

## A point-by-point reply to each query/comment

To: Ruo-Yu Ma  
Science Editor, Editorial Office  
Baishideng Publishing Group Inc

Dear Ruo-Yu Ma edito and reviewers,  
I would like to thank you for your interesting in this manuscript. We would like to reply or explaine a point-by-point following.

Reviewer #1: Serum HBV RNA is a predictor of HBeAg seroconversion and virological response with entecavir treatment in CHB patients In this study, the authors aimed to investigate whether HBV RNA can predict virological response or HBeAg seroconversion during ETV treatment when HBV DNA is undetectable. Thirty treatment-naïve individuals were included in the study. They found that HBeAg seroconversion was more likely in CHB patients with HBV RNA levels below 4.12 log<sub>10</sub> copies/ml before treatment. They have concluded that Serum HBV RNA can predict HBeAg seroconversion and partial virological response during treatment. In the partial virological response group, serum HBV RNA showed an increasing trend. I think this is a good study, and the manuscript is well written; also the tables are all appropriate.

**Reply :** Thanks very much for the valuable and helpful comments.

Reviewer #2:

GENERAL COMMENTS: Other studies have shown that in HBV patients while HBV DNA is found in serum, there is at levels at least 1,000-fold lower, HBV RNA. And, yet other studies have shown that if HBV DNA levels are lower, then antiviral treatments are more likely to succeed. The present studies would like to test/assert that serum HBV RNA, although more difficult to detect, might be a better way to predict/confirm success in antiviral therapies. A major problem of the present study is the limited number of patients with which to test the hypothesis. The accepted patient groups contain only 10 and 15 individuals, with 5 uninfected controls. This major problem remains unsolved even though the authors have provided an heroic attempt at evaluating data for statistical significance.

**Reply:** Thanks very much for the valuable comments. We have the limitation that the number of enrolled patients were small, we have added it in the discussion.

What might be a second problem is the specificity of the RNA assays. The assays might yet be detecting residual HBV DNA. That is, since the HBV DNA is initially in an excess of at least 1,000 fold, the RNA isolation/assay must be much greater than 99.9% greater in removing/detecting DNA. This reviewer did not see control data, obtained in the absence of the reverse transcription step.

Reply : Thanks for your suggestions. We have checked the instruction of QIAamp Viral Mini Kit, which we used to detect HBV RNA. The Kit have the DNA enzyme to avoid detecting residual HBV DNA.

SPECIFIC COMMENTS: Abstract Remove use of first person. Introduction In 1996 Kock first demonstrated that ... HBV RNA levels in serum were ... characteristics of alterations of serum HBV RNA were ... Patients The criteria for inclusion were: (a) patients ... The criteria for exclusion were: ... Informed consent was obtained for all enrolled patients and the study protocol ... by the Ethics Committee ... Results (83%) (37 +/- 6 vs. 33 +/- 12) (3.1 +/- 1.4 vs. 5.5 +/- 1.5) Not convincing that this is a statistically significant difference!! various personal background!! Define fIRNA and trRNA Table 3 HBeAg positive

Reply : Thank you very much for the valuable and helpful comments. We have removed use of first person which was in the page 5. The errors you mentioned were revised.

Reviewer #3:

Name of Journal: World Journal of Gastroenterology Manuscript Type: OBSERVATIONAL STUDY Serum HBV RNA is a predictor of HBeAg seroconversion and virological response with entecavir treatment in CHB patients Generally, the idea of this study is good and the manuscript is well written although it needs minor error editing Title is ok Abstract is simple and please change word discussion to conclusion Key words are enough Introduction, materials and methods are clear. Results contains enough tables and figures but there is several error editing in tables- Please what about relation between HBV DNA and HBsAg Discussion is ok although it is better if it is more longer with more references

Reply : Thanks for the valuable suggestion. The errors you mentioned were revised. The discussion was changed to conclusion. The error in tables were corrected.