

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 67799

**Title:** Hepatitis B virus/hepatitis D virus epidemiology: changes over time and possible future influence of the SARS-CoV-2 pandemic

**Reviewer's code:** 02623966

**Position:** Editorial Board

**Academic degree:** MD, MSc, PhD

**Professional title:** Attending Doctor, Research Scientist

**Reviewer's Country/Territory:** Greece

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-05-02

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-05-03 15:01

**Reviewer performed review:** 2021-05-03 15:02

**Review time:** 1 Hour

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 Grade E: Do not publish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



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#### **SPECIFIC COMMENTS TO AUTHORS**

According to my knowledge, it is a novel paper in its field opening new horizons for further evidence. In addition, the object as well as the results are appropriately discussed in the context of previous literature explaining the importance of the manuscript in its field. Authors succeed to present their data in a clear way adding information to the existing literature. Therefore, I have no corrections or further work to propose for the improvement of the manuscript and therefore it can be published unaltered.

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**Name of journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 67799

**Title:** Hepatitis B virus/hepatitis D virus epidemiology: changes over time and possible future influence of the SARS-CoV-2 pandemic

**Reviewer's code:** 05402068

**Position:** Peer Reviewer

**Academic degree:** MD, MSc

**Professional title:** Doctor

**Reviewer's Country/Territory:** United States

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-05-02

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-05-04 06:13

**Reviewer performed review:** 2021-05-04 06:16

**Review time:** 1 Hour

<b>Scientific quality</b>	<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
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

This work is well done and should be accepted for publication

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 67799

**Title:** Hepatitis B virus/hepatitis D virus epidemiology: changes over time and possible future influence of the SARS-CoV-2 pandemic

**Reviewer's code:** 05872850

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Academic Research

**Reviewer's Country/Territory:** Iran

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-05-02

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-05-05 07:26

**Reviewer performed review:** 2021-05-05 08:24

**Review time:** 1 Hour

<b>Scientific quality</b>	<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
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

Do you think that if the incidence of COVID-19 decreases, the increase in the incidence of hepatitis will stop?

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 67799

**Title:** Hepatitis B virus/hepatitis D virus epidemiology: changes over time and possible future influence of the SARS-CoV-2 pandemic

**Reviewer's code:** 05907822

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Professor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-05-02

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-05-02 13:19

**Reviewer performed review:** 2021-05-05 14:02

**Review time:** 3 Days

<b>Scientific quality</b>	<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
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

I have read the manuscript entitled HBV/HDV epidemiology: changes over time and possible future influence of the SARS-COV-2 pandemic, submitted to World Journal of Gastroenterology. In this paper, the authors aimed to review the epidemiological changes HBV/HDV and possible future influence on humanbeings during the COVID-19 pandemic. The article is presented in an intelligible fashion and written in standard English. I have no questions to ask.



## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 67799

**Title:** Hepatitis B virus/hepatitis D virus epidemiology: changes over time and possible future influence of the SARS-CoV-2 pandemic

**Reviewer's code:** 05915429

**Position:** Peer Reviewer

**Academic degree:** BSc, MSc

**Professional title:** Research Assistant Professor

**Reviewer's Country/Territory:** India

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-05-02

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-05-02 13:04

**Reviewer performed review:** 2021-05-09 19:12

**Review time:** 7 Days and 6 Hours

<b>Scientific quality</b>	<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
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
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## **SPECIFIC COMMENTS TO AUTHORS**

First: This study proposed that HDV virus may exist along with HBV and due to existing SARS-CoV-2 pandemic diagnosis of HDV is under reported and this may lead to a catastrophic event caused due to hepatitis in near future. Therefore authors suggested to closely monitor the COVID-19 patient's serum anti-HDV during hospital admission with SARS-CoV-2 infection. Second: The quality is good however slight changes are suggested. This review showed the epidemiology of HDV in covid-19 patients and showed very few studies are actually reporting HDV in patients. Yes the conclusion was summarized appropriately. This study showed that the prevalence rate of HBV/HDV decreased in current population, but there could be rise in this rate if it remains unnoticed within population. The reasons why a hepatitis outbreak occurs are discussed along with the reasons why the numbers are reducing at present but why the numbers will again increase dramatically are also discussed very thoughtfully and provided several evidences. Third, the future directions of the topic described in this manuscript suggested that due to existing focus on COVID-19 the HDV prevalence rate may increase in global population. This study will impact the basic science as well as the clinical practice since it suggests the diagnosis of HDV infection in COVID-19 patients. The limitations, the questions/issues that remain to be solved are listed below; 1. A comma was inadvertently placed after and kindly place it after cases "Peg-interferon alfa, the only recommended therapy, clears HDV in only 10-20% of cases and, consequently, new treatment strategies are being explored". 2. First sentence of Introduction section, the word "liver-tropic" please mention as "liver tropic virus" remove the hyphen or else mention as "hepatotropic". 3. "Chronic HDV infection is the most severe and rapidly progressive form of chronic hepatitis, leading to cirrhosis in 70% of patients in 5-10 years." Please replace the "in 5-10 years" with "within". 4. "Comparing HBV

