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OPEN PEER REVIEW

Comparison of Characteristics and Outcomes of Hepatitis B and Hepatitis C Patients in the Fars Hepatitis Registry

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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

5 comments · 23 Jul 2024 – 2 Aug 2024

Referee 1 Reviewer

MINOR REVISION 23 Jul 2024

1. The title does not reflect the content appropriately. The title is “Epidemiology of viral hepatitis in southern Iran, a cross sectional register based study on 6,690 patients,” but in the study, hepatitis B and C have been compared.
2. The flow of the paper is reasonable and has a logical flow.
3. There are no significant language issues.
4. Many studies have been done in this field, but it might help to compare all of these side by side. Also, the provided statistics are valuable.

Referee 2 Reviewer

MINOR REVISION 30 Jul 2024

Comments to the authors:
1. English writing needs to be checked and improved.
2. Introduction. The reason for the comparison between HCV and HBV in terms of risk factors, etc., is not well described.
3. Method. Inclusion and exclusion criteria are not described well.
4. Method. This study is retrospective. Did you collect data by reviewing patients' files or conducting interviews? You mentioned that patients were referred to the clinic. Please describe these items clearly.
5. Discussion. Line 155. 78.5% of the group. Which group does 'the group' refer to?
6. Discussion. Line 161. The mean age of patients in our study was 52.56 years, indicating that hepatitis infections disproportionately affect older individuals in this region. Did you record the age of patients at the time of disease onset? And was the mean age at the time of disease diagnosis 52.26 years?
7. Discussion. Please discuss the possible or probable reasons for the higher prevalence of the disease among males.

Referee 3 Reviewer

MAJOR REVISION 2 Aug 2024

Dear AE,
I had the privilege of reviewing this study. Here are some suggestions and comments that should be addressed:
Addressing these flaws will strengthen the study's reporting quality and ensure it adheres to the CONSORT guidelines, enhancing transparency, replicability, and reliability:

-Please try to improve the quality of academic writing in the manuscript with the help of a native English-speaking writer or a person proficient in academic English. It needs revision throughout.

-Some sentences lack references. All sentences quoted from other articles must have references at the end. For example, the following sentences:
"Iran, a country home to more than 80 million people, has launched a number of programs to reduce the incidence of viral hepatitis."

"With a population of over 3 million, Fars province is a significant region in southern Iran and offers a useful case study for examining the regional hepatitis epidemiology."

-I could not find the exclusion criteria for patients. Expand the exclusion criteria to include all relevant factors, such as specific health conditions that may affect the outcomes.

-How was the sample size calculated? Which formula was used? Explain it.

-The selection bias is overt.

Associate Editor

MAJOR REVISION 2 Aug 2024

Dear EIC,
I thank the authors and express my appreciation to the researchers. The manuscript presents valuable research. But some revisions are needed. The authors should revise it based on the comments. Also, minor changes should be made in the abstract:
1- The study design should be mentioned in the first line of the method section of the ABSTRACT.
2- A summary of the statistical analysis results should be mentioned in the result section of the ABSTRACT.

Dear EIC,
I thank the authors and express my appreciation to the researchers. The manuscript presents valuable research. But some revisions are needed. The authors should revise it based on the comments. Also, minor changes should be made in the abstract:
1- The study design should be mentioned in the first line of the method section of the ABSTRACT.
2- A summary of the statistical analysis results should be mentioned in the result section of the ABSTRACT.

Editor-in-Chief

MAJOR REVISION 2 Aug 2024

Dear Author,
Thank you for submitting the article. It needs some revision. Please revise it based on the reviewers' and AE's comments.

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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.

Dear Editor-in-Chief of Hepatitis Monthly,

We would like to thank you for the email dated 3-Aug-2024, and the opportunity to resubmit a revised version of the manuscript, entitled “Epidemiology of viral hepatitis in southern Iran, a cross sectional register based study on 6,690 patients” (Submission ID 150623, the title is changed to “Comparison of characteristics and outcomes of hepatitis B and hepatitis C patients in the Fars hepatitis registry”). We would also like to take this opportunity to express our thanks to the reviewers for the positive feedback and helpful comments for correction or modification, which led to major revision of the work and helped its improvement. We have addressed each of the reviewer’s comments as outlined below. All corrections are highlighted in the main text in yellow.

