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
Article DOI: 10.5812/hepatmon.101516
Published in: Hepatitis Monthly: 20(6); e101516

Peer Review Report for "Impact of Apo Lipoprotein E Gene Polymorphism on Hepatitis C Virus Disease Progression and Response to Direct Acting Antivirals in the Egyptian Population"

Author(s): Monkez M Yousif, Fayrouz Othman Selim, Ayaat Mohamed Zedan, Ghada Mohamed Samir , Ahmed Elsadek Fakhr

Review Timeline:

Submit Date: 22 Feb 2020
Revised Date: 24 May 2020
Accepted Date: 1 Jun 2020

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) 27 Mar 2020

Dear AE,
The manuscript describes No Impact for Apo lipoprotein E Gene Polymorphism on Hepatitis C Virus Disease Progression nor Response to Direct Acting Antivirals. Overall the manuscript seems scientifically good. However, there are some comments:
The manuscript is suitable for publication in the hepatitis monthly journal with a minor revision.
1. The references didn't match the journals format.
2. According to the information released on the 9th of July 2019 at https://www.who.int/news-room/fact-sheets/detail/hepatitis-c, there is "Globally, an estimated 71 million people have chronic hepatitis C virus infection."
3. In the aim part of the abstract, to should start with capital T.
4. In the abstract part, the word Keywords is one word so it doesn't have space between key and word.
Thanks.

REFEREE: Reviewer | **Revision** (0) 29 Mar 2020

Dear AE,
The study “No Impact for Apolipoprotein E Gene Polymorphism on Hepatitis C Virus Disease Progression nor Response to Direct-Acting Antiviralsis” is notable because there are limited studies on this topic in the literature.
Here is a suggestion to add to the discussion: The authors should point out the impact of Apolipoprotein E Gene Polymorphism in response to Peg- IFN and Ribavirin which was published before.
They should report the impact of Apolipoprotein E Gene Polymorphism and response to Peg-IFN and Ribavirin among patients if there’s available history.
Thanks.

REFEREE: Reviewer | **Revision** (0) 3 Apr 2020

Dear AE,
The authors of the manuscript (ID:101516) entitled: “No Impact for Apo lipoprotein E Gene Polymorphism on Hepatitis C Virus Disease Progression nor Response to Direct Acting Antivirals present” presented valuable data over HCV. However, the manuscript needs minor revision before the next steps.
Introduction
1- This part needs to be started with the viral hepatitis program and relation with the present study (+references).
2- situation of Egypt in case of HCV should be added (+references)
3- This part should present a better definition of Apo for readers.
Materials and methods
4- Mentioned primers and thermal profiles of PCR can be framed in a table.
Results
5- The format of tables should be checked by the published articles in Hepatitis Monthly
Discussion
6- Instead of repeating “in agreement”, authors can use “in line with/ corroborate with
General comments
English writing needs serious polishing. Authors should keep unity in the format of alphabetic or numbering (ninety-six or 96) in the whole text.
Thanks.

Heidar Sharafi: Associate Editor | **Revision** (0) 8 Apr 2020

Dear EIC,
The manuscript was evaluated by the peer-review team. The study is interesting with including the assessment of host genetics on response to HCV treatment using an IFN-free regimen. However, there are major concerns with the study design and presentation which enforce me to ask authors to majorly revise their manuscript to have a chance for acceptance.
1. I would like to ask authors to reform their manuscript to a brief report as the journal's

authors' instruction and submit the revision as a brief report.
2. The manuscript should be sent out to professional language and academic edit to improve its presentation.
3. The study is not a clinical trial so, needs no clinical trial registration code.
4. No need of presenting the "ethical approval" and "Informed consent" in Arabic language. They can include if the study has an ethical approval at the responsible committee in their institute as well as the study ethical approval code.
5. In the introduction, "Impact of Apolipoprotein E isoforms on hepatitis C virus disease progression and response to interferon therapy had been shown in different studies (12)". Different studies and citing only one study.
6. The final sample size is small (83). How did the sample size calculated for this study? It is important to see if the study has statistical power with the current sample size.
7. Why did they use nested PCR for amplification of the human genome? Nested PCR routinely used when the target sequence has a small number in the extracted material.
8. The Table for band sizes should be numbered and referred in the manuscript body.
9. where did they use one way ANOVA in the statistical analysis?
10. Tables 1 and 2 can be merged as a single table.
11. Cirrhosis can be included in the above-mentioned table in comment 10 and compared in those with or without SVR.
12. Figures 1 and 2 can be deleted.
13. I don't get the analysis included in Tables 3, 4, and 5. The Fisher exact test is based on a 2 by 2 table while these tables are 2 by 5. how did they conduct the comparisons. I guess they need the consultation of an expert in statistical analysis.
14. Figures 3 and 4 can be deleted.
15. I have a major concern with the study participant selection. The real-world response to IFN-free regimens is higher than 95% in the clinical setting. in this study, among 83 included individuals, 18 (21.7%) had treatment failure. Is there any bias toward the selection of those with treatment failure or any particular reason for high treatment failure?
Regards

Seyed Moayed Alavian: EIC | **Revision** (**0**) 10 Apr 2020

Dear Author,
Your article is reviewed by the reviewers carefully. According to their comments, this document needs major revision. Please follow their comments as requested.
Thanks.

