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OPEN PEER REVIEW

Association of Epstein–Barr Virus and Cytomegalovirus Infections with Esophageal Carcinoma

Jamal Sarvari, Ahmad Habibi, Afagh Moattari, Amir Taher Eftehkar Sadat, Mahin Ahangar Oskouee

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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

1 comment · 18 Apr 2021

Referee 1 Reviewer

MINOR REVISION 18 Apr 2021

Regarding the manuscript entitled “Association of Epstein–Barr virus and cytomegalovirus infections in patients with esophageal carcinoma in Tabriz, northwest of Iran”
The information presented in this manuscript can be beneficial to other researchers. However, there are some points that need to be addressed, as listed below for the authors.

-Abbreviations should be defined at first mention in the abstract and main manuscript and used consistently thereafter. For example, ESCC and EAC in the abstract.

-Is it possible to extract the DNA directly from the paraffin-embedded biopsy samples using a DNA extraction kit? Please mention the deparaffinization of samples before extraction.

-The first paragraph of the discussion needs a reference: There is a compelling evidence that support a direct and crucial role of EBV infection in development of several malignancies including Burkit lymphoma, nasopharyngeal carcinoma, gastric cancer, B-cell non-Hodgkin’s, and Hodgkin’s lymphoma

-The phrase “rule out” in the following sentences in the discussion and conclusion sections needs to be edited: However, further comprehensive studies are needed to rule out the potential association between these viruses and different types of esophageal cancer. Indeed, “rule out” is not appropriate for this sentence; using “decipher” instead is suggested.

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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 Professor Akbari

Editor in Chief of "International Journal of Cancer Management"

Thank you so much for your letter and the comments from the referees about our manuscript (Manuscript ID: 114566). The content of manuscript was revised based on the reviewers' comments. The fowling is point-by-point responses to the reviewers' comments.

Reviewers' Comments:

Reviewer 1:

Regarding the manuscript entitled "Association of Epstein–Barr virus and cytomegalovirus infections in patients with esophageal carcinoma in Tabriz, northwest of Iran"
The information presented in this manuscript can be beneficial to the other researchers. However, there are some points that need to be dealt with and listed below for the authors.

1-Abbreviations should be defined at first mention in the abstract and main manuscript and used consistently thereafter. For example, ESCC and EAC in the abstract.

Reply: Corrected.

2 -Is it possible to extract the DNA directly from the paraffin-embedded biopsy samples by DNA extraction kit? Please mention to de-paraffinization of samples before extraction.
Reply: De-paraffinization stage on paraffin embedded section was added to the materials and method section of the abstract and body of the manuscript before DNA extraction.

3-The first paragraph of the discussion needs a reference: There is a compelling evidence that support a direct and crucial role of EBV infection in development of several malignancies including Burkit lymphoma, nasopharyngeal carcinoma, gastric cancer, B-cell non-Hodgkin's, and Hodgkin's lymphoma.

Reply: References' was added in view of this comment.

4-The "rule out" in the following sentences in the discussion and conclusion sections needs to be edited: However, further comprehensive studies are needed to rule out the potential association between these viruses and different types of esophageal cancer. Indeed, rule out is not appropriate for this sentence; it would be suggested using "decipher" instead of it.

Reply: Corrected

Reviewer 2:

The study highlights the possible role of EBV and HCMV in esophageal adenocarcinomas and esophageal squamous cell pathogenesis, respectively. This report adds some useful data to the growing body of viral oncogenesis. Therefore, I recommend the respected editor-in-chief to consider the manuscript for possible publication after major revisions were made by the authors.

1. Manuscript has many English language and editing issues, for examples only in the abstract, page 2 line 38: “fragment DNA” is a grammatical error, line 39 need to add “, respectively” at the end of the sentence which is an editing error, in line 41: “inpatient” needs space which is a typing error and in line 49: types should be replaced instead of “type”. Therefore, please ask a native speaker to read the whole manuscript thoroughly to fix them all.

Reply: Manuscript was carefully checked for type and syntax errors and necessary changes were made, where needed.

2. In page 3 lines 61 and 63 need references.

Reply: Reference was added in view of this comment.

3. In page 3 line 86: please introduce the abbreviated form of BART.

Reply: The abbreviated of BART was added to the text.

4. Authors have reported that negative samples were excluded from the study (line 17, page4), however, all 200 samples are included in the study. Please verify if you have not excluded any sample in the result section.

Reply: Five samples were negative for beta globin gene that was excluded from the study. It mention in the material and method section of the manuscript.

