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

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- 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

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Peer Review Report for "The Frequency of CD4+ T Cells in Women with Hashimoto's Thyroiditis"

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Review Timeline:

Submit Date: 4 Oct 2020
Revised Date: 14 Aug 2021
Accepted Date: 1 Sep 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) — 6 Dec 2020

Dear AE,
Thank you for inviting me to review this manuscript.
This is obvious that the manuscript has been written based on a part of a research project. The manuscript needs a major revision. I have added my comments to the PDF file. The authors need to pay special attention to the "discussion" and made an extensive revision in this section.
Best regards

REFEREE: Reviewer | **Revision** (0) — 26 Feb 2021

Dear AE,
Specific Comments to Authors:
Thanks for submitting your paper. The manuscript aims to analyze, and hence challenge the current concepts surrounding, the balance and/or imbalance of some T-Cell subsets in Hashimoto's Thyroiditis (HT). As it is widely known in the field, conducting studies that try to address the mechanism(s) of AITD is challenging and the gathered data through studies such as yours are quite valuable. However, the complexity of interactions between the

immune system and the thyroid, as well as between different components of the immune system in the context of autoimmunity makes generalizing the findings of such studies extremely difficult. This feature limits the scope of the manuscript and the generalizability of the findings. Moreover, your manuscript is not drafted sufficiently clearly and does a disservice to itself by not clarifying the specific knowledge gap it tries to answer in the context of existing literature. The following comments should be considered in revising this manuscript:

1. The Introduction needs to be restructured and framed in a more coherent manner so that the research gap is highlighted and communicated more effectively.
2. The rationale for grouping the patients the way you have done needs to be clarified
3. In the “Methods” section, please describe the exact criteria used for establishing the diagnosis of HT.
4. It would be worthwhile, and necessary, to clarify and explain the baseline and clinical characteristics of the patients such as time since diagnosis, the treatment received response/resistance to treatment regimens used, thyroid function tests, whether pathology reports were used or not, and other basic information (preferably in the form of a table at the beginning of “Results” section).
5. The Discussion section would benefit from a revision considering what was mentioned in previous items. Specifically, the relation between autoantibodies and the cellular immune response in HT, as a disease the main proposed mechanism for it is cellular immunity, can be clarified and highlighted. Accordingly, the findings can be interpreted in this context.
6. The manuscript will benefit from more stringent English language editing.

Thanks.

REFEREE: Associate Editor | **Revision** (0) 6 Mar 2021

Dear EIC,

Based on the reviewers' comments the manuscript needs major revision.

Thanks.

REFEREE: EIC | **Revision** (0) 6 Mar 2021

Dear Authors,

The manuscript needs extensive revision before it can be accepted for publication.

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.

Dear Prof. Fereidoun Azizi & Dr. Azita Zadeh-Vakili

We really appreciate the time and efforts by the editor and referees in reviewing the manuscript # *110013*, entitled: "Evaluation of the frequency of $CD4^+$ T cells in women with Hashimoto's thyroiditis" We have addressed all issues raised by the editor-in-chief and reviewers and believed that the revised version can meet the journal publication requirements. The reviewer's comments and the author's responses were written in normal and italic fonts respectively.

Response to Comments of Reviewer #1

Comment 1

The introduction needs to be restructured and framed in a more coherent manner so that the research gap is highlighted and communicated more effectively.

Response to comment 1

We appreciate the reviewer's insightful attention. The Introduction has been edited on lines 51 to 66.

Comment 2

The rationale for grouping the patients the way you have done needs to be clarified

Response to comment 2

Thanks for the comment. We've added the reviewer's suggestion on lines 64 to 66.

Comment 3

In the "Methods" section, please describe the exact criteria used for establishing the diagnosis of HT

Response to comment 3

Thanks for the comment. In fact, patients have been diagnosed by endocrinologists and these diagnoses have been made based on the guideline. This criterion has been mentioned on lines 74 to 77.

Comment 4

It would be worthwhile, and necessary, to clarify and explain the baseline and clinical characteristics of the patients such as time since diagnosis, the treatment received,

response/resistance to treatment regimens used, thyroid function tests, whether pathology reports were used or not, and other basic information (preferably in the form of a table at the beginning of "Results" section).

Response to comment 4

Thanks for the comment. The requested data were added in Table 1.

Comment 5

The Discussion section would benefit from a revision considering what was mentioned in previous items. Specifically, the relation between autoantibodies and the cellular immune response in HT, as a disease the main proposed mechanism for it is cellular immunity, can be clarified and highlighted. Accordingly, the findings can be interpreted in this context.

Response to comment 5

Thanks for your valuable comments. The sentences were changed in lines 191 to 194 the new sentences have been added in lines 188 to 190.

