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Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road,
Wan Chai, Hong Kong, China

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 4559

Title: HBsAg levels in HBeAg-positive chronic hepatitis B patients with different immune conditions

Reviewer code: 00503062

Science editor: Zhai, Huan-Huan

Date sent for review: 2013-07-06 17:57

Date reviewed: 2013-07-14 21:46

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This paper described serum HBsAg levels in patients of HBeAg-positive chronic hepatitis B under different immune conditions. Basically, the manuscript is well written and the conclusion is clear. But, there are several points to be improved. Major points 1. Authors grouped CHB patients to IT group, IC-Mild group, and ACLF group. The rationale of this grouping is not clear. Authors should explain the reasons for this grouping in more detail. 2. Tables. Explanation or legends of tables is not enough. Authors should describe tables more correctly and reader-friendly. Table 1. Just show some mistakes or inappropriate points. (1) The location of “(median, interquartile range)” is strange. The explanation should be in the table legend and should be described more correctly. (2) “Gender (M/F)” should be “Gender (male/female)”. (3) “10” in “log10 IU/mL” should be subscribed. (4) “Total Bilirubin” should be “total bilirubin”. Why do authors capitalize only “Total Bilirubin”? Table 2. (1) Authors described “r” values in the text (page 8, lines 18-20). Authors should add the data in Table 2. (2) Explain “beta”. 3. Figures. Figure legends are too short and not enough. (1) Dots in figures are too weak! (2) “10” in “log10 IU/mL” should be subscribed. 4. Statistical analysis. . Description of “Kruskall-Wallis ANOVA” (page 6, line 3 from the bottom) is wrong. Kruskal-Wallis is a non-parametric statistical analysis method and ANOVA is a parametric method. They are different statistical method! Minor points There are many careless mistakes through the manuscript. Authors should check and correct them. Some of them are listed below. Page 2, line 3. Add “(CHB)” after “chronic hepatitis B”. Page 2, line 7 from bottom. Spell out “INR” when it comes out first. And explain INR somewhere in the manuscript. INR is not familiar for readers whose expertise is not in hepatitis. Page 3, line 10. Remove “infection”. Page 3, line 21. Add a space between “Serum” and “HBeAg”. Page 5, line 5. Spell out “ULN” when it comes out first. And explain ULN.



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Page 6, line 8. Remove “and”. Page 6, line 20. Remove “Germany”. It already appeared in line 17. Page 6, lines 20, 21. “if HBsAg level > 250 IU/ml” should be “if the HBsAg levels were more than 250 IU/ml”. Page 6, line 23. “for the samples with HBV DNA > 108 IU/ml” should be “for the samples with > 108 IU/ml HBV DNA level”. Page 7, line 3. “San Diego” should be before “USA”. Page 7, line 4. “P” should be italicized. Page 8, line 16. The subtitle should be “Correlation between serum HBsAg levels and serum HBV DNA levels”. Page 9, line 3. Add “significantly” after “serum HBsAg levels”. Page 9, line 5. “and” reads “or”. Page 10, line 10. “triggled” reads “triggered”. Page 10, lines 11, 12. “HLA-class I antigen-restrict cytotoxic T lymphocyte” reads “HLA class I-restricted cytotoxic T-lymphocyte”. Page 10, line 14. “destroied” reads “destroyed”. Page 10, line 20. Add “be” before “related”. Page 10, line 22. “predominantly” reads “predominant”. Page 11, line 7. “number” reads “amounts”. Page 11, line 8. “Peg-IFN” should be spelled out when it appears first and explain it. Page 11, line 14. Remove “of”. Page 11, line 18. “greater” should be after “102 to 105”. Page 12, line 5 from bottom. “crossection” reads “cross-section”. The format of References section should be followed to the format described in Instructions for Authors of WJG.



