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A Survey of HBV Core/Pre-Core Mutations in Iraqi Patients with Chronic Hepatitis

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

3 comments · 19 Jul 2023 – 28 Jul 2023

Referee 1 Reviewer

MAJOR REVISION 19 Jul 2023

Title and Abstract: The title should clearly state the objective of the study, but it is vague and does not convey the specific focus on HBV Core/Pre-Core mutations. The abstract lacks important information such as the methodology used and the key findings of the study.

Introduction: The introduction should provide a comprehensive background on the topic, including the global and local prevalence of HBV, its association with hepatocellular carcinoma (HCC), and the significance of studying HBV genotypes and mutations. The current introduction lacks relevant information and references.

Methods: The sample size of 134 patients is mentioned without clear justification or explanation of how it was determined. The lack of information on HBeAg status is a limitation, as it is a critical marker in the progression of CHB. The sample collection and storage methods are not described, and there is no mention of any inclusion/exclusion criteria for patient selection.

Results: The presentation of results lacks clarity. The specific nucleotide and amino acid alterations are mentioned, but their clinical implications or significance are not discussed. The statistical analyses are not described in detail, and the results are not adequately linked to the objectives of the study.

Discussion: The discussion is brief and lacks depth. The comparison of results with other studies is limited, and the interpretation of findings is not comprehensive. The limitations of the study are mentioned, but they are not thoroughly discussed. The discussion does not provide meaningful insights into the field or suggest directions for future research.

Conclusion: The conclusion is too general and does not adequately summarize the key findings of the study. It does not provide any recommendations or implications for clinical practice or further research.

Referee 2 Reviewer

MINOR REVISION 26 Jul 2023

This study was undertaken to evaluate the biological diversity pattern of chronic HBV among patients in an Iraqi province. In this present investigation, a total of 134 patients were included for evaluation. To cover the C gene in human-infecting hepatitis B viruses, two specific PCR fragments were designed. The PCR products from the clinical viral samples were subsequently subjected to direct sequencing using the Sanger method. Ultimately, the researchers identified twenty-one variants within the coding sequences of the C gene. The findings of this study indicate that genotype D predominates among the identified viral infections. Moreover, the results suggest the potential utility of the evaluated fragment for HBV genotyping purposes.
1. Provide a comprehensive account of the study's context, pertinent locations, and relevant dates, encompassing periods of recruitment, exposure, follow-up, and data collection.
2. Were there any missing data, and if so, how did you handle them?
3. How did you sample the cases?

Associate Editor

MAJOR REVISION 28 Jul 2023

Dear EIC,
Thanks to the authors and appreciation to the researchers. The manuscript is a valuable piece of research. But some revisions are needed.
ABSTRACT:
1- The study design should be mentioned in the first line of the methods section of the ABSTRACT.
2- A summary of the statistical analysis results should be mentioned in the results section of the ABSTRACT.

2

Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

We sincerely thanks the associated editor, EIC and dear reviewers for the time and efforts. The mentioned comments for reviewers and associated editor were revised in the text in a point-by-point fashion. The revised based on the reviewer 1 comments highlights by yellow color, the revised based on the reviewer 2 and associated editor where highlighted by green and blue color respectively.

Thank you for your efforts,

Reviewer 1:

Title and Abstract: The title should clearly state the objective of the study, but it is vague and does not convey the specific focus on HBV Core/Pre-Core mutations. The abstract lacks important information such as the methodology used and the key findings of the study.

Thank you for your consideration and efforts, Based on the reviewer comment the objective of study in abstract and the text. Based on the dear reviewer comment we rewrite the method and results sections of the abstract in more informative form. (Page 1, lines 5-17)

Introduction: The introduction should provide a comprehensive background on the topic, including the global and local prevalence of HBV, its association with hepatocellular carcinoma (HCC), and the significance of studying HBV genotypes and mutations. The current introduction lacks relevant information and references.

Based on the dear reviewer comment the introduction was edited and some sections about global and local prevalence of HBV, its association with hepatocellular carcinoma (HCC), and the significance of studying HBV genotypes and mutations were added to the text. (Page 2, lines 40-44, 52-54, 57-61, 73-74)

Methods: The sample size of 134 patients is mentioned without clear justification or explanation of how it was determined.

The mentioned section were completely revised and replace with “In the current cross-sectional study, we evaluates 134 CHB patients for mutations in Pre-Core/Core gene. All patients with inclusion criteria during the study period were included. The inclusion criteria were serological or molecular confirmed CHB, written ethical consent form and age>18 years old. The exclusion criteria were include not enough sample, and age less than 18. ” (Page 3, lines 77-80)

The lack of information on HBeAg status is a limitation, as it is a critical marker in the progression of CHB.