Comment 6

The manuscript will benefit from a more stringent English language editing

Response to comment 6

All sentences were revised and major changes were performed for this manuscript.

Response to Comments of Reviewer #2

Comments of reviewer #2

Comments are given in the article and highlighted.

Response to Comments of Reviewer #2

The authors are very grateful for the very precisionist review and helpful comment provided by the respected reviewer #2 to edit the manuscript. We have responded to the comments in the same PDF file.

As you request to edited lines 11 to 12, 16, and 42 the edit has been done.

Comment 1

The exact criteria used for establishing the diagnosis of HT is based on the guideline?

Response to comment 1

In fact, patients have been diagnosed by endocrinologists and these diagnoses have been made based on the guideline anyway we change this reference.

Comment 2

Do you have an Ethical statement for sampling of healthy women?

Response to comment 2

In fact, this project was part of a bigger project, and the ethical approval for the whole project was taken with one ethical code. The approval number is IRCT2016110130644N1

Comment 3

What is the volume of fresh blood and what is the density of ficoll and what is the company?

Response to comment 3

The volume of fresh blood was 15 ml and we used ficoll in 1.077 g/ml from Amersham company.

Comment 4

What is the MACS column Company and which method is used to separate cells?

Response to comment 4

The MACS column Company was Miltenyi and cell sorting has been done via depletion of non-target cells, a negative selection.

Comment 5

Why cells are cultured and then Incubated?

Response to comment 5

Because the cells had to be stimulated with PMA to produce cytokines in the culture medium and this is a part of the specified protocol for the estimate of LT intracellular cytokines by flow cytometry.

Comment 6

Introduce & bring more details about isotype control

Response to comment 6

Thanks for the comment. The requested data were added in lines 113 to 115.

Comment 7

Explain and discuss more line 195

Response to comment7

Thanks for the comment. This change has been done in lines 228 to 231.

Comment 8

Discusses and explain more about line 236 and study this article
DOI: 10.1007/s00262-015-1705-5. Epub 2015 May 14.
Cytokine production in patients with papillary thyroid cancer and associated autoimmune Hashimoto thyroiditis
Response to comment 8

Thanks for introducing this article, but in this article, the TH 2 population in people with Hashimoto's thyroid was lower than in healthy people, although this difference was not significant.
More explanation about line 160 is given in lines 188 to 190.

As mentioned at the end of the manuscript discussion, the authors confirmed this study is a preliminary investigation and further studies are necessary to explore the exact pathogenic mechanisms of Hashimoto's thyroiditis.

Kind regards

Saboor

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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.

REFEREE: Reviewer | **Revision** (1) — 12 Jun 2021

Dear AE,
The recommended changes have been made properly but a few small changes in references are required before the manuscript can be accepted for publication.
A PDF file containing the comments has been uploaded.
Thanks.

REFEREE: Reviewer | **Revision** (1) — 1 Aug 2021

Dear AE,
I have reviewed the revised version of manuscript #110013 along with the comments by the author. The authors have applied all the changes suggested by the reviewers and the manuscript is a good fit for the Journal and its readership. I strongly believe that the authors can improve on the design of their subsequent studies as the concept they are addressing is of value to the field.
Thanks.

REFEREE: Associate Editor | **Revision** (1) — 2 Aug 2021

Dear EIC,
The manuscript will be acceptable after minor revision.
Thanks.

REFEREE: EIC | **Revision** (1) — 2 Aug 2021

Dear Authors,
The manuscript needs revision before it can be accepted for publication.
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.

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Response to Comments of Reviewer #1

Comment 1

The recommended changes have been made properly but a few small changes in references is required before the manuscript can be accepted for publication.

Insert a reference at the end of each paragraph

Response to comment 1

Thanks for your valuable comments. Unless paragraphs explained our results, we added references at the end of each paragraph.

Comment 2

Please explain further about line 195. By critique the findings and other similar reference

Response to comment 2

We appreciate the reviewer's insightful attention. The reviewer's suggestion was added in lines 195 to 198 and 203 to 205.

Comment 3

More than half of the references date back more than 10 years. Please include some new references in the introduction and discussion.

Response to comment 3

Thanks for the comment. Some old references were replaced by new related references and some new references were added. The number of new references is 2, 3, 5, 8, 9,10,11,16 and 17.

Response to Comments of Reviewer #1

I have reviewed revised version of the manuscript 110013 along with the comments by the author. The authors have applied all the changes suggested by the reviewers and the manuscript is a good fit for the Journal and its readership. I strongly believe that the authors can improve on the design of their subsequent studies as the concept they are addressing is of value to the field.

Response to comment 1

We are very pleased with your good opinion and we will do our best to improve the next our studies.

Kind 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.

REFEREE: EIC | **Revision** (2) 1 Sep 2021

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