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Journal Name:	**International Journal of Biochemistry Research & Review**
Manuscript Number:	**Ms_IJBCRR_31609**
Title of the Manuscript:	**Circulating Survivin and TIMP-1 in Hepatitis C Virus Associated Liver Fibrosis**
Type of the Article	**original research article**

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty'**, provided the manuscript is scientifically robust and technically sound.
To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

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PART 1: Review Comments

	Reviewer's comment	**Author's comment** *(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)*
Compulsory REVISION comments	**The manuscript describes the evaluation of circulating survivin and TIMP-1 and their ratio as non-invasive biomarkers of liver fibrosis in HCV patients and concluded that these parameters represent promising novel biomarkers for prediction and discrimination of different stages of HCV associated liver fibrosis**. Major concerns 1-The limitations of liver biopsy is well known, however, several non-invasive blood-based panels including APRI, FIB-4, Fibrotest, Hepascore, and ELF score, in addition to transient elastography for liver stiffness measurement, were developed and validated for liver fibrosis prediction in chronic HCV and other liver diseases with high diagnostic accuracy for fibrosis staging especially for defining liver cirrhosis (The most important). Therefore, I disagree with the author general statement "a reliable non-invasive method for accurate assessments of different stages of liver fibrosis is still missing" (line 48, 49 page 3). In addition, the word "novel" in the conclusion in not appropriate here as TIMP-1, for example, was already included in ELF score for fibrosis prediction (Lichtinghagen et al., 2013, PMID:23523583) and survivin (as survivin-IgM immune complex was also evaluated before for fibrosis prediction in HCV patients (Matteucci et al, 2014, PMID:24102797). 2-We see that survivin, TIMP-1, their ratio was not significantly different between F0, F1 stages, and F3,	Ok, it is modified All authors see that the current distribution of the disease groups is the ideal for the study target.

	F4 stages (Table 2), why the authors not try to combine fibrosis groups, for example, F0-F1 (early stages) and F2-F4 (moderate/advanced stages) for better interpretation of results and to demonstrate the diagnostic accuracy of their markers to discriminate advanced disease from early disease (not fibrosis vs control) which is the most important, especially that their markers levels in the early stages (F0-F1) were not significantly different from controls. 3-The ROC curve level is not enough for fibrosis prediction, a univariate and multivariate logistic regression analysis should be done to determine the predictor variables (and perhaps their combination) could be significant predictors. 4- The authors should try to compare the performance of his markers (For example, in terms of AUC) with existing fibrosis panels such as APRI or FIB-4. 4-How the authors concluded that "Circulating survivin could be considered as a potential valuable tool for **the detection of the early asymptomatic stage of liver fibrosis** in HCV-infected patients with high sensitivity and specificity" while survivin was not significantly different in early fibrosis (F0 and F1) from controls (Table 1)?. I will be correct for advanced disease (F3/F4) as survivin is significantly different for early stages and controls.	We will do that in our currently arranged future study incorporating a large scale population. Since a lot of the enclosed patients in this study could no longer be still surviving, we can do that in our currently arranged study with a larger scale. Ok, it is modified

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Minor REVISION comments	1- In figure 1, the AUC, P values for ROC curves should be mentioned. And AUC 95% confidence intervals should be mentioned in the results description under ROC analysis. 2-The results under Western blott and mRNA expression, also Figure 2, can't be interpreted without p values and error bars (figure 2), the use of overexpression or gradual increase without mentioning the significance level is misleading. 3--The discussion is repeating the results description. For example, the significance of the observed correlations found should be discussed. The comparison of survivin, TIMP-1, and their ratio with other fibrosis prediction markers or models should be discussed also.	It was modified It was modified It was modified
Optional/General comments		