Reviewer Comments:

Reviewer #1:

1.The title does not reflect the content appropriately. The title is Epidemiology of viral hepatitis in southern Iran, a cross sectional register based study on 6,690 patients but In the study, hepatitis B and C have been compared.

Thank you for your thoughtful comment. The title was revised as follows:

Comparison of characteristics and outcomes of hepatitis B and hepatitis C patients in the Fars hepatitis registry

2.The flow of the paper is reasonable and has a logical flow.

Thank you for your positive feedback.

3.There are no significant language issues.

Thank you for your positive feedback.

4.Many studies have been done in this field but It might help to compare all of these side by side. Also, the provided statistics are valuable.

Thank you for your positive comment.

Reviewer #2:

Comments to the authors:

1. English writing needs to be checked and improved.

Thank you for your comment. English revision was conducted.

2. Introduction. The reason for the comparison between HCV and HBV in terms of risk factors and etc is not well described.

Thank you for your comment. The reason was added to the revised manuscript.

Numerous investigations have examined the incidence of HBV and HCV in Iran. (8) However, there isn't a thorough analysis that makes use of information from a sizable, dedicated registry. By examining data from the Fars hepatitis registry, this study seeks to fill this gap by examining the prevalence, demographics, and possible risk factors related to HBV and HCV infections. Our goal in evaluating this data was to provide important new information about the hepatitis epidemiology that exists in southern Iran at the moment. The burden of hepatitis in our community can eventually be decreased by using this knowledge to guide focused interventions.

3. Method. Inclusion and exclusion criteria are not described well.

Thank you for your comment. The inclusion and exclusion criteria is added to the revised manuscript.

In the current cross-sectional descriptive-analytical investigation study, we included a total of 6,690 adult patients who had enzyme immunoassay-confirmed HBV and HCV infections with a minimum of six months elapsed since their diagnosis and were included in the Fars hepatitis registry. Patients with other known hepatic diseases, malignancies, co-infections of HBV and HCV, acute hepatitis, and severe comorbid conditions (e.g., heart failure, chronic kidney disease) were excluded from current study.

4. Method. This study is retrospective. Did you collected data through reading patients files or interview. You mentioned patients were referred to the clinic. Please describe clearly these items.

We retrospectively analyzed data from the Fars Hepatitis Registry, which was gathered prospectively. We revised the manuscript in this regard.

In the current cross-sectional descriptive-analytical investigation study, we included a total of 6,690 adult patients who had enzyme immunoassay-confirmed HBV and HCV infections with a minimum of six months elapsed since their diagnosis and were included in the Fars hepatitis registry. Patients with other known hepatic diseases, malignancies, co-infections of HBV and HCV, acute hepatitis, and severe comorbid conditions (e.g., heart failure, chronic kidney disease) were excluded from current study.

The Fars hepatitis registry is affiliated with the Shiraz University of Medical Sciences, located at the Gastroenterohepatology Research Center within the Motahhari Referral Clinic in Shiraz, Iran. Eligible subjects were referred to the clinic by gastroenterologists. The collection of patients' data began in 1995 and continued until 2023. However, the first patient included in the records was diagnosed in 1991. Before being admitted to this facility, the goals of the present study were communicated to the patients, and signed agreement was obtained from each individual. Following that, data pertaining to the timing of diagnosis, demographic characteristics, medical background, progression of the disease (including symptoms at the beginning), laboratory results, and history of exposure to potential transmission routes and risk factors, and family history of hepatitis infection were gathered from patients, while anthropometric variables were measured. The enrolled patients were monitored at six-month intervals using telephone interviews and in-person visits conducted by gastroenterologists.

5. Discussion. Line 155. 78.5% of the group. 'the group' is which group?

Thank you for your comment. The sentence was deleted.

6. Discussion. Line 161. The mean age of patients in our study was 52.56 years, indicating that hepatitis infections disproportionately affect older individuals in this region. Did you record age of patients at the time of the disease onset? And mean of age at time of the disease diagnosis was 52.26 years?

Thank you for your thoughtful comment. The reported age is related to the patients' age at time of inclusion to the registry. So, these sentences were deleted.

