

Reviewer 1	Answer
<p>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.</p>	<p>Only the control group is diabetic free, as for all of the other groups; diabetes is a risk factor. All of the 192 HCC patients diabetic or not were used in the mathematical modeling. It is explained clearly in the text. Corrected</p>
<p>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?</p>	<p>All missing information was added .thanks for your important comments. Corrected</p>
Reviewer 2	Answer
<p>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 β-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.</p>	<p>Added to M&M.</p>
<p>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.</p>	<p>None of the subjects is alcoholic (statement were added to M&M).</p>

Why?	
<p>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?</p>	<p>Please note that fig.4 (the schematic representation) is differentiation between the HCC and the Non-HCC in the second step.</p> <p>As the first model is differentiating the control group from the diseased group. And the second model is differentiating the HCC group from (the LC and the CHC) so at this step HCC is completely differentiated from the non-HCC.</p> <p>Also , in table 7, this equation</p> $(-1.227(E+01)+(3.299)* \text{Proteasome} +(4.002E-04)*\text{IL-8}+(1.548E-03)*\text{sICAM-1}+(6.803E-04)* \text{sTNF-RII} +(2.936E-01)* \beta\text{-Catenin} +(1.981E-02)*\text{AFP})$ <p>is directly differentiating between HCC and the non-HCC.</p>
<p>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.</p>	<p>The conclusion was reformulated</p>
<p>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?</p>	<p>Simplified and added</p>

<p>6. Serum levels of IL-8, sICAM-1, sTNF-RII, Proteasome and β-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</p>	<p>Re-edited</p>
<p>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</p>	<p>Full name were added</p>
<p>Tables and Figures Three-line tables should be used.</p>	<p>Reformulated</p>
<p>The English language should be improved</p>	<p>done</p>