OPEN PEER REVIEW

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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

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Peer Review Report for "Molecular Evaluation of Human Enterovirus-Related Aseptic Meningitis in Isfahan, Iran 2017"

Author(s): Maryam Ansari Chaharsoughi , Behrooz Ataei, Farzin Khorvash, Kiana Shirani, Morteza Pourahmad

Review Timeline:

Submit Date:	19 Oct 2019
Revised Date:	7 Mar 2020
Accepted Date:	9 Mar 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)

2 Jan 2020

Dear AE,

Thank you for inviting me to review the manuscript entitled “Molecular evaluation of human enterovirus related aseptic meningitis in Isfahan, Iran 2017”. Although the topic is interesting and some of the results are interesting too, the manuscript was not well written, and also my major concern is the small sample size.

• The English needs to be improved in terms of grammar and structure.

ABSTRACT

• “Human enterovirus (HEVs)” should be changed to “Human enteroviruses”.

• “This virus is a common” should be changed to “These viruses” because these viruses comprise more than 80 serotypes.

• The method for detection of virus is better to be added in Abstract.

• The result section is confusing and should be revised and rewritten in plausible form.

• The lumbar puncture (LP) sample, in conclusion, has to mention in the material and methods section.

• “significant in pediatric patients (9.5%)” in conclusion: what your mean is? Generally, the significance has indicated with “p-value”

INTRODUCTION

• The frequency of these viruses in Iran has to mention in this section. Which serotypes of these viruses are common in Iran?
• “Direct detection of virus in CSF samples”: I couldn’t understand what your mean is? What is direct detection for detection of these viruses?
• What is the gold standard test for the detection of viruses?
MATERIAL AND METHODS
• Page 5: The number of samples hasn’t mentioned in this section.
• Page 6: Has the real-time PCR designed by authors? Can this method detect different serotypes of these viruses?
RESULTS
• The result section is confusing and should be revised and rewritten in plausible form.
• Table 1: what is the mentioned p-value?
• Page 9: “CSF PCR for enteroviruses was positive in 2 samples of 70 samples (2.8%)”. This sentence is repeated above.
DISCUSSION
• There are several studies in Iran that have shown the frequency of these viruses in Iran. The authors have to compare this study with other studies in Iran.
Thanks.

REFEREE: Reviewer | **Revision** (0) 14 Jan 2020

Dear AE,
There are some comments which should be addressed by the author:
- Is the extraction kit used is one-step? Otherwise, please write the cDNA synthesis method.
- Please delete repetitive contents in the results section. (Below table 1).
Thanks.

REFEREE: Associate Editor | **Revision** (0) 1 Feb 2020

Dear EIC,
The manuscript entitled "Molecular evaluation of human enterovirus related aseptic meningitis in Isfahan, Iran 2017" could be published after major revision.
Thanks.

REFEREE: EIC | **Revision** (0) 11 Feb 2020

Dear Author,
Thank you for submitting your manuscript to JJM. I have completed the review of your manuscript and a summary is appended below (Pleases find attached files). The reviewers recommend reconsideration of your paper following major revision. I invite you to resubmit your manuscript after addressing all reviewer comments. Please answer point by point to reviewer's comments on a separate sheet under WORD format and write your modifications in the revised version (WORD format) in colored or highlighted letters. Your answers to reviewers’ queries are not only for the Editorial Board but for the readers and should be included, when appropriate, in the manuscript for improvement and a better understanding. When resubmitting your manuscript, please carefully consider all issues mentioned in the

reviewers' comments, outline every change made point by point, and provide suitable rebuttals for any comments not addressed. In addition JJM INSTRUCTION attached to mail, Pleases find it.

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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 Sir/Madam

.We have revised the article based on the comments from your reviewers

Following are the main parts of our revision. (the revised parts are in yellow highlight)

:ABSTRACT

ABSTRACT

• *"Human enterovirus (HEVs)" should be changed to "Human entroviruses".*

These viruses are

• *"This virus is a common" should be changed to "These viruses" because these viruses comprise more than 80 serotypes.*

Has been changed

• *The method for detection of virus is better to be added in Abstract.*

EV RNA was extracted with Roch extraction Kit and Entroviral infection was detected by RT-PCR test.

• *The result section is confusing and should be revised and rewritten in plausible form.*

Entero viruses were detected in 2cases out of 70 patients (2.8%). Two cases are in children group (9.5%). The relationship between gender and prevalence was not significant. Two cases were found in summer and winter.

