

The *World Journal of Clinical Cases* is a high-quality, online, open-access, single-blind peer-reviewed journal published by the BPG.

The following peer-review report and comments from the Editorial Office (Science Editor, Editorial Office Director, and Company Editor-in-Chief) are provided for your reference.

1 Peer-review report

Reviewer #1: 1. The units should be the standard unit eg. BUN mg/dL, CHE U/L etc. 2. The abbreviation should be arranged as A to Z. 3. The references should be modified as correct format.

Reply: Thanks for your comments. We have corrected the units and the abbreviations in the tables.

Reviewer #2: General comment

I. The accurate prognosis of HBV-related ACLF is an important topic, particularly in China. The authors emphasize the usefulness of GP73 as a prognostic marker for survival and the necessity of a liver transplantation. They present a table with a large number of prognostic markers but they somehow fail to prove that GP73 is really superior to many other markers (point 15) except for the well-known old-fashioned MELD score.

Reply: Thanks for your comments. In this study, the prognostic model (GP73-ACLF) was established based on the variables screened out by Cox regression analysis. The model was named GP73-ACLF because GP73 was included in the model.

II. The discussion of HBV markers is almost completely neglected. More importantly, the role of previous or ongoing antiviral therapy of the patients is kept secret (point 8 and 12).

Reply: Thanks for your comments. Patients in this study received entecavir or tenofovir dipivoxil antiviral therapy after admission, and no post-treatment indicators were collected. Due to the retrospective nature of this study, we think this is the limitation of this study. We appreciate your kind suggestion very much, and we will supplement this part of data content in future experiments.

III. Methodological data are highly incomplete.

Reply: Thanks for your comments. We have supplemented the information about the indicators. The revised contents are as follows:

General Information: Gender and age.

Coagulation function: Prothrombin time (PT), INR.

Routine blood test and coagulation function were analyzed by Sysmex XN (Sysmex, Kobe, Japan) automatic analyzer with Sysmex kit reagent. The indicators included Neutrophil-to-lymphocyte ratio (NLR) and platelet count (PLT).

Blood biochemistry: Alanine aminotransferase (ALT), aspartate aminotransferase (AST), Tbil, albumin (ALB), cholinesterase (CHE), blood urea nitrogen (BUN), creatinine (Cr), blood glucose (Glu), sodium (Na). The TBA120FR automatic biochemical analyzer (Toshiba, Japan) was used for analysis. The kit was purchased from Beijing Kangda Taiké Medical Technology Co., LTD.

Tumor markers: Alpha-fetoprotein (AFP) was analyzed by Cobas E601 biochemical immunoanalyzer (Roche Diagnostics, Germany). The kit was purchased from Roche Diagnostics (Shanghai) Co., LTD. Golgi protein 73 (GP73) was detected by ELISA, which was provided by Beijing Reking Biotechnology Co., LTD.

Virological indicators: HBV DNA was determined by fluorescence quantitative PCR. Taq enzyme,

deoxyuracil nucleoside triphosphate and uracil glycosylation enzyme were purchased from Shanghai Huamei Biological Engineering Company. Standard substance, negative and positive control substance and PCR buffer were purchased from Shanghai Fosun Industrial Company. Primer sequences were synthesized by Shanghai Shenyong Co., LTD. Fluorescence quantitative gene amplifiers were produced by Roche Light Cycler Co., LTD. HBV markers were measured by electrochemiluminescence assay using Cobas 6000 biochemical immunoassay [Roche Diagnostics (Shanghai) Co., LTD.] The kit was purchased from Roche Diagnostics (Shanghai) Co., LTD

Complications: Hepatic encephalopathy, hepatorenal syndrome, spontaneous peritonitis, gastrointestinal bleeding, pulmonary infection. (Line 127 to 151)

IV. The discussion of the data as well of the relevant literature is superficial.

Reply: Thanks for your comments. We have supplemented more discussion. The revised contents are as follows:

TBIL and INR have been recognized as prognostic indicators of viral hepatitis - associated liver failure^[12]. As liver damage worsens, the liver's ability to clear endotoxins decreases. The accumulation of endotoxin in turn induces platelet aggregation, activation and damage, resulting in a decrease in platelet count. On the other hand, hypersplenism secondary to cirrhosis can also cause a decrease in platelet count. Therefore, platelet level can reflect liver function and degree of cirrhosis to a certain extent. The results of this study suggest that platelets may play a role in predicting the prognosis of chronic subacute liver failure. (Line 231 to 240)

GP73 is expressed in hilar bile duct epithelial cells, with little or no expression in normal liver cells, and increased in autoimmune hepatitis or hepatitis B or C virus infection^[17]. Iftikhar found that GP73 was mainly derived from hepatocytes and activated hepatic stellate cells, suggesting that serum GP73 could better reflect the pathological changes of liver^[9]. (Line 251 to 255)

Although the exact mechanism of GP73 on liver injury is not clear, studies have shown that GP73-deficient mice are more likely to develop severe liver cell injury, suggesting that GP73 levels have a certain role in predicting the severity of liver injury^[21]. (Line 264 to 267)

V. Furthermore, the text contains many mistakes as pointed below.

Reply: Thanks for your comments. We have asked for language polishing.

