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PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 40837

Title: Iron metabolism disorders in patients with hepatitis B-related liver diseases

Reviewer's code: 02439220

Reviewer's country: Australia

Science editor: Ruo-Yu Ma

Date sent for review: 2018-07-17

Date reviewed: 2018-08-06

Review time: 20 Days

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[ ] Grade E: Do not publish		[ ] Rejection	[Y] Advanced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

SPECIFIC COMMENTS TO AUTHORS

1) The title does not reflect accurately the findings from this study. Serum hepcidin levels were reported to be decreased in HBV-related disease (Fig 1) and correlated with HBV-DNA (Table 2) but no data demonstrated that hepcidin levels were correlated with liver iron deposition or in fact any serum iron parameters or markers of liver injury

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(Table 2). Liver iron was increased with liver fibrosis scores but hepcidin was not measured in different stages of fibrosis and was unchanged with Child-Pugh or BCLC scores (Fig 2&3). The title needs to be amended. 2) The abstract results and conclusions do not reflect the data presented in manuscript. a) Serum ferritin and transferrin saturation levels increased with poorer Child-Pugh scores (Fig 2) but there was no direct evidence that they increased with fibrosis levels as stated. Child-Pugh is a classification of cirrhosis not fibrosis. Metavir score is for fibrosis. b) Hepatic iron staining levels were not positively correlated with fibrosis stage. It increased at stage 3 and 4 only but not stage 1 and 2. Amend this sentence. c) Abstract conclusions were not consistent with the results. Serum ferritin not serum iron levels were significantly higher in HBV-related disease. Serum iron was increased in CHB subjects only (Fig 1). Ferritin is an acute phase protein and may reflect the presence of hepatic inflammation or iron stores. d) There was no direct evidence from this study that lower hepcidin levels were associated with higher liver iron staining or severity of liver injury in HBV related disease. In fact hepcidin levels were decreased in CHB compared to healthy controls and relatively increased with more severe LC or HCC disease compared to CHB. The conclusions need to be moderated. 3) Core tips need to be modified as outlined in comment 2 above. 4) In the methods section state whether all healthy controls have normal serum iron parameters and describe how liver iron levels were quantified? Results 5a) p9 para 2. Fig 2 demonstrated serum ferritin and transferrin saturation changed with severity of cirrhosis not fibrosis. Also TIBC and TF levels were significantly decreased with an "increased" in Child-Pugh scores. Amend text. 5b) p10 para 2. In Figure 4, it is not stated how many liver samples were tested. Were liver iron levels measured in all HBV patients? What changes were seen across the 4 HBV groups and how did the liver iron levels change with serum hepcidin? It is necessary to do this analysis before you can state that serum hepcidin changes with liver iron and injury in HBV patients.

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Discussion 6a) p12 para 2. Again there is no direct evidence to show "that a decreased serum hepcidin levels correlated with excessive iron accumulation in patients with HBV-related liver disease." 6b) p13 para 3. In the conclusion the text needs to be changed as outlined before (2c and 2d). Other comments 7a) Change total iron binding force to total iron binding capacity (Abstract para 3; p7, para 3; p9 para 1). 7b) Fig 1-3. Include units on y-axis. State whether results are expressed as mean ± SEM or median ± range; n=? 7c) Define what fibrosis stage (S0-S4) is shown in Figs 4a-e. In Fig 4f state whether the results are expressed as mean ± SEM or median ± range; n=?

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

[ ] The same title

[ ] Duplicate publication

[ ] Plagiarism

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Name of journal: World Journal of Clinical Cases

Manuscript NO: 40837

Title: Iron metabolism disorders in patients with hepatitis B-related liver diseases

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			Conflicts-of-Interest:
			[ ] Yes
			[Y] No

SPECIFIC COMMENTS TO AUTHORS

The manuscript written by Gao et al. describes that serum levels of hepcidin were negatively correlated with iron deposit in the liver. Serum levels of hepcidin were also negatively correlated with HBV DNA levels and iron deposit in the liver was increased according to the progression of liver fibrosis. Since iron metabolism in HBV-related liver

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disease has not been well analyzed, the data are interesting and important. However, there are some concerns that need to be addressed. Major points 1. Both age and HBV DNA levels showed statistically significant association with serum hepcidin levels. The results corrected by age should be analyzed and shown. 2. A figure showing the association between serum HBV DNA and hepcidin should be shown. Minor point 1. The possible mechanism by which HBV overload or replication affect hepcidin levels should be discussed. 2. How the data lead to the conclusion that hepcidin may function as an therapeutic target for liver injury is unclear.

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