OPEN PEER REVIEW

Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
- More motivations for all involved roles in the review process
- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://sites.kowsarpub.com/kowsar/knowledgebase/category/tree.html#opr.html

Hepatitis Monthly
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Peer Review Report for "Clinical Course and Outcome of Liver Transplantation in Patients with Hepatitis C in Iran"

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Review Timeline:

Submit Date: 11 Aug 2020
Revised Date: 5 May 2021
Accepted Date: 5 May 2021

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | Revision (0)

21 Mar 2021

Dear AE,
In this paper, the clinical course and outcome of patients with end-stage chronic hepatitis C that have undergone liver transplantation are evaluated after the advent of direct antiviral drugs in an Iranian liver transplantation center. The authors have shown a very good outcome which is comparable with well-known international centers. The manuscript is well-written and addresses a very important issue. Therefore, I recommend its publication. However, I suggest the following modifications for the authors before publication:
1. Was the protocol biopsy performed on all cases? If yes, how many of them showed evidence of rejection and/or hepatitis C recurrence in the patients without abnormal liver biochemistries?
2. What has been the frequency of antibody-mediated rejection?
3. As the authors have mentioned the 1-year survival of transplanted hep C patients, that was previously reported by Dr. Malek Hossieni from the same center (Malek Hosseini SA, Nikeghbalian S, Salahi H, Kazemi K, Shemsaeifar A, Bahador A, Dehghani M, Imanieh MH, Tabrizi R, Lankarani KB. Evolution of Liver Transplantation Program in Shiraz, Iran.

Hepatitis Monthly. 2017 Nov 1;17(11).), has been the same as this study i.e., 85%. As that study belonged to the pre-DAA era, how can this finding be explained?
Does it mean that DAA does not affect the 1-year outcome? What has been improved in comparison to the pre-DAA era?
4. Line 60: “in” is repeated.
5. Line 100: “trough" level not “through” level.
6. Line 136: Were rejections confirmed with liver biopsy in all cases?
7. Line 139: How was the patient, with concomitant HCV recurrence and mild acute rejection, diagnosed? How was he/she treated?
8. Line 139-140: It is mentioned that no patient with rejection had HCV rejection. But it has been stated that one of the patients with HCV recurrence had mild acute cellular rejection (lines 138-139). These statements seem to be contradictory. How can it be explained?
9. Table 4: line 289: There are two cases of myocardial infarction but only one interval to death is given in the table.
Thanks

REFEREE: Reviewer | **Revision** (0) 27 Mar 2021

Dear AE,
This manuscript needs some major revision.
Thanks.

REFEREE: Reviewer | **Revision** (0) 29 Mar 2021

Dear AE,
Many thanks for your kind invitation. I read the manuscript carefully and tried to review it. Based on the authors’ statement, this project is the first one that evaluates the hepatitis c virus (HCV) course among liver transplanted patients (LTP) in Iran. Here you can my find comments on this project:
1- Authors should select more appropriate keywords. Some of them should cover treatment aspects of HCV among LTP. They can use treatment or direct-acting antivirals or interferon …. Also, all of the used keywords should be selected according to the MeSH database.
2- In the introduction section, the authors can add some statistics about the status of HCV prevalence and treatment in Iran.
3- CRRT should be completely spelled out in the first use.
4- Authors should provide separate parts in the methods section for settings of the study/Eligibility criteria/ Ethical approval/
5- Study type (retrospective cohort ?) should be mentioned.
6- Authors have mentioned P-value in the results section. However, they did not cite using of analytical test in the methods section.
7- The discussion section is too long and should be summarized.
8- Authors should provide a detailed list of their limitations in this project.
9- I think the manuscript can be and should be formatted as a brief report.
10- Tables should be reformatted based on Hepatitis monthly journal instructions.
In conclusion, I think that this project should be majorly revised and then evaluated for possible publication in the HM journal.
Best

REFEREE: Associate Editor | **Revision** (0) 30 Mar 2021

Dear EIC,
The authors should make major revisions as suggested by the reviewers and resubmit highlighting the changes made , This may be considered for publication provided the necessary changes are made.
Thanks.

