

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 44765

Title: Clinical characteristics of non-alcoholic fatty liver disease in Chinese adult hypopituitary patients

Reviewer's code: 02860814

Reviewer's country: Greece

Science editor: Ruo-Yu Ma

Date sent for review: 2019-01-29

Date reviewed: 2019-02-03

Review time: 19 Hours, 5 Days

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 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

1. The authors should check the relevance of some references. e.g. "Approximately 20-30% of NAFLD patients develop NASH, which includes a 20% risk of further causing cirrhosis [2]". "However, the pathogenesis of NAFLD and its progression is a complex

process, and the “multiple-hit” hypothesis proposed by Buzzetti et al. in 2016 suggested that simple steatosis and NASH not only exhibited different risk of progression but might also reflect different disease entities in terms of pathogenesis [4]. Multiple insults including insulin resistance, obesity and gut microbiota contribute to the development of steatosis and liver inflammation [4].” “This percentage was significantly higher than that of the general adult population in China (approximately 15%), which was reported in 2013 [18]”. The authors should check again all the references one-by-one to find the mismatches and correct accordingly. 2. An incorrect statement occurs in abstract that BMI and HOMA-IR of the cirrhotic patients were higher than those of the NAFLD patients. Firstly, P values were not significant (P 0.912 and 0.539 respectively), and secondly mean values of BMI was 27.9 in NAFLD group (higher than that of Cirrhosis group, 27.7 kg/m²). 3. The authors should discuss about the sensitivity and specificity of ultrasound to diagnose NAFLD. 4. How many of 7 cirrhotic patients were decompensated? 5. The second paragraph in page 15 should be checked and written again because many false statements exist. a. “Approximately 20 -30% of NAFLD patients develop NASH and this carries a 20% risk of causing cirrhosis [2]. However, only seven patients in the present study were diagnosed with cirrhosis”. Actually, the incidence of cirrhosis in the present study population (patients with hypopituitarism and NAFLD) is calculated 7 patients with cirrhosis out of 27 patients with NAFLD (7/27 = 28%), while in general NAFLD population the incidence of cirrhosis is around 3%. So, the proportion of cirrhotic patients is high, and an explanation should be given in discussion for this high prevalence of cirrhosis, considering also that cirrhotic patients in this study were very young [mean age 21 years, range 19-25.2 years]. What do we know about rapidly progressive NAFLD due to hypopituitarism? What do other studies describe about cirrhosis prevalence in patients with hypopituitarism? b. “Thus, only two of our patients underwent liver biopsy. Therefore, we could not distinguish simple



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steatosis and NASH from NAFLD, and the incidence of cirrhosis might be misleading". Liver biopsy is to distinguish steatosis from NASH. c. Epistaxis is not a manifestation of cirrhotic decompensation. 6. Did delay in diagnosis and treatment initiation contribute to progression to cirrhosis? 7. An increased HOMA-IR was found to cirrhotic patients and this finding was presented as a potential factor that lead to progression to cirrhosis. However, as we know liver cirrhosis and particularly portal hypertension could lead to insulin resistance and this probability should be discussed. 8. Plasma osmolality and sodium concentration was statistically significant higher in cirrhotic patients when compared only to NAFLD group. Why wasn't this difference found between cirrhotic and NAFLD (-) patients?

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
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- ☐ Plagiarism
- ☐ [Y] No

BPG Search:

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- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ [Y] No

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 44765

Title: Clinical characteristics of non-alcoholic fatty liver disease in Chinese adult hypopituitary patients

Reviewer's code: 04091933

Reviewer's country: Russia

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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:
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			Conflicts-of-Interest:
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			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The study is interesting, given the increasing prevalence of NAFLD. However, publication can be recommended only with a major revision. In the section "Association with metabolic syndrome" there is an incorrect statement that "the median

HOMA-IR of the cirrhotic, the NAFLD (+) and the NAFLD (-) groups was 9.57, 3.92 and 2.60, respectively": there should be "the NAFLD group" (as indicated in Table 1) or "the NAFLD patients". I also recommend removing from the abstract: "The parameters BMI and HOMA-IR of the cirrhotic patients were ... higher than those of the NAFLD patients" as incorrect and/or not significant. "The plasma osmolality and serum sodium levels of hypopituitary patients with cirrhosis were higher than subjects with NAFLD and those without NAFLD" is a false statement, because levels were "significantly higher than those of the NAFLD patients". The statement, "that hyperosmolality might be a contributor to the deterioration of NAFLD in hypopituitary patients" cannot be considered valid only on the basis that "the plasma osmolality and serum sodium concentration of the cirrhotic patients were ... were significantly higher than those of the NAFLD patients", because there were no differences with patients without NAFLD. In addition, since it is known that hyponatremia, but not hypernatremia, is a frequent feature of hypopituitarism, this should be discussed in relation to NAFLD. The text states "that there were no significant differences in ... diastolic blood pressure (DBP) between NAFLD (+), and NAFLD (-), patients ($P = 0.050$), respectively", but the Table 1 shows a significant difference. Statement "that the hyperosmolar state may aggravate NAFLD in hypopituitary patients by exacerbating insulin resistance" needs to be confirmed, since it is well known that NAFLD is intimately related to insulin resistance, and the osmolality was statistically significant higher in cirrhotic patients when compared only to NAFLD patients in the study. The correlation between the HOMA-IR and the osmolality should be calculated. The article lacks the latest references (2017-2018), and all available references should be carefully checked for relevance.

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