mono-infected patients with the HBV/HDV co-infected, the latter show a better outcome if reinfection is prevented by the continuous administration of nucleos(t)ide analogues and of hepatitis B immune globulins (HBIG)". Please remove the second "of" not necessary. 5. "Further changes are expected in this era of the COVID-19 pandemic, which might involve, among others, a lower possibility of screening and access to treatment and a reduced effectiveness of the vaccination policy against HBV infection and of the management of patients with severe chronic hepatitis." Please mention "for the management of patients with severe chronic hepatitis". 6. "These epidemiological changes, of great impact on the health and quality of life of human beings, are the subject of this review", please rewrite as "These epidemiological changes has great impact on the health quality of life of human beings, are the subject of this review". 7. Some of the sub-headings are in caps while some are not, please maintain as per journal's instruction. 8. Please correct the tense of this sentence "HDV is spread all over the world, with a global disease burden around 62-72 million HBV/HDV co-infected subjects". 9. The country "French Guiana" is an old term or former name, please write it as French Guyana or mention formerly known as French Guiana. 10. "in Yucpa Indians in Venezuela" please rewrite as "Yucpa Indians of Venezuela" also "in 8 city hospitals in Mongolia" change to in 8 city hospitals of Mongolia. 11. Under the sub-headings in this sentence "To offer the readers an overview of the worldwide variability of the prevalence of anti-HDV among HBV chronic carriers, we report data recorded at different times in some countries", please mention the year range in which the varying studies were performed across various geographical locations within bracket example (1977-2015). 12. Please check the spacing between these two words "data recorded" of the above mentioned sentence. 13. Similar, to the addition done as per point 11 please do it for the next paragraph for low prevalence too. 14. Last sentence of page 12 it should be "patient's fear". 15. It is important to mention that HBV patients are at high

risk of acquiring SARS-CoV-2 infection. 16. Under subheading "SARS-COV-2 PANDEMIC: REDUCED OPPORTUNITY FOR SCREENING, MANAGEMENT, AND TREATMENT" sixth sentence "Overall, all hepatology activities," better to mention as "Overall, hepatological activities. 17. Please put the reference 29 in the last sentence of the paragraph. 18. Page 12 "intra-family spread and men-who-have-sex-with men[44,50,67,93-95] " better to mention the word "homosexual and heterosexual" as this will help to find the article more rapidly during Google search. 19. Please add the data for sex workers as well since very are vulnerable to viral hepatitis. 20. The epidemiological information given under subheading "HDV/HBV Chronic Infection" has to be segregated from the information given about the reasons for reduced prevalence rate. Please segregate and make two different paragraphs. 21. It would be best if the epidemiological findings are segregated as per the decades irrespective of the countries where the studies were conducted and accordingly the sub-headings can be changed. If you are not willing to do so atleast align the sentence with epidemiological information in year wise chronological manner. 22. "The epidemiology of HDV infection has changed a lot in nearly every country since its first identification 55 years ago" Please add a citation for this and below it place the sentence "Outbreaks of fulminant hepatitis were first described in the Amazon Basin, in French Guiana, in Yucpa Indians in Venezuela and in the Central African Republic[14-19]. Small but similar outbreaks have been observed also in northern Colombia and designated as hepatitis of Santa Marta (de sierra Nevada)[20-22]. Please add the year of occurrence for the respective regions. Earliest discovery of HDV in patients can be mentioned in a separate paragraph and can be added in the introduction section. Now if these studies [Reference 14-22] if they have found that acute liver failure in patients then what was the exact number of deaths please mention it. 23. Better to merge the acute infections in geographic location [Reference 23-28] with hospitalized acute infection [Reference 29-32]

into one example - Acute hepatitis cases, please choose a suitable sub-heading. 24. These sentences need citation and mention the year "In patients with fulminant hepatitis, morphologic studies showed marked liver steatosis with characteristic "morular hepatocytes", cells with small droplets of fat and central pycnotic nuclei. Worthy of note, some similarities in the clinical presentation of fulminant hepatitis Delta with that of yellow fever has led to the hypothesis that some of the outbreaks occurring in the past in the Amazon basin and attributed to yellow fever, may have been due to HBV/HDV co-infection". 25. Please refer if any research article showed superinfection of HBV/HDV, HIV and COVID-19 in a single patient. 26. Reference [14] is incomplete I am unable to refer it in Google. 27. No need of this sentence please remove it "To provide readers with an organic view of the spread of HDV infection around the world over the past 5 decades, we will separately analyze published epidemiological data concerning both acute HDV infections, observed during outbreaks or in planned clinical studies, and chronic HDV infection and then make some conclusive remarks". 28. Please mention the disease name as COVID-19 not just covid. 29. The occurrence of HDV and HIV super-infection in patients was not mentioned at all, it has to be mentioned. Please provide the epidemiological data relevant to it. 30. Often test with anti-HDV IgM, hepatitis D antigen (HDAg) or HDV RNA as an initial test are not considered accurate as these are inconsistently expressed markers of HDV infection. However, here it was not considered please explain.