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

Archives of Pediatric Infectious Diseases
Article DOI: 10.5812/pedinfect.103904
Published in: Archives of Pediatric Infectious Diseases: 9(1); e103904

Peer Review Report for "Human Cytomegalovirus and Human Herpesvirus-6 and Wilms Tumor: Is There a Link?"

Author(s): Maryam Kazemi Aghdam, Seyed Alireza Nadji , Maliheh Khoddami, Mohamad Mahdi Tehrani

Review Timeline:

Submit Date: 19 Apr 2020
Revised Date: 18 Jul 2020
Accepted Date: 5 Aug 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) — 29 May 2020

Dear AE,
1. This study is a cross-sectional study, not a case-control
2. Part 3.2 should be written as “inclusion and Exclusion criteria”
3. This manuscript needs some grammar corrections
Regards

Babak Abdolkarimi: Reviewer | **Revision** (0) — 23 Jun 2020

Dear AE,
Thanks for your study in pediatric oncology
1. I think that you should consult with a pediatric oncologist before design this study, In order to the unknown idea for this study.I can,t pluralization that, how you result from the theoretical correlation of viruses with solid tumor etiology especially Wilms tumor?
2. Viruses especially herpes family have an etiologic role in hematologic malignancies, but I didn't find any evidence for this relation in solid tumors.
3. Incidentally infection by viruses isn't sufficient evidence as an etiologic role
4. Most pediatric tumors have multi-factorial etiology. Hodgkin lymphoma has a confirmed

relation with EBV because of EBV genome is a part of the genome in Reedstrenburg cell. Therefore, the selection of title study should have a firm theory, and not a random title.
5. With the detection and treatment of oncovirus infection we can,t prevent cancer in the future because cancer is the result of interaction with viruses and patients' immune systems.
Thanks.

REFEREE: Reviewer | **Revision** (0) 24 Jun 2020

Dear AE,
The authors tried to find an association between HHV-6, CMV, and Wilms tumor. They showed that there was no statistically significant difference between the patients and the control group. Although this is the first report of its kind, there are some major concerns:
Major issue:
1. This is a case-control study with a limited number of patients. You can not speak about the casualty with this study design. Instead, a cohort study would be more appropriate. At best, you can only assess the associations. The small number of cases is also a limitation. These issues should be explained in the Discussion part as the limitations of the study.
Minor issues:
1. The exclusion criteria are somehow vague. what do you mean by " lack of infectious diseases or immunosuppressive therapy"? It was also written as criteria for inclusion under the subheading Exclusion criteria.
2. English needs to be improved.
3. The statistics should be explained more explicitly in the Methods section.
Thanks.

REFEREE: Associate Editor | **Revision** (0) 25 Jun 2020

Dear EIC,
Comments for authors
- Your manuscript has been reviewed by three reviews whose comments are appended.
- All found aspects of the work interesting, but there are significant objections to your manuscript being published in its current form. Therefore, I am rejecting it.
Thank you for considering the “Archives of Pediatric Infectious Diseases” for publication of your work.
Thanks.

REFEREE: EIC | **Revision** (0) 3 Jul 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 (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.

Reviewers' Comments: Answer to

:Reviewer 1

I think think that you should consult with a pediatric oncologist before design this study,In .1 order to unknown idea for this study.I can,t pluralization that,how you result theoretical ?correlation of viruses with solid tumor etiology especially Wilms tumor

viruses especially herpes family have etiologic role in hematologic malignancies,but I didn,t .2 .find any evidence for this relation in solid tumors

Answer: We consulted a Pediatric Oncologist before the study was designed and it was .approved by her

There is no definitive proof for etiologic role of the herpes viruses in solid tumors, however, :there are some researches on this matter as mentioned in the manuscript

Ref. 8- Scheurer ME, Bondy ML, Aldape KD, Albrecht T, El-Zein R. Detection **of human cytomegalovirus** in different histological types of **gliomas**. Acta Neuropathol. 2008 .Jul;116(1):79-86

Ref. 9- Samanta M, Harkins L, Klemm K, Britt WJ, Cobbs CS. High prevalence of **human cytomegalovirus** in prostatic intraepithelial neoplasia and **prostatic carcinoma**. J Urol. 2003 .Sep;170(3):998-1002

Ref. 10- Melnick M, Sedghizadeh PP, Allen CM, Jaskoll T. **Human cytomegalovirus** and **mucoepidermoid carcinoma of salivary glands**: cell-specific localization of active viral and oncogenic signaling proteins is confirmatory of a causal relationship. Exp Mol Pathol. 2012 ..Feb;92(1):118-25