5. In page 4 line 110, the authors could possibly need to specify the types and numbers of each “benign esophageal tissues” (e.g. 10 Leiomyoma tissues, 10 cyst tissues…. etc.).

Reply: Unfortunately, we have not data regarding the type of benign samples to include in the manuscript.

6. In page 4 lines 116 and 120, please provide primers' references. You need to add these references in table 1, as well.

Reply: The references of primes were added to the text as well as table1.

7. In page 4 line 116: please verify the meaning of consensus primers here.

Reply: It was deleted from the text in view of this comment.

8. Page 5 line 122: the phrase "Samples negative for β-globin gene were excluded from the study." was repeated in the previous page line 117.

Reply: The repeated sentence was deleted.

9. Since gender had not any effect on the frequency of EBV and CMV in the ESCC and EAC groups, it seems there is no need to explain it in details at the first part of the result section (page 5 lines 140-148). In addition, all these data are available in the provided tables 2 and 3. Hence, it needs to be shortened.

Reply: This sentences "Out of 70 ESCC, 37 were male and 33 females, and out of 30 EAC, 16 were male and the rest were female. Gender had not any effect on the frequency of EBV and CMV in the ESCC and EAC groups (P 0.05)" were deleted from the result section of the manuscript.

10. Please check the sequences and the mentioned PCR product sizes in table 1.

For example, the standard PCR using PCO3 and PC04 primers is 110 bp.

Reply: the sequences and the PCR product sizes were cheeked and corrected in the table1.

11. Tables 2 and 3 need to be reformatted to allow for easier interpretation by the readers. For example, what dose "EBV Yes" mean in tables 2 and 3?

Reply: Corrected

12. All tables should be self-explanatory; therefore, spell out terms even if they have been introduced in the text. For example, please define ESCC and EAC abbreviations in the table 3 note.

Reply: Corrected

13. Please add the p value to the table 3 in regard to gender association with ESCC and EAC.

Reply: p value was added to the table 3 in view of this comment.

2 Revision 1

2 comments · 14 Aug 2021 – 16 Aug 2021

Ali Mehrabi Tavana Reviewer

MINOR REVISION 14 Aug 2021

Dear Authors,

1-With regard to Reviewer 1's comments, you should also explain the abbreviations. 1-Abbreviations should be defined at first mention in the abstract and main manuscript and used.
2-It is better to edit your article again; for example, “table” is not correct; “Table” is correct.

3-In my opinion, your article must be updated by using very recent references in both the introduction and discussion sections.
4-In addition, write a paragraph for the public about the public health aspect of these findings at the end of your article.

Referee 2 Reviewer

ACCEPT 16 Aug 2021

The revised manuscript has been improved and is coherent.

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Revision 2

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 Professor Akbari

Editor in Chief of "International Journal of Cancer Management"

Thank you so much for your letter and the comments from the referees about our manuscript (Manuscript ID: 114566). The content of manuscript was revised based on the reviewers' comments. The fowling is point-by-point responses to the reviewers' comments.

Reviewers' Comments:

Reviewer 1:

The revised manuscript has been improved and coherent.

Thank you very much for your consideration to this article.

Reviewer 2:

Dear Authors,

1-With regard to comments which requested by reviewer 1 you should explain about abbreviation too. 1-Abbreviations should be defined at first mention in the abstract and main manuscript and used

Reply: Abbreviations were corrected.

2-It is better to edit your article again for example table not correct Table is correct.

Reply: The manuscript was revised for English editing

3-in my opinion your article must be up-dated by using very new references in both introduction and discussion section too.

Reply: Some old references were replaced with new once such as references No. 5, 6 and 37

4-in addition write a paragraph about public health aspect of this findings for public at the end of your article too.

Reply: A paragraph regarding the public health aspect of this findings was included at the end of article.

Reviewer 3:

Dear Editor-in-chief,

I have checked the revised manuscript and happy with the changes implemented. You may consider it for publication.

Many thanks for your consideration to this article.

Please just make sure that authors need to remove “PCO4:” and “GH20:” from the second column of table 1.

Reply: PCO4:” and “GH20:” were removed from the second column of table 1.

Reviewer 4:

All the comments has been addressed by the authors.

Many thanks for your consideration to this article.

Associate Editor's Comments:

Associate Editor 1:
according to the reviewer:
your article must be up-dated by using very new references in both introduction and discussion section too.

Reply: The article was up-dated by using very new references in both introduction and discussion section where possible.

in addition write a paragraph about public health aspect of this findings for public at the end of your article too.