Unfortunately, we did not access to the HBeAg status and in this regard, we added this to the study limitations. (Page 5, line 191)

The sample collection and storage methods are not described, and there is no mention of any inclusion/exclusion criteria for patient selection.

By the favor of dear reviewer, the sample storage and collection method added. The inclusion and exclusion criteria added. (Page 84-87)

Results: The presentation of results lacks clarity. The specific nucleotide and amino acid alterations are mentioned, but their clinical implications or significance are not discussed. The statistical analyses are not described in detail, and the results are not adequately linked to the objectives of the study.

We tried to revise the results section in a more clear way. The clinical implication of mentioned mutations discussed in dissection section as much as relevant literature with direct mention to these mutations were available. The statistical tests were added in the table 2 and the text. we completely understand the reviewer concern and tried to provide more details in the supplementary data to summarize the body of text of article and this might be a reason for this complication. We sincerely thanks the reviewer for the valuable comments. (Page 4, line 134, lines 136-146)

Discussion: The discussion is brief and lacks depth. The comparison of results with other studies is limited, and the interpretation of findings is not comprehensive. The limitations of the study are mentioned, but they are not thoroughly discussed. The discussion does not provide meaningful insights into the field or suggest directions for future research.

More literature added to the discussion section. Limitation were discussed with more depth and completely revised. We tried to provide a scope for future studies. All changes were highlighted by yellow color. (Page 5, 177-188, Page 6, 207-233)

Conclusion: The conclusion is too general and does not adequately summarize the key findings of the study. It does not provide any recommendations or implications for clinical practice or further research.

More descriptions added to the conclusion. A future perspective added to the conclusion. The conclusion section were completely revised. (Page 6, 220-233)

Reviewer 2:

This study was undertaken to evaluate the biological diversity pattern of chronic HBV among patients in an Iraqi province. In this present investigation, a total of 134 patients were included for evaluation. To cover the C gene in human-infecting hepatitis B viruses, two specific PCR fragments were designed. The PCR products from the clinical viral samples were subsequently subjected to direct sequencing using the Sanger method. Ultimately, the researchers identified twenty-one variants within the coding sequences of the C gene. The findings of this study indicate that genotype D predominates among the identified viral infections. Moreover, the results suggest the potential utility of the evaluated fragment for HBV genotyping purposes.

1. Provide a comprehensive account of the study's context, pertinent locations, and relevant dates, encompassing periods of recruitment, exposure, follow-up, and data collection.

Firstly, we thank dear reviewer for the time, efforts, valuable comments, and concerns. Based on the dear reviewer comment we added some sections in interdiction for more clarification of frame work (Page 2, lines 40-44, 52-54, 57-61, 73-74), patients location and date collection (Page 3, lines 89-90). Some items include encompassing periods of recruitment, exposure and follow-up period is not applicatable or available which we added all of them into the study limitations. (Page 6, lines 212-213)

2. Was there any missing data and how did you handle it, if any?

Patients with missing data (only about the mentioned data in article) were excluded before the genotyping and patients with no missing data evaluated in next steps. By the favor of dear reviewer a statement about this added into the method section. (Page 3, lines 90-94)

3. How did you sample the cases?

The inclusion criteria and sampling criteria about this study added in method, the sampling was randomly based on the inclusion criteria in mentioned study period. (Page 3, lines 77-81).

> Associate Editor's Comments:

Associate Editor 1:

Dear EIC,

Thanks to the authors and appreciation to the researchers. The manuscript is a valuable research. But some revisions are needed.

ABSTRACT:

1- Study design should be mentioned in first line of method section of ABSTRACT

Thank you for your consideration and efforts, the study design were added in the abstract in method section. (Page 1, line 8)

2-Summary of Statistical analysis results should be mention in result section of ABSTRACT.

Statistically analysis result were added into the abstract in results section. (Page 1, lines 17-19)

2 Revision 1

3 comments · 30 Aug 2023 – 12 Sep 2023

Referee 1 Reviewer

ACCEPT 30 Aug 2023

Dear AE,
I reviewed the manuscript again. The great effort in improving the manuscript is highly appreciated.
The authors have addressed all comments.
Thank you

Referee 2 Reviewer

ACCEPT 9 Sep 2023

Dear authors,
Thank you very much for the revisions.
Best regards

Associate Editor

ACCEPT 12 Sep 2023

Dear EIC,
I reviewed the manuscript again. The great effort in improving the manuscript is highly appreciated.
The authors have addressed all comments.
Thank you