Seyed Moayed Alavian: EIC | **Revision** (0) 30 Mar 2021

Dear Authors,
Thanks for your submission. Please submit a revision based on the peer-review comments.
Regards,

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear editor.

Thank you and your reviewers for reviewing our paper and precise comments. We revised the paper according to the reviewers' comments. The Changes related to Referee No. 2 are highlighted in yellow and changes related to Referee No. 3 are highlighted in blue.

Also reviewer 2 has suggested that "*the manuscript can be and should be formatted as a brief report*". With all respects, we prefer to publish this paper as an **"Original Article".**

Sincerely yours

Response to Reviewer 2:

1- Authors should select more appropriate keywords. Some of them should cover treatment aspects of HCV among LTP. They can use treatment or direct-acting antivirals or interferon .... Also, all of the used keywords should be selected according to the MeSH database.

- The changes were done according to Mesh Database

2- In the introduction section, the authors can add some statistics about the status of HCV prevalence and treatment in Iran.

- Thank you. We added some epidemiologic data about HCV prevalence in Iran.

3- CRRT should be completely spelled out in the first use.

- Continues Renal Replacement Therapy was spelled completely

4- Authors should provide separate parts in the methods section for settings of the study/Eligibility criteria/ Ethical approval/

- The changes were made in the methods section.

5- Study type (retrospective cohort ?) should be mentioned.

- Thank you for your comment. The study type was cohort. We add this to the paper.

6- Authors have mentioned P-value in the results section. However, they did not cite using of analytical test in the methods section.

- Thank you for this comment. We only use T-test for compare the men age between male and female patients. Which was not significant. Other parameter are descriptive type. We add this to the paper.

7- The discussion section is too long and should be summarized.

- We did our best to reduce the "discussion" size and summarized

8- Authors should provide a detailed list of their limitations in this project.

- Thank you. We added the limitations to the paper.

9- Tables should be reformatted based on Hepatitis monthly journal instructions.

- Correction was done

Response to Reviewer 3:

1-Was the protocol biopsy performed on all cases? If yes, how many of them showed evidence of rejection and/or hepatitis C recurrence in the patients without abnormal liver biochemistries?

- Thank you for your comment. We do not perform routine liver biopsy in our center. We perform liver biopsy if we suspect to rejection.

2- What has been the frequency of antibody-mediated rejection?

- Generally we have a few cases of C4D+ antibody medicated rejection in all rejection cases.and No C4D+ rejection observed among our HCV patients.

3- As the authors have mentioned the 1-year survival of transplanted hep C patients, that was previously reported by Dr. Malek Hossieni from the same center (Malek Hosseini SA, Nikeghbalian S, Salahi H, Kazemi K, Shemsaeifar A, Bahador A, Dehghani M, Imanieh MH, Tabrizi R, Lankarani KB. Evolution of Liver Transplantation Program in Shiraz, Iran. Hepatitis Monthly. 2017 Nov 1;17(11).), has been the same as this study i.e., 85%. As that study belonged to the pre-DAA era, how can this finding be explained? Does it mean that DAA does not affect the 1-year outcome? What has been improved in comparison to the pre-DAA era?

- Thank you for your comment. In that paper , HCV hepatitis included in the "Other" causes category and there was no direct discussion about its properties.

4- Line 60: “in” is repeated.

- Correction was made.

5- Line 100: “trough" level not “through” level.

- Thank you. We corrected that

6- Line 136: Were rejections confirmed with liver biopsy in all cases?

- Thank you for your comment. Yes. We added it to the text.

7- Line 139: How was the patient, with concomitant HCV recurrence and mild acute rejection, diagnosed? How was he/she treated?

- The patient treated as acute cellular rejection with no Antiviral therapy (at that time; IFN base therapy)

8- Line 139-140: It is mentioned that no patient with rejection had HCV rejection. But it has been stated that one of the patients with HCV recurrence had mild acute cellular rejection (lines 138-139). These statements seem to be contradictory. How can it be explained?

- We meant that 17 patients had acute rejection, 6 other patients had HCV recurrence (without rejection) and 1 patient had concomitant acute rejection and recurrence.

9-Table 4: line 289: There are two cases of myocardial infarction but only one interval to death is given in the table.

- Thank you. We corrected that.