Reply: A paragraph regarding the public health aspect of this findings was included at the end of article.

EIC Decision:

In order to access the comments of the reviewer, Please see the attached file.
Also, all Abbreviations in tables should be defined.

Reply: Abbreviations in tables were defined

In addition, It is necessary to add the ORCID id of at least the first and corresponding authors.

Reply: The ORCID of first and corresponding authors include:

3 Revision 2

0 comments

No public comments in this round.

4

Revision 3

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 Professor Akbari

Editor in Chief of "International Journal of Cancer Management"

Thank you so much for your letter and the comments from the referees about our manuscript (Manuscript ID: 114566). The content of manuscript was revised based on the reviewers' comments. The fowling is point-by-point responses to the reviewers' comments. All the changes appear with green color.

Reviewers' Comments:

Reviewer 1:
Q: The revised manuscript has been improved and coherent.

R: Thank you very much for your consideration to this article.

Reviewer 2:
Dear Authors,

Q: [reviewer's first question] : With regard to comments which requested by reviewer 1 you should explain about abbreviation too. 1-Abbreviations should be defined at first mention in the abstract and main manuscript and used

R: [author's first reply]: Abbreviations were corrected (Line 15, 23 and 67).

Q: [reviewer's two question] -It is better to edit your article again for example table not correct Table is correct.

R: [Author's two replies]: The manuscript was revised for English editing (Line 15, 31 and 81)

Q: [reviewer's three question] -in my opinion your article must be up-dated by using very new references in both introduction and discussion section too.

R: [author's three reply]: Some old references were replaced with new once such as references No. 5, 6 and 37

Q: [reviewer's four question] in addition write a paragraph about public health aspect of this findings for public at the end of your article too.

R: [author's four reply]: A paragraph regarding the public health aspect of this findings was included at the end of article (line 204 and 205).

Reviewer 3:
Dear Editor-in-chief,

I have checked the revised manuscript and happy with the changes implemented. You may consider it for publication.Many thanks for your consideration to this article.

Q: [reviewer's first question] : Please just make sure that authors need to remove "PCO4:" and "GH20:" from the second column of table 1.

R: [author's first reply]: PCO4:" and "GH20:" were removed from the second column of table 1.

Reviewer 4:
Q: [reviewer's first question] : All the comments has been addressed by the authors.

R: [author's first reply]: Many thanks for your consideration to this article.

Associate Editor's Comments:

Associate Editor 1:
Q: [reviewer's first question] : according to the reviewer:your article must be up-dated by using very new references in both introduction and discussion section too.

R: [author's first reply]: The article was up-dated by using very new references in both introduction and discussion section where possible (references No. 5, 6 and 37).

Q: [reviewer's two question]: i n addition write a paragraph about public health aspect of this findings for public at the end of your article too.

R: [author's two reply]:A paragraph regarding the public health aspect of this findings was included at the end of article (line 204 and 205).

EIC Decision:

Q: [reviewer's first question] In order to access the comments of the reviewer, Please see the attached file.
Also, all Abbreviations in tables should be defined.

R: [author's first reply]:**:** Abbreviations in tables were defined (Line 362)

Q: [reviewer's two question] In addition, It is necessary to add the ORCID id of at least the first and corresponding authors.

R: [Author's two replies]:The ORCID of first and corresponding authors include:

Jamal Sarvari: 0000-0002-2259-0836

Mahin Ahangar Oskouee: **0000-0002-9682-8835**

In-text comments:

For an analytical title, there is no need to specify the place.

Response: The place and time were removed from the title of the article (lines 1 and 2).

The method of selecting the test and control samples should be described.

Response: Owing to the word limit of the abstract, the method of selecting the samples was added to the Methods section of the article (lines 98, 99, and 100).

The conclusion of the abstract should be rewritten; it is written like the results, not a conclusion.

Response: The conclusion of the abstract was changed according to the respected reviewer's comment (lines 32 and 33).

The control and test groups have not been defined.

Response: The test and control groups were explained in the Methods (lines 95, 96, and 97).

If parentheses are used, there is no need for ±.

Response: In accordance with the respected reviewer's suggestion, ± was removed from the Results section (lines 129 to 135).

Given the type of study, all results should be reported separately for the test and control groups.

Response: In accordance with the respected reviewer's comment, the results of the two study groups have been described in the Results section (lines 134 and 135).

[Translated from Persian by the Brieflands editorial office.]

4 Revision 3

0 comments

No public comments in this round.