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.

Reply to the reviewers' comments

	Original comments of the reviewer	Reply by the author(s)	Changes done
1.	Start with viral hepatitis program	Done	Marked in yellow
2.	Situation of Egypt in HCV	Done	Mark in yellow
3.	Better definition of Apo E	Done	Mark in yellow
4.	Primers and thermal profile in table	Done	Table (1)
5.	Check published tables	Done	Tables 3,4,5,6
6.	Replace in agreement in discussion	Done	Mark in yellow
7.	Number 96 or ninety six	Done	Not marked
8.	References	Done	New references marked in yellow ,others revised and corrected in the references
9.	71 million have globally HCV globally	Done	Mark in yellow in introduction
10.	Abstract: correct keywords	Done	Mark in yellow

11.	Aim	Corrected	Mark in yellow
12.	Discussion :apo E and peg IFN in patient of available history	Can not understand what is needed	
13.	Manuscript type as brief report	Will be done in resubmission	
14.	Language	Done	
15.	No trial registration code	Will be done in resubmission	
16.	Do not present ethical approval /informed consent	Will be done in resubmission	
17	Introduction: different studies	Changed and replaced by David	Mark in yellow
18	Sample size	By assuming that the effect of Apo E in hepatitis C Virus infection is 50 %(Hishiki, et. al , 2010) and total number of patients attending Zagazig viral hepatitis treatment center during one year is 31266 with confidence level 95% and power of test 80% by using Epi-Info version 6 so calculated sample size is 96	
19	Why nested PCR	We follow the same protocol developed by Fabris et al, 2011 for amplification and RFLP. May	

		be to decrease the chance for non-specific amplification if go directly into the inner primers.	
20	Table for band size	Numbered and referenced	Table (2) and reference 27
21	Merge table 1 ,2	Done	In table (3)
22	Cirrhosis in comment 10 and compared with /without SVR	Cannot understand what is needed	
23	Figure 1,2	Deleted	
24	Where one way ANOVA is used	Not used	Removed from the paragraph
25	Analysis on table 3,4,5	Done	Mark in yellow below each table 4,5,6
26	Fisher exact test	Already calculated for by 2 by 2	
27	Selection of participants	Done randomly and systematically	

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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) 13 May 2020

Dear EIC,
The authors addressed most of the comments however, few major concerns remained:
1. The manuscript should be restructured as a brief report mainly reducing the word count of the manuscript body. In this regard, the abstract, Introduction, Methods, and discussion can be edited to reduce the content.
2. The English and scientific presentation of the manuscript should be improved. I suggest authors to ask a colleague who is expert in academic writing to help them.
3. Regarding adding the cirrhosis, they should add and compare the proportion of patients with cirrhosis in those with and without SVR (the same as sex and viral load).
4. The analysis in Tables 4, 5 and 6 is unclear. The P in 2 by 2 tables are a result of comparing 2 groups. I don't get what each P is presenting in these Tables. They can include one P for comparing all those genotypes or include 1 genotype as a reference and compare other genotypes with the reference. I strongly recommend them to have advice of an expert in statistical analysis.
5. And my last main concern, I asked about patient selection and they replied to me "Done randomly and systematically". It is not an appropriate response to my concern. This concern mainly came from the high rate of treatment failure. If they did a random sampling of those treated for HCV using DAA, then they should justify the high rate of treatment failure (22%).
Regards

Seyed Moayed Alavian: EIC | **Revision** (1) 15 May 2020

Dear Author,
The reviewers' comments are mentioned. Please correct the details as mentioned above carefully according to reviewers' request.
Thanks.

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.

Reply to the reviewers' comments

	Original comments of the reviewer	Reply by the author(s)	Changes done
1.	Restructure manuscript as brief report	Done by reducing word count in abstract , introduction ,methods, discussion ,reference and by removal of table 3 and merging tables 4, 5 and 6 References were done using Mendeley Reference management software	Done
2.	Revision of manuscript for scientific presentation and language	Done by Dr. Ahmed Elsadek Fakhr	Done
3.	Cirrhosis as variable in table 3	Table 3 is removed in reconstruction of manuscript as a brief report	Not included in manuscript but can be available as a supplementary table
4.	Reference category in table 4,5,6	Table 4,5,6 were merged as one table to meet criteria for brief report and statistical data were revised	Done
5.	Sample	Sample size is determined to be 96 and then divided into 2 groups (SVR=76 and Non SVR=20). For comparison purposes the whole number of non SVR without exclusion criteria and with written approval were included within the period of sample collection, while SVR group were chosen randomly. Thus this ratio is not revealing failure rate.	Explained

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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) 30 May 2020

Dear EIC
Based on the authors' answers to the reviewers' comments, the reviewer(s) have recommended publication.
Kind regards.

Seyed Moayed Alavian: EIC | **Revision** (2) 1 Jun 2020

Dear Author,
The document is reviewed carefully by the reviewers. According to their comments and your revisions as requested, this manuscript is accepted.
Thanks.