7. Discussion. Please discuss the possible or probable reasons for higher prevalence of the disease among male gender.

Thank you for your comment. According to our comment following sentences were added to the manuscript:

Additionally, we observed a higher proportion of HCV patients being male compared to HBV patients, a finding that warrants further investigation into potential sex-specific risk factors or healthcare-seeking behaviors. There is conflicting evidence regarding the sex differences in the prevalence of hepatitis. While some studies support the notion that HCV has a higher prevalence and more rapid progression among men, as well as a greater prevalence of intravenous drug use as a risk factor for HCV in this population, other studies have reported contradictory findings

Reviewer #3:

Dear AE,

I had the privilege of reviewing this study. Here I have some suggestions and comments that should be addressed:

Addressing these flaws will strengthen the study's reporting quality and ensure it adheres to the CONSORT guidelines, enhancing transparency, replicability, and reliability:

1-Please try to improve the quality of academic writing in your manuscript by a native-writer or a person proficient in Academic English!!!! It needs revision, totally.

Thank you for your comment. English revision was conducted.

2-Some sentences lack references. All sentences quoted from other articles must have references at the end of themselves.

For example below sentences:

Iran, a country home to more than 80 million people, has launched a number of programs to reduce the incidence of viral hepatitis.

With a population of over 3 million, Fars province is a significant region in southern Iran and offers a useful case study for examining the regional hepatitis epidemiology.

Thank you for your comment. Appropriate references were added to the manuscript.

3-I could not find the exclusion criteria of patients. Expand the exclusion criteria to include all relevant factors, such as specific health conditions that may affect the outcomes.

Thank you for your comment. The inclusion and exclusion criteria is added to the revised manuscript.

In the current cross-sectional descriptive-analytical investigation study, we included a total of 6,690 adult patients who had enzyme immunoassay-confirmed HBV and HCV infections with a minimum of six months elapsed since their diagnosis and were included in the Fars hepatitis registry. Patients with other known hepatic diseases, malignancies, co-infections of HBV and HCV, acute hepatitis, and severe comorbid conditions (e.g., heart failure, chronic kidney disease) were excluded from current study.

4-How did you calculate the sample size? Which formula? Explain it.

We included all patients who were referred to our clinic from 1995 until 2023. This is mentioned in the manuscript.

The Fars hepatitis registry is affiliated with the Shiraz University of Medical Sciences, located at the Gastroenterohepatology Research Center within the Motahhari Referral Clinic in Shiraz,

Iran. All eligible subjects were referred to the clinic by gastroenterologists. The collection of patients' data began in 1995 and continued until 2023.

5-The selection bias is overt.

Thank you for your comment. This limitation is mentioned in the revise manuscript.

Firstly, the study design may introduce biases related to data collection and patient selection.

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. Authors should revise it based on comments. Also minor changes should be done in abstract:

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

Thank you for your comment. The study design now is mentioned in first line of method section of ABSTRACT.

Methods: In this cross-sectional study, a total of 6,690 eligible patients, including 3,840 (57.4%) with HBV and 2,820 (42.6%) with HCV, were assessed from the database spanning 1995 to 2023.

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

Thank you for your comment. The summary of statistical analysis results now is mentioned in result section of ABSTRACT.

Results: The average age of the patients was 52.56 years (standard deviation: 13.24). Significant differences were found between HBV and HCV patients in terms of sex, marital status, education level, family history of HBV and HCV, smoking status, drug use, and body mass index ($P<0.001$ for all). HBV patients had a higher prevalence of dental procedures ($P<0.001$) and uncertain sexual contacts ($P=0.009$), while blood transfusion, intravenous drug use, major thalassemia ($P<0.001$ for all), tattoos ($P=0.004$), and hemodialysis ($P=0.001$) were more common in HCV patients. HCV patients showed higher levels of liver enzymes ($P<0.001$) and total bilirubin ($P=0.002$) but lower levels of albumin ($P<0.001$) and prothrombin time ($P=0.034$) compared to HBV patients. Cirrhosis was also more common in HCV patients ($P<0.001$).

2 Revision 1

5 comments · 21 Aug 2024 – 6 Sep 2024

Referee 1 Reviewer — ACCEPT 21 Aug 2024

Thank you for the corrections.

Referee 3 Reviewer — ACCEPT 26 Aug 2024

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 2 Sep 2024

The manuscript has been revised according to the comments.

Associate Editor — ACCEPT 6 Sep 2024

Dear EIC,
I read the manuscript, and the authors corrected the requested items. The article could be accepted at this stage.
Sincerely;

Editor-in-Chief — ACCEPT 6 Sep 2024

Dear Author,
Your revisions have significantly improved the article, and it is now deemed acceptable for publication.
Congratulations on your hard work and dedication to enhancing the quality of your work.