• *The lumbar puncture (LP) sample in conclusion has to mention in material and methods section.*

Diagnosis of meningitis was made on clinical symptoms and lumbar puncture samples. Inclusion criteria were: Normal CSF glucose level, normal or high normal CSF protein level, WBC count < 300 /$mm^{3,}$ Lymphocyte Dominant,

• *"significant in pediatric patients (9.5%)" in conclusion: what your mean is? Generally, the significantly has indicated with "p-value"*

(statistically p value=0.026

INTRODUCTION

• The frequency of these viruses in Iran has to mention in this section. Which serotypes of these viruses are common in Iran?

In a similar study in Iran, serotype EV71,was the major causes of the disease, especially in very young children. (17)

• "Direct detection of virus in CSF samples": I couldn't understand what your mean is? What is direct detection for detection of these viruses?

A specific virologic diagnosis of enteroviral meningitis depends on isolation of virus from the CSF in tissue culture (16).

• What is the gold standard test for detection of viruses?

PCR is the most promising alternations to viral culture for the diagnosis of EV meningitis (16).

MATERIAL AND METHODS

• Page 5: The number of samples hasn't mentioned in this section.

At last 70 eligible person entered in this study (21 children and 49 adults).

• Page 6: Has the real-time PCR designed by authors? Can this method detect different serotypes of these viruses?

Enterovirus RNA was detected by 2-steps RT-PCR Kit. This test can not be used for differentiation of enterovirus subtypes. Briefly5 g total CSFRNA with primer mixture (0.2 of Random hexamer (and top up 12.5 of water) were incubated at ❑❑ c for 5min and chilled on ice. The cDNA synthesis mixture was prepared in the following order :4 of 5x reaction Buffer,0.5 of thermo Scientific Ribolock RNase inhibitor ,2 dNTP Mix 10mM each, 1 (200U) RevertAid Reverse transcriptase. Then top up to 20 , mixed gently and centrifuged, incubated 10min at ❑❑ followed by 60 min at ❑❑ c and

terminated the reaction by heating at ❑□ c for 10min then 2µ l of the reaction mixed to perform PCR in 50µl volume.

RESULTS

• The result section is confusing and should be revised and rewritten in plausible form.

Has been changed

• Table 1: what is the mentioned p-value?

in age groups

• Page 9: "CSF PCR for enteroviruses was positive in 2 samples of 70 samples (2.8%)". This sentence is repeated above.

Has been changed

DISCUSSION

• There are several studies in Iran that have shown the frequency of these viruses in Iran. The authors have to compare this study with other studies in Iran.

In a similar study in Ahwaz, southwest of Iran, the prevalence of enterovirus was considerably high (59.6%). (18)

In a study which is conducted on children below 8 years old in Iran, the frequency of positive CSF PCR has been reported 32.2% for HEV. (14) In contrast to our study, the mean age of the cases in these studies has been mainly below the 8 years

Another study in children medical center in Tehran showed the "enterovirus detection rate" in all 118 CSFs was 10/16% and most patients were 0-2 year (40/67%). (15)

Reviewer 2:
-Is the extraction kit used is one-step? Otherwise, please write the cDNA synthesis method.

Enterovirus RNA was detected by 2-steps RT-PCR Kit. This test can not be used for differentiation of enterovirus subtypes. Briefly5 g total CSFRNA with primer mixture (0.2 of Random hexamer (and top up 12.5 of water) were incubated at ❑❑ c for 5min and chilled on ice. The cDNA synthesis mixture was prepared in the following order :4 of 5x reaction Buffer,0.5 of thermo Scientific Ribolock RNase inhibitor ,2 dNTP Mix 10mM each, 1 (200U) RevertAid Reverse transcriptase. Then top up to 20 , mixed gently and centrifuged, incubated 10min at ❑❑ followed by 60 min at ❑❑ c and terminated the reaction by heating at ❑❑ c for 10min then 2µ l of the reaction mixed to perform PCR in 50µl volume.

-Please delete repetitive contents in the results section. (Below table 1)

Has been changed

Thanks

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Revision (1)

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REFEREE: EIC | **Revision (1)** 9 Mar 2020

Dear Authors
According to the associated editor report, your manuscript is accepted for publishing in JJM and send to the publisher for the next process.
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