

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 47640

**Title:** Liquid biopsy for non-invasive assessment of liver injury in hepatitis B patients

**Reviewer's code:** 00036801

**Reviewer's country:** Spain

**Science editor:** Jia-Ping Yan

**Reviewer accepted review:** 2019-03-27 12:47

**Reviewer performed review:** 2019-04-03 09:37

**Review time:** 6 Days and 20 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

This is an interesting manuscript about a model to predict the severity of liver injury in patients infected by hepatitis B virus using serum parameters (liquid-biopsy). The final model combines ALT, bilirubin, and plasma DNA levels as the parameters that better correlated with marked-severe liver inflammation. A diagnostic tool such as the

proposed by authors is, no doubt, very interesting and potentially useful. However, several doubts about the method followed to build the model must be answered by the authors: 1 – Statistical analysis: the statistical methods used and described in the manuscript are the Spearman's rank correlation test and the AUC of the ROC. However, a logistic regression model (binary or ordinal if several liver inflammation categories are considered) is the best and more specific method to build a predictive model. Why the authors have excluded the logistic regression model in their methods?. The authors must build a logistic regression model using as independent variables ALT, bilirubin, plasma DNA, HBV DNA, AST, albumin and controlling by variables such as age, drinking, and gender (since they show significant differences in table 1) and then fit the best and harmonic model. The model's AUC can be used to measure the predictive information provided by the model. 2 – Statistical analysis: multiple comparisons are made in data analysis (table 1). A correction for multiple comparisons must be done and new p values should be indicated on the table. 3 – healthy controls with a history of drinking alcohol had higher ALT, AST, bilirubin, and plasma DNA levels. Were these patients true healthy controls? How the authors discharged an alcoholic liver disease? 4 – How the authors combine serum ALT, bilirubin and plasma DNA to calculate AUC of ROC? Authors must explain the followed method in the statistical methods section.

## **INITIAL REVIEW OF THE MANUSCRIPT**

### ***Google Search:***

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No



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- ☐ No

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 47640

**Title:** Liquid biopsy for non-invasive assessment of liver injury in hepatitis B patients

**Reviewer's code:** 00646291

**Reviewer's country:** United Kingdom

**Science editor:** Jia-Ping Yan

**Reviewer accepted review:** 2019-05-10 22:36

**Reviewer performed review:** 2019-05-14 08:36

**Review time:** 3 Days and 10 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

The experimental approaches used should be described in more details. In particular, the primers and probes as well as the conditions used for the duplex real-time PCR and the quantification of the serum HBV DNA by real-time PCR should be included. In addition, a brief description of the experiments carried out to measure the ALT, AST, bilirubin and



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albumin should be included. Minor comments Lack instead of lackness "The similar results were found in serum AST." Delete the word The. The sentence "This suggests that nearly half of the patients with severe liver injury that was diagnosed only based on serum ALT or AST levels may have a missed diagnosis" is grammatically incorrect. In the Tables 1 and 2 correct the spelling of the word "Groups"

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

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- ☐ No

##### ***BPG Search:***

- ☐ The same title
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- ☐ Plagiarism
- ☐ No

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 47640

**Title:** Liquid biopsy for non-invasive assessment of liver injury in hepatitis B patients

**Reviewer's code:** 00630200

**Reviewer's country:** United States

**Science editor:** Jia-Ping Yan

**Reviewer accepted review:** 2019-05-11 01:07

**Reviewer performed review:** 2019-05-15 01:48

**Review time:** 4 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
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		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
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			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS

Xia et al. studied the idea that measuring free DNA in plasma may aid in the diagnosis of HBV related liver injury. Their results suggest that free DNA may improve diagnosis in patients combined with other markers and may prevent the need for liver biopsy. Specific comments: The abstract should have all abbreviations spelled out.



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Introduction: “especially in China”. Perhaps this statement should be re-worded to express the specific problem (I’m guessing quality and access to health care) rather than stating that the entire country of China has this problem. I imagine China has a spectrum of quality health care. Results: check spelling on “Billirubin” in several locations. P-values listed as 0.000 should be listed as <0.01, or some appropriate value. ‘Sex’ is the appropriate word in regards to biological males and females. ‘Gender’ is not the correct word. Spelling ‘gruops’ in Table 2. Discussion: “lackness” is not a word. Use ‘lack of’ Discussion: The authors need to provide references in regards to the sex-based differences in enzyme levels that are discussed. For instance the following statement needs to be substantiated: “While males have a higher basal metabolic rate than females, a higher activity rate of liver cells can lead to more ALT, AST and genomic DNA released from apoptotic liver cells into the blood.” Studies have reported differences based on sex and various liver enzymes. Including fibrosis stages in Fig. 4 would be informative.

## INITIAL REVIEW OF THE MANUSCRIPT

### *Google Search:*

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- ☐ Plagiarism
- ☐ No

### *BPG Search:*

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism



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[ Y ] No