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OPEN PEER REVIEW

Aspartate Aminotransferase to Platelet Ratio Index Before and After the Treatment of Chronic Hepatitis C Patients with Sofosbuvir/Daclatasvir

Mohammad Javad Pourgholamali, Parvin Khalili, Vahid Mirzaei, Zahra Jamali, Zohreh Rajabi, Afshin Tahmasbi

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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 · 11 Jun 2023 – 8 Jul 2023

Referee 1 Reviewer

MAJOR REVISION 11 Jun 2023

Dear AE,
The study lacks a control group for comparison. Without a control group, it is difficult to determine the effectiveness of the treatment (Sovodak) in reducing liver fibrosis. A control group receiving a placebo or alternative treatment would provide a basis for comparison and help establish the efficacy of Sovodak.

Referee 2 Reviewer

MAJOR REVISION 8 Jul 2023

In the manuscript entitled "Aspartate aminotransferase to platelet ratio index (APRI) before and after treatment of chronic hepatitis C patients with Sovodak", the authors evaluated the change in APRI score after HCV treatment in 45 patients. Although the topic is novel, the manuscript still has potential to contribute to the literature given the limited data from Iran. However, I still have some concerns about the methodology, statistical analysis, and discussion. More detailed comments are as follows:
1- In the title and abstract, the authors used "Sovodak" to refer to sofosbuvir and daclatasvir. It seems that it is the commercial name of this medicine in Iran. The authors are recommended to use the generic name; otherwise, it will not be understood by the audience outside Iran.
2- Abstract: "APRI level decreased significantly after treatment with Sovodak in all patients". Please report the median score before and after treatment and also the p-value.
3- The Introduction needs to be shortened and should include content more relevant to the current study. Some parts of the Introduction (e.g., the parts about diagnosis or natural history of HCV) are not directly relevant to the focus of this study and are not really necessary for the audience of a journal that specializes in liver diseases.
4- Introduction: "In Iran, the prevalence of hepatitis C disease is on average less than 0.5% in the normal population". "Normal population" is not clear. I think the authors meant "general population".
5- Introduction: Reference #4 (Pawlotsky 2018) does not look relevant to the statement for which it was used.
6- Introduction: The format of reference #7 is distorted.
7- Methods: The authors have referred to the "hepatitis C eradication plan" as the backbone of this current study. More details about this project are needed. For example, I was wondering what the components of this project were. I assume HCV screening and treatment were the main components. Are there other components as well (e.g., education)? How was the screening conducted? Was it based on on-site testing, or were people invited to the health care centers? How were the HCV-positive people referred? Was the "Hepatitis Clinic" mentioned by the authors a public or private center? Was it run by specialists or primary care clinicians?
8- Methods: The authors mentioned "people living in hangouts and camps", which was not clear to me.
9- Methods: "viral infection was checked by PCR using the MIC device (SINMOOO1456bms)". Please report the commercial name of the assay and the manufacturer.
10- Statistical Analysis: "Wilcoxon test was used to evaluate the APRI score before and after treatment". It is not clear if the authors used the Wilcoxon signed rank test or Wilcoxon rank-sum test for comparisons. This is very important, given that only the Wilcoxon signed-rank test is a valid test to compare paired samples.
11- Statistical Analysis: It is very important that the authors also evaluate how many of the participants with pre-treatment APRI>1 had post-treatment APRI<1. Although APRI is a score, it is more commonly used as a binary measure for the diagnosis of cirrhosis. Thus, an APRI<1 for ruling out cirrhosis is more important clinically than the actual score. This should be considered in the analysis comparing APRI before and after

treatment as well.
12- Findings: “13 people due to non-referral were excluded”. It is not clear what the author meant by “non-referral”.
13- Table 1: Please also report how many participants injected drugs at the time of enrollment (ongoing injecting drug use).
14- Table 2: The format of all the numbers is incorrect and confusing. For example, 0/68 should be 0.68.
15- The main limitation of the Discussion is the lack of focus on the objectives of the current study. The main finding of this study is about the change in APRI score following HCV treatment. However, I did not find any parts of the Discussion in which the authors referred to other similar studies and compared their results with those of these studies. Instead, for example, they had a detailed discussion about HIV-HCV co-infection, which is not really the focus of this current study.

