Reviewer's report

Title: Alpha-Fetoprotein Level as a Biomarker of Liver Fibrosis Status in 621 consecutive patients with Chronic Hepatitis B

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Reviewer: Vincenza Calvaruso

Reviewer's report:

In this manuscript Liu and co-workers aimed at identifying the role of Alpha-Fetoprotein Level as a biomarker of liver fibrosis in a cohort of patients with chronic hepatitis B.

However, there are several limitations of the manuscript:

One of the main features of chronic hepatitis B is the occurrence of acute flares which have an important role in the progression of the disease. However this significant difference of the inflammation grade during the time, make extremely difficult the evaluation of performance of fibrosis biomarkers. This is particularly evident for a marker which is strongly influenced by inflammation like AFP.

A repeated and dynamic evaluation of the biomarker may be more useful in this setting.

The performance of AFP in the evaluation of the different grades and stages could be not considered satisfactory (AUROC always lower than 0.80).

A proof of the unreliability of the AFP in this setting is demonstrated also by the fact that the median values of AFP at liver inflammation stages null (6.1 ng/ml) was higher than the median value of stage G1-G3.

Moreover the analysis using with AFP cut off > 400 ng/ml should be eliminated because a test with high specificity but so low sensitivity is not clinically relevant. I suppose that only a very few number of subjects had AFP higher than 400 ng/ml.

As the author stated in the discussion they applied the accepted pathological staging system used in China but there are no known comparisons between this system and other universal systems. This is an important limitation of the study.

The discussion is too long and the session explaining the performances of the available not invasive tests of liver fibrosis should be eliminated.

All figures showing the histological features of the differences stages of liver fibrosis did not add any informations to the study results and should be eliminated.

Level of interest: An article of insufficient interest to warrant publication in a scientific/medical journal
Quality of written English: Acceptable

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

Declaration of competing interests: No competing interests to declare