned, since they had significant findings, they should discuss it in greater details and even change the title of the paper. If not, they should write another manuscript on the association between iron in groundwater and lung cancer.

4. As townships with serious land subsidence had significant higher iron concentration and HCC mortality ASR than those without the problem, land subsidence might be a confounder of the association between iron in groundwater and liver cancer.

5. Statistical test should be performed to evaluate the differences shown in Table 2.
6. The authors showed information on in Figure 3, but the title of the paper shows that the focus was on iron in groundwater. A figure showing iron levels in groundwater should be more important.

Minor Essential Revisions

The authors mentioned that viral hepatitis is an important risk factor of liver cancer in Taiwan. The possible effects of this factor on the results of this study should be discussed if there were no data to adjust for its effects.

Discretionary Revisions

Reporting the p values to the third digit under the decimal point should be sufficient.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.