OPEN PEER REVIEW

Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Heidar Sharafi: Associate Editor | **Revision** (1) 19 Apr 2021

Dear EIC,
Thanks for submitting the revision. I have few more amendments and comments for the authors:
1. The updated figures of the number of individuals with HCV infection in world is not 170 million anymore. They estimated it around 71 million. Take a look at: Polaris Observatory HCV Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Lancet Gastroenterol Hepatol. 2017 Mar;2(3):161-176. doi: 10.1016/S2468-1253(16)30181-9. Epub 2016 Dec 16. PMID: 28404132.
2. "Acute HCV is clinically mild and usually unrecognized and is frequently undiagnosed." better to use "Early HCV infection is clinically ...".
3. The prevalence of HCV Ab in Iran was estimated around 0.6%. Mirminachi B, Mohammadi Z, Merat S, Neishabouri A, Sharifi A H, et al. Update on the Prevalence of Hepatitis C Virus Infection Among Iranian General Population: A Systematic Review and Meta-Analysis, Hepat Mon. 2017 ; 17(2):e42291. doi: 10.5812/hepatmon.42291.
4. It should be a retrospective cohort. Please mention it.
5. Please merge Tables 1 and 2, and construct a new Table for presentation of participants characteristics including Age, gender, HCV RNA level, HCV genotype, history of HCV antiviral treatment, HBV coinfection, HCC, and every other baseline characteristics.
6. "Seven patients had biopsy proven HCV recurrence". Its confusing, we investigate HCV recurrence using RT-PCR rather than histology.
7. Were all those with HCV recurrence from the HCV untreated group? Please mention it.
Regards,

Seyed Moayed Alavian: EIC | **Revision** (1) 19 Apr 2021

Dear Authors,
Please submit a revision.
Regards,

OPEN PEER REVIEW

Revision (2)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear Associate Editor
Thank you and your comments. We revised the paper according to your comments. The Changes are highlighted in yellow

Sincerely yours

The Associate Editor comments:
1. The updated figures of the number of individuals with HCV infection in world is not 170 million anymore. They estimated it around 71 million. Take a look at: Polaris Observatory HCV Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Lancet Gastroenterol Hepatol. 2017 Mar;2(3):161-176. doi: 10.1016/S2468-1253(16)30181-9. Epub 2016 Dec 16. PMID: 28404132.

- Thank your comment. We corrected the text and replaced the reference.

2. "Acute HCV is clinically mild and usually unrecognized and is frequently undiagnosed." better to use "Early HCV infection is clinically ..."

- We replaced it.

3. The prevalence of HCV Ab in Iran was estimated around 0.6%. Mirminachi B, Mohammadi Z, Merat S, Neishabouri A, Sharifi A H, et al. Update on the Prevalence of Hepatitis C Virus Infection Among Iranian General Population: A Systematic Review and Meta-Analysis, Hepat Mon. 2017 ; 17(2):e42291. doi: 10.5812/hepatmon.42291.

- Thank your comment. We corrected the text and replaced the reference.

4. It should be a retrospective cohort. Please mention it.

- Thank you for your comment. We mentioned it.

5. Please merge Tables 1 and 2, and construct a new Table for presentation of participants characteristics including Age, gender, HCV RNA level, HCV genotype, history of HCV antiviral treatment, HBV coinfection, HCC, and every other baseline characteristics.

- thank you. We made the changes

6. "Seven patients had biopsy proven HCV recurrence". Its confusing, we investigate HCV recurrence using RT-PCR rather than histology.

- These patients had a rise in the level of aminotransferases lever, biopsy was done for rejection and if the patients had pathological evidence of HCV recurrence, it was confirmed by PCR study. We correct the text.

7. Were all those with HCV recurrence from the HCV untreated group? Please mention it.

- Thank for your interesting comment. We mentioned the detailed information in the paper.

Regards,

OPEN PEER REVIEW

Revision (2)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Heidar Sharafi: Associate Editor | **Revision** (2) 5 May 2021

Dear EIC,
The authors have addressed all my comments correctly. I have no more comments.
Regards

Seyed Moayed Alavian: EIC | **Revision** (2) 5 May 2021

Dear Authors,
I am delighted to inform you that your manuscript is accepted for publication in the Hepatitis Monthly journal.
Regards,