Associate Editor

MAJOR REVISION 8 Jul 2023

Dear EIC,
It is a useful study but needs some revision. All comments should be addressed by the authors, and changes should be made based on the 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.

Response Letter

Dear Editor-in-Chief of Journal of Hepatitis Monthly

Subject: Resubmission of Manuscript No: 138049

We thank the editors for giving us the opportunity to re-submit a revised version of an original article entitled “Aspartate aminotransferase to platelet ratio index (APRI) before and after treatment of chronic hepatitis C patients with Sovodak” to be considered for publication in the International Journal of Hypertension.

We provide below point-by-point responses to the comments made by the reviewers from our initial submission. All changes have highlighted in yellow in the text. On behalf of all co-authors, I would like to take the opportunity to thank the Editorial Boards for considering our paper and the reviewers for their helpful comments. On behalf of all co-authors, I would like to take this opportunity to thank the reviewers for their insightful comments, which have improved the quality of the paper, and the Editorial Board for considering our work.

We sincerely hope that the revised version will satisfy the reviewers and the editors, and that the revised manuscript will be acceptable in the current form. We look forward to hearing from you.

*(Corresponding author): Afshin Tahmasabi, Department of Internal Medicine, Faculty of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

Reviewer 1:

In the manuscript entitled “Aspartate aminotransferase to platelet ratio index (APRI) before and after treatment of chronic hepatitis C patients with Sovodak”, the authors evaluated the change of APRI score after HCV treatment in 45 patients. Although the topic is novel, the manuscript still has potential to contribute to the literature given limited data from Iran. However, I have still some concerns about the methodology, statistical analysis, and discussion. More detailed comments come as follow:

1- In the title and abstract, the authors used “Sovodak” to refer to sofosbuvir and daclatasvir. It seems that it is the commercial name of this medicine in Iran. The authors are recommended to use the generic name, otherwise it will not be understood by the audience outside Iran.

Thanks for valuable comment. The generic name of Sovodak was used.

2- Abstract: “APRI level decreased significantly after treatment with Sovodak in all patients”. Please report the median score before and after treatment and also the p value.

Thanks for valuable comment, the median score before and after treatment and also the p value were reported.

3- Introduction needs to be shortened and should include the content more relevant to the current study. Some parts of the Introduction (e.g., the parts about diagnosis or natural history of HCV) are not directly relevant to the focus of this study and not really necessary for the audience of a journal which is specialised for liver diseases.

Thanks for valuable comment. Introduction was shortened.

4- Introduction: “In Iran, the prevalence of hepatitis C disease is on average less than 0.5% in the normal population”. “Normal population” is not clear. I think the authors meant “general population”.

Thanks for valuable comment. "General population" was used instead of “Normal population”.

5- Introduction: Reference #4 (Pawlotsky 2018) does not look relevant to the statement that it was used for.

After we shortened the introduction, reference #4 was deleted.

6- Introduction: The format of reference #7 is distorted.

After we shortened the introduction, reference #7 was deleted.

7- Methods: The authors have referred to the “hepatitis C eradication plan” as the backbone of this current study. More details about this project are needed. For example, I was wondering what the components of this project were. I assume HCV screening and treatment were main components. Are there other components as well (e.g., education)? How was the screening conducted? Was that based on on-site testing or people were invited to the health care centres? How were the HCV positive people referred? Was the “Hepatitis Clinic” mentioned by the authors a public or private centre? Was it run by specialists or primary care clinicians?