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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 4559

Title: HBsAg levels in HBeAg-positive chronic hepatitis B patients with different immune conditions

Reviewer code: 00035760

Science editor: Zhai, Huan-Huan

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The authors have investigated the role of quantitative HBsAg in HBeAg-positive IT, IC and ACLF patients. They have shown modest correlation of HBsAg levels with HBV DNA and differences in HBsAg levels in the 3 categories of the patients. The study has a number of shortcomings: 1. The English language needs significant improvement. There are numerous spelling mistakes, and places where the space between words is missing. 2. There is no new message from the study – similar studies with similar results have already been published in HBeAg-positive patients. The authors contradict themselves by stating in the Introduction that there are no studies in the IC group while in Discussion, they cite studies in IC patients while comparing their results with those studies. 3. The majority of the patients in the ACLF group seem to have low platelets (Table 1) and hence likely cirrhotic. As such the statement in the Methodology regarding exclusion of cirrhotics patients is misleading and in my opinion can be removed. I cannot understand the rationale for excluding cirrhosis, particularly since the study does not aim to study the histological stage in relation to HBsAg levels. 4. Were patients excluded if they had recently received chemo/immunotherapy? This is important since the mechanism for immune response in such patients is externally stimulated, and hence the HBsAg response may potentially be also different. The authors should clearly state whether such patients were included and if so, then I recommend that this category of patients be excluded from the analysis. 5. The inclusion exclusion criteria are lacking in comprehensiveness. For instance, were pediatric patients included; HCC; chemo/immunotherapy? 6. The authors should clarify how patients were determined to have normal ALT (how many recordings?), how many HBV DNA recordings, at what time intervals, etc? It is well known that patients may have fluctuating ALT levels and this may impact on patient categorization. Note that the authors mention that ALT for IC group



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were <2 ALT. I assume this is a typo and I assume the authors mean to say ALT >2 and <10 ULN. 7. It is unclear when the serum samples were collected. Were they collected at the time of the 1st visit or subsequently, since this will clarify if patients with ACLF had samples collected during the disease flare? 8. I'm confused about the multivariate analysis - what exactly is the outcome measure here? I assume its HBsAg levels. If so, what level? Clearly then, there should be a cutoff level. If the outcome measure is the predictability to be in a particular category (as defined in the study) based on HBsAg level, then which category was the outcome measure? This entire objective, its methodology, its reporting in the results, the associated table and the discussion should be re-written completely. At present I fail to understand what the authors are aiming to perform. 9. The statement in the discussion "HBsAg production is significantly correlated with viral replication ($r = 0.30$, $p = 0.09$)." is misleading and incorrect. The result (of the previous study) cited is not significant. This should be changed. 10. I'm unclear why patient categories definitions were chosen from 2 different guidelines (APASL and Chinese). I recommend categorization based on a single guideline in order to maintain uniformity and consistency.



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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 4559

Title: HBsAg levels in HBeAg-positive chronic hepatitis B patients with different immune conditions

Reviewer code: 00506564

Science editor: Zhai, Huan-Huan

Date sent for review: 2013-07-06 17:57

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

Authors have performed an interesting and straightforward study. Although sample size is not very large and main limitation comes from being a cross-sectional study, results are of value. However, some points should be addressed in order to improve the manuscript. Major points - How did authors exclude other liver diseases? I understand that autoimmune hepatitis was ruled out according to autoantibody testing but what was the threshold for alcohol consumption to rule out alcoholic liver disease? - Multivariate regression with such a small sample size is well known to be unreliable and prone to overfitting. Thus, it is likely that INR as a predictive factor for HbsAg is just a marker for hepatic failure. I recommend that authors perform multivariate linear regression considering all patients as a whole, in order to analyze which factors predict HbsAg in these kind of patients, but not in every specific subgroup, since sample size does not allow to do that. - Discussion is rather long and should be shortened and focused on author's findings. Also reference list. - Please kindly revise the paper by a native English speaker since there are many mistakes. E.g., "andused" instead of "and has been used", "host's immune" instead of "host immune" or "understanting" instead of "understanding", and other minor mistakes and typos. Minor points - Please, P (p-value) should be italicized and in upper cases. - Since only ultrasound cannot completely rule out or confirm cirrhosis, authors should state that patients had no clinical or ultrasonographic findings of cirrhosis, instead of "Ultrasound B test was conducted and revealed that all of the patients did not suffer from cirrhosis" - ULN has not been defined. - Figure 3 is not referenced in the text. And figure 2 and "figure 2A" are incorrectly referenced. - Bilirubin levels are expressed in mol/L and mg/dL. Please unify.