

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 63382

Title: Present and future management of viral hepatitis

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05561766

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: United States

Author's Country/Territory: Spain

Manuscript submission date: 2021-01-27

Reviewer chosen by: Jin-Lei Wang

Reviewer accepted review: 2021-03-04 14:08

Reviewer performed review: 2021-03-04 15:56

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

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

SPECIFIC COMMENTS TO AUTHORS

González Grande et al. present an ambitious review of all forms of viral hepatitis, ranging from acute to chronic hepatitis. The efforts required in the undertaking of such a project should be commended. The overall quality of the references is excellent, however a few suggestions in order to improve the manuscript follow. Major comments: -The scope and aim of this article should be revised in order to render the message of the article more powerful, for instance highlighting the specific challenges for every single viral hepatitis. -The discussion of each viral hepatitis is uneven; while some delve into epidemiological details others focus on treatments. A more uniform discussion of future directions for each viral hepatitis would strengthen this manuscript. -Numerous sentences from the first two paragraphs in the HEV section are taken quasi-verbatim from the EASL practice guidance. Although the source is cited, reformulation is recommended. This includes the first four sentences of the first paragraph, and the second, third and fourth sentences from the second paragraph. Minor comments: HEV section -The link from reference 21 is inactive and the accuracy of the statement should be confirmed as the authors also state in the article that "HBV is the leading cause of morbidity and mortality of hepatic origin in the world" -Reference 30 refers to a Scottish cohort of 80 patients and this cannot be equated to all cases of liver failure in Europe -The sentence referring to the diagnosis of HEV is superfluous as a stand-alone paragraph without further development. - The following sentence from the last paragraph on HEV "Currently, screening for HEV is advisable in all cases of acute hepatitis, including those with suspected drug-induced liver injury, particularly if patients have higher levels of transaminases, in which case acute HEV must be excluded systematically" should be moved to the paragraph detailing screening in other

populations. HBV section -The EASL classification from the 2017 practice guidance refers to "infection" vs "hepatitis". Would therefore recommend replacing the word "disease" with "hepatitis" -The authors mention the long-term safety of NAs but omit to discuss effects on bone health and renal function -Would recommend changing the formulation of the following sentences: "the latter drug has recently been ratified in a meta-analysis" (page 10, paragraph on HCC) and "Up until a few years ago patients who required a liver transplant due to HBV had a very high risk of recurrence of the infection in the graft" (page 10, paragraph on liver transplantation) as the authors later discuss HBIG and NAs which were introduced two decades ago. -Please clarify the reference to HBV DNA when describing functional cure on page 11 HDV section -The authors should clarify which patients require screening for HDV: all HBsAg patients or select groups (page 16) -It is important to make clear that NAs are not recommended for treatment of HDV while acknowledging the contradictory anecdotal evidence regarding HBsAg and HDV reduction in patients (most often HIV positive) HCV section -The reference to "baby boom" on page 18 should be reformulated. Does it refer to the prevalence of HCV in the Baby boomer generation? -In the same paragraph "naive" should be replaced with "treatment-naive" - The following statement does not belong in a paragraph on treatment and should be in the introduction instead: "HCV, an RNA virus with seven genotypes, was discovered in 1989, before which time it was referred to as non-A non-B" (page 18) -A mention of the challenges of treating HCV in patients with cirrhosis (especially decompensated liver disease) and an emphasis on the impact of HCC due to resolved HCV infection would strengthen the discussion of future management in HCV

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Academic degree: MD, PhD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Spain

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
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Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statementsConflicts-of-Interest: [] Yes [**Y**] No**SPECIFIC COMMENTS TO AUTHORS**

Although spectacular advances in HCV treatment have been made in recent years, viral hepatitis is still a threat to human health. In this review, the author provided an overview of the current situation, recent advances and future perspectives in the approach to viral hepatitis. The author concluded that it is still necessary to persist with, and even boost studies designed to find efficient new therapies, though without forgetting the implementation of preventive measures. This review is described in detail, which, as valuable information, could help the readers to better understand the transmission mechanisms, the pathogenesis, the vaccines and the new highly-efficient, potent drugs of different types of viral hepatitis. If possible, please add the data about hepatitis A and hepatitis E vaccination and briefly introduce the protective effects. This review is recommended to be published in the journal.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Reviewer's Country/Territory: China

Author's Country/Territory: Spain

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
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Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This review is described in detail, which, as valuable information, could help the readers to better understand the new development of different types of viral hepatitis. Recommended for publication.