Thanks for your attention. The components of this project were screening, treatment and also education. Based on on-site testing, of all people with suspected hepatitis C infection including all prisoners, people living in de-addiction camp, people who live in hangouts or go to these places to use drugs, blood samples were collected. Then, HCV Ab test was performed for rapid test. if the test was positive, the person was referred to the Hepatitis clinic, a public center located in the main health center which run by primary care clinicians.

These sentences were added to method section.

8- Methods: the authors mentioned “people living in hangouts and camps” which was not clear to me.

Thanks for your attention. De-addiction camp is a place that provides treatment and de-addiction treatment for addicts with official permission from welfare. In these centers, all the stages of treatment are done under the supervision of medical and psychological experts, and they try to treat the damaged body and mind of the addict together.

Hangouts is a place where addicts gather and use drugs or buy and sell drugs.

9- Methods: “viral infection was checked by PCR using the MIC device (SINMOOO1456bms)”. Please report the commercial name of the assay and the

manufacturer.

Thanks for your attention. Based on your valuable comment, commercial name and the manufacturer of MIC devise was reported in method section.

10- Statistical Analysis: “Wilcoxon test was used to evaluate the APRI score before and after treatment”. It is not clear if the authors used the Wilcoxon signed rank test or Wilcoxon rank-sum test for comparisons. It is very important, given that only Wilcoxon signed-rank test is a valid test to compare paired samples.

Thanks for your comment. Based on your good suggestion, Wilcoxon signed-rank test was used. However, in this test, the p value was also the same as Wilcoxon test. In statistical analysis, Wilcoxon test changed to Wilcoxon signed-rank test.

11- Statistical Analysis: It is very important that authors also evaluate how many of participants with pre-treatment APRI>1 had post-treatment APRI<1. Although APRI is a score, but it is more commonly used as binary for diagnosis of cirrhosis. Then an APRI<1 for ruling out of cirrhosis is more important clinically than the actual score. It should be considered for analysis of comparing APRI before and after treatment as well.

Thanks for your attention. Based on your valuable comment for analysis of comparing APRI before and after treatment, categories of APRI (<1 and >1) using Mcnemar Test was used and added to Statistical Analysis section. The new result was reported in Table3.

12- Findings: “13 people due to non-referral were excluded”. It is not clear what the author meant by “non-referral”.

Thanks for your attention This sentence was revised.

13- Table 1: Please also report how many participants injected drugs at the time of enrolment (ongoing injecting drug use).

In the present study, this question was asked the patients: have you injected drugs in the last 12 months. We revised this variable in results of Table 1 and throughout the manuscript.

14- Table 2: The format of all the numbers is not correct and is confusing. For example, 0/68 should be 0.68.

Thanks for your attention. Table 2 was corrected.

15- The main limitation of the Discussion is lack of focus on the objectives of the current study. The main finding of this study is about the change in APRI score following HCV treatment. However, I did not find any parts of the Discussion in that the authors referred to the other similar studies and compared their results with those studies. Instead, for example, they had a detailed discussion about HIV-HCV co-infection which is not really the focus of this current study.

Thanks for your comment. Based on your good suggestion, we carefully read the discussion and revised the discussion.

Reviewer 2:
Dear AE,
The study lacks a control group for comparison. Without a control group, it is difficult to determine the effectiveness of the treatment (Sovodak) in reducing liver fibrosis. A control group receiving a placebo or alternative treatment would provide a basis for comparison and help establish the efficacy of Sovodak.

Thanks for your comment. Lack of a control group for comparison was mentioned in limitation section.

2 Revision 1

3 comments · 2 Oct 2023 – 11 Oct 2023

Referee 1 Reviewer

ACCEPT 2 Oct 2023

Dear AE.
I reviewed the manuscript again. The great effort in improving the manuscript is highly appreciated. The authors have addressed all comments that were related to my review.
Thank you

Referee 2 Reviewer

ACCEPT 11 Oct 2023

Most of the comments were addressed properly.

Associate Editor

ACCEPT 11 Oct 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