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E-mail: z.m.gong@wjgnet.com

Dear editor Gong,

Thank you very much for your decision letter regarding our manuscript entitled “Serum ceruloplasmin levels are negatively associated with liver fibrosis: a promising novel non-invasive model to predict liver fibrosis in chronic hepatitis B virus patients with normal or minimally raised ALT” (ESPS manuscript No: 28307). We also thank the reviewers for their valuable comments and suggestions. Based on the comments and suggestions from the reviewers, we have made major revisions in the manuscript. All amendments are highlighted in red in the revised manuscript. In addition, point-by-point responses to the comments are listed as follows:

## **COMMENTS TO AUTHOR**

**Reviewer #1:** 1. Major – briefly but better introduce the significance of ceruloplasmin in human biology and pathophysiology and previous studies involving cp in humans (Marano et al. 2015)

**Response:** Thank you for your suggestion. In the revised introduction, we have more precisely mentioned the significance of ceruloplasmin from both its biological and pathophysiological aspects and quoted some previous studies about CP (page 6).

2. Major – comment as a limitation of the study the methodological approach in dosing Cp in the human serum considering other possibilities as evaluating the cp activity (Siotto M et al. Automation of o-dianisidine assay for ceruloplasmin activity analyses: usefulness of investigation in Wilson's disease and in hepatic encephalopathy. J Neural Transm (Vienna). 2014 Oct;121(10):1281-6.)

**Response:** We agree with the Reviewer. However, in our lab, we had only the possibility to test serum CP by nephelometry. The advantages of automation of the o-dianisidine assay and disadvantages of the nephelometric test have now been considered in the revised manuscript (page 15) to address this issue.

3. Minor – declare the exclusion criteria

**Response:** Thanks for the suggestion. We have now added the subject exclusion criteria in the revised manuscript (page 5) as follows:

Patients with the following conditions were excluded from the study: i) presence of other types of viral hepatitis, ii) hepatocellular carcinoma, iii) alcoholic liver disease and non-alcoholic fatty liver disease, iv) decompensated cirrhosis, v) autoimmune hepatitis, vi) concurrent infection with human immunodeficiency virus (HIV), vii) hereditary liver diseases, and viii) drug-induced liver injury (page 8).

We once again thank you and the reviewers for evaluating of our manuscript. We believe that the quality of our manuscript has been significantly improved after revising it according to the comments and suggestions.

We hope that the revised manuscript is now acceptable for publication in *World Journal of Gastroenterology*.

Yours sincerely,

Yue-Yong Zhu, MD, PHD

Liver Center, The First Affiliated Hospital

Fujian Medical University

Fuzhou, Fujian Province, China, 350005

Tel: +86-591-87981660

Fax: +0591-83356180

Email: ezhu066@sina.com