

## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 23555

**Title:** Early detection of hepatocellular carcinoma co-occurring with hepatitis C virus infection: A mathematical model

**Reviewer's code:** 02860848

**Reviewer's country:** Germany

**Science editor:** Jing Yu

**Date sent for review:** 2015-12-02 10:09

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<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"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

In the current manuscript, the authors Zekri et al. provide a potential novel biomarker combination useful also for early diagnosis for patients with cHCV. This is an interesting study, yet there is an unclear issue, which is to be clarified: ----- The authors mention (in the methods part) that they excluded "diabetes, patients HBV infection and patients with (HCC, LC, and CHC) who received treatment or antiviral therapy for HCV" from their study. In Table 1, the authors show 43 patients from 192 are diabetic. From the table 2, I consider that all 192 patient samples were used for mathematical modeling. ----- The authors did not distinguish between diabetic and non-diabetic patients? Both cases (1. the authors eliminated 43 D.M. cases and they used 148 cases for mathematical analysis or 2. They used all 192 patients) are acceptable, however this should be mentioned in the manuscript (and methods part) in clearer manner. ----- Minor point: In HCC case (Table 1), Sum Gender Male and Female 191, Smoker Yes and No 190, D.M. Yes and No 191, HCV Ab Present and Absent 189, Ascites Yes and No 182. These factors are less than 192. What happened to the missing numbers? Just unknown?

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

**ESPS manuscript NO:** 23555

**Title:** Early detection of hepatocellular carcinoma co-occurring with hepatitis C virus infection: A mathematical model

**Reviewer's code:** 02451558

**Reviewer's country:** China

**Science editor:** Jing Yu

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<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"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

This study was designed to explore the mathematical model for early detection of hepatocellular carcinoma on top of HCV infection. However, the mathematical model is very complex. For the clinical practice, it is very difficult. In addition, some important risk factors have not been controlled, for example alcohol drinking. The English language should also be improved. Major comments: 1. Measurement of serum biomarkers Serum levels of sICAM-1, IL-8 and sTNF-RII were measured by ELISA kit from (R&D Systems, Inc., USA), Proteasome was measured by ELISA kit from (Enzo Life Sciences, Inc., Switzerland) and  $\beta$ -catenin was measured by ELISA kit from (Glory Science Co., Ltd, USA) according to the manufacturer's instructions. Please provide the simple operation processes of these methods. 2. Clinical data of the studied groups Alcohol drinking is one of the most important risk factors for HCC. However, it has not been considered. Why? 3. Title: Mathematical model for early detection of hepatocellular carcinoma on top of HCV infection Abstract: Results: For the discrimination of HCC group from LC group For the discrimination of HCC group from CHC group The objective of this study was designed to explore the mathematical model for early detection of

hepatocellular carcinoma on top of HCV infection. However, in the section of results, the authors did not shown the discrimination of HCC group from non-HCC group. Why? 4. Conclusion: Our proposed mathematical models can differentiate not only between HCC and other studied groups but also between all studied groups in non-invasive, inexpensive and rapid manner. The conclusion has been exaggerated. We could not draw the conclusion on the basis of the results which were provided in the section of results. 5. For the discrimination of HCC group from LC group, using a mathematical model  $[-1.133(E+01) + 7.380 * \text{Proteasome} + (1.081E-03) * \text{sICAM-1} + (2.574E-01) * \beta\text{-catenin} + (1.597E-02) * \text{AFP}]$  with cutoff 0.6552 has achieved 98.8% specificity and 89.1% sensitivity. The mathematical model is very complex. For the clinical practice, it is very difficult. Could the authors simplify the mathematical models for clinical practice? Minor comments: 1. Serum levels of IL-8, sICAM-1, sTNF-RII, Proteasome and  $\beta$ -catenin were measured in 479 subjects, 192 with HCC associated with HCV infection, 96 with HCV related liver cirrhosis (LC), 96 with chronic hepatitis C (CHC) and 95 healthy controls. Should be: were measured in 479 subjects, including 192 with HCC 2. 192 with HCC associated with HCV infection Can be: 192 with HCC and HCV infection 3. ROC curve analysis over pairs of groups was used to find the best cutoffs differentiating among different groups. For the first time of emergence, the full name should be provided, such as ROC. 4. Tables and Figures Three-line tables should be used. 5. The English language should be improved.