Specific points

Replace antiHBe and HBcAb by antiHBe and antiHBc throughout the text.

Reply: Thanks for your kind suggestion. We have corrected this writing mistake.

L45. Abstract and later. Replace “Golgi apparatus 73” by “Golgi protein 73” (GP73).

Reply: Thanks for your comments. We have corrected this writing mistake.

L50. Abstract and later. What is IgHBsAg? Shall this be the log 10 of the HBsAg concentration in IU/mL? Lg should be replaced throughout by log. LgHBsAg could be misunderstood as large HBsAg.

Reply: Thanks for your comments. We have corrected this writing mistake.

L93. Introduction. What is meant here by “international standard value” as a substitute for prothrombin? Should

it be INR?

Reply: Thanks for your comments. We have corrected this writing mistake. It should be “international normalized ratio”. The revised contents are as follows:

Recent studies found that age, hepatic encephalopathy, total bilirubin, prothrombin or international normalized ratio, alpha-fetoprotein and other indicators have certain value in the prognostic evaluation of liver failure. (Line 70 to 72)

L101-104. It should be briefly mentioned what the biological function of GP73 is.

Reply: Thanks for your comments. We have supplemented more information about GP73 in the introduction section. The revised contents are as following:

Kladneyd et al.^[8] found high expression of Golgi 73 in hepatocytes of giant cell hepatitis. Iftikhar found that GP73 is a novel marker for the evaluation of advanced liver disease and hepatocellular carcinoma (HCC)^[9]. (Line 79 to 81)

L127. M&M. Exclusion criteria. “Other hepadnavirus (hepatitis A,C,D,V); “ Replace “hepadnavirus” by “hepatitis viruses”. HAV, HCV and HDV are not hepadnaviruses. What is meant by hepatitis V?

Reply: Thanks for your kind suggestion. The abbreviation for Hepatitis E is HEV We have corrected this writing mistake. The revised contents are as follows:

Exclusion criteria: 1. Other hepatitis viruses (hepatitis A, C, D, E) infections. (Line 108)

L129. Were HBV-related HCC cases excluded?

Reply: Thanks for your kind suggestion. The patient was examined for primary liver cancer by color ultrasound after admission. We have made additional clarification in the sixth exclusion criterion. The revised contents are as follows:

6. Malignancy including HBV-related HCC. (Line 110)

L130 or elsewhere. Mention whether the patients received antiviral therapy, for how long and with which drugs. (See point 12).

Reply: Thanks for your kind suggestion. We have supplemented the information about patients’ antiviral therapy. The revised contents are as follows:

All patients underwent venous blood and color doppler ultrasound examination and received antiviral therapy within 24 hours after admission. The antiviral treatment of choice is entecavir or tenofovir dipivoxil. (Line 99 to 102)

9. L 139-144. Staging. The text is confusing. Shall “30%

Reply: Thanks for your kind suggestion. We have adjusted the description of staging. The revised contents were as following:

Early stage: the prothrombin time activity (PTA) was between 30%-40% or $1.5 \leq \text{INR} < 1.9$; There were no complications and other extrahepatic organ failure.

Middle stage: the PTA was between 20%-30%, or $1.9 \leq \text{INR} < 2.6$; There was 1 complication and/or 1 extrahepatic organ failure.

Late stage: the PTA was less than 20% or $\text{INR} \geq 2.6$; There was 2 complications and/or 2 extrahepatic organ failure.(Line 118 to 123)

2 Editorial Office's comments

1) Science Editor: In this study, the authors highlight the value usefulness of GP73 as a prognostic marker for survival and the necessity of liver transplantation. However, the data do not show that these markers are superior to others. Therefore, comparisons among other HBV-related markers and treatment should not be overlooked in this context. The material method section should be thoroughly reviewed. In particular, abbreviations should be written in a standard. In addition, the unit values used should be clearly stated. Table 1 should contain more detailed information. The discussion should be handled more comprehensively. Findings showing that GP73 is a vital marker should be highlighted. References should be reviewed. Spelling errors throughout the text should be corrected. The manuscript should be revised according to the comments of the referees

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade D (Fair)

Reply: We have revised the manuscript according to the comments and responded point by point.

2) Editorial Office Director: I recommend the manuscript to be published in the World Journal of Clinical Cases.

Reply: Thanks very much.

3) Company Editor-in-Chief: I recommend the manuscript to be published in the World Journal of Clinical Cases.

Reply: Thanks very much.