Ref. 11- Wolmer-Solberg N, Baryawno N, Rahbar A, Fuchs D, Odeberg J, Taher C, et al. Frequent detection **of human cytomegalovirus in neuroblastoma**: a novel therapeutic target? .Int J Cancer. 2013 Nov;133(10):2351-61

Ref. 13- Harkins L, Volk AL, Samanta M, Mikolaenko I, Britt WJ, Bland KI, et al. Specific localization of human **cytomegalovirus** nucleic acids and proteins in **human colorectal cancer**. .Lancet. 2002 Nov 16;360(9345):1557-63

Ref. 14- Crawford JR, Santi MR, Thorarinsdottir HK, Cornelison R, Rushing EJ, Zhang H, et al. Detection of **human herpesvirus-6** variants **in pediatric brain tumors**: association of viral .antigen in low grade gliomas. J Clin Virol. 2009 Jun;46(1):37-42

Ref. 15- Crawford JR, Santi MR, Cornelison R, Sallinen S-L, Haapasalo H, MacDonald TJ. Detection of human herpesvirus-6 in adult central nervous system tumors: predominance of early and late viral antigens in glial tumors. J Neurooncol. 2009 Oct;95(1):49-60. doi: .10.1007/s11060-009-9908-2. Epub 2009 May 8

Ref. 22- Saravani S, Miri-Moghaddam E, Sanadgol N, Kadeh H, Nazeri MR. Human Herpesvirus-6 and Epstein–Barr Virus Infections at Different Histopathological Grades of Oral .Squamous Cell Carcinomas. Int J Prev Med. 2014 Oct;5(10):1231-8

incidentally infection by viruses isn,t sufficient evidence as an etiologic role.3

Answer: We did not mean to prove an etiologic role of the viruses, we just looked for presence .of the virus tin tumoral tissue

most of the pediatric tumors have multi factorial etiology.Hodgkin lymphoma has a confirmed .4 relation with EBV because of EBV genome is a part of genome in Reedstrenburg .cell.Therefore,selection of title study should have firm theory, and not randomly title

Answer: We agree with the reviewer. This study can be considered as the first step. In the event significant number of cases had been positive for the virus, the second step would have been .detecting the virus in the genome of tumor cells

with detection and treatment of oncoviruses infection we can,t prevent cancer in future because.5 of cancer is result of intraction with virus and patient,s immune system

Answer: Detection and prevention of viruses such as HBV and HPV has proved to be effective .in preventing virus-related cancers. Besides, we don’t know what future holds

:Reviewer 2

Major issue:

1. This is a case-control study with a limited number of patients. You can not speak about the casualty with this study design. Instead, a cohort study would be more appropriate. At best, you can only assess the associations. The small number of cases is also a limitation. These issues should be explained in the Discussion part as the limitations of the study.

Answer: Revised and limitations of the study are included in the discussion.

Minor issues:

1. The exclusion criteria are somehow vague. what do you mean by " lack of infectious diseases or immunosuppressive therapy"? It was also written as criteria for inclusion under the subheading Exclusion criteria.

Answer: Corrected.

2. English needs to be improved.

Answer: Reviewed and revised.

.The statistics should be explained more explicitly in the Methods section .3

.**Answer:** More information is added to this part

Reviewer 3:

1. This study is a cross sectional study not a case control

Answer: Corrected.

2. Part 3.2 should be written as “inclusion and Exclusion criteria”

Answer: Corrected.

3. This manuscript needs some grammar corrections

Answer: Corrected.

Reviewer 4:

Paper is not bad, but they can say that we couldn’t find any association between WT and these .viruses (Not cause and relationship)

.**Answer:** Corrected

Also they can describe discussion better than the present one

Answer: Discussion is revised .

Reviewer 5:

1-In introduction it is better authors focus on effect of this research on treatment protocol .for example target therapy for viruses , because prevention of infection with CMV somehow impossible

Answer: Revised.

2-inclusion criteria: 3-2 exclusion criteria: The criteria for inclusion were absence of tumor, absence of infectious disease and lack of history of corticosteroid and immunosuppressive therapy. It seems it is about inclusion criteria for control group …please correct this

Answer: Corrected.

3-result: The control specimens included normal kidneys from autopsy specimens and nontumoral and noninfectious kidney specimens. It is methodology not result

Answer: Corrected.

4- discussion need to revise

.**Answer:** Discussion is revised

OPEN PEER REVIEW

Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Associate Editor | **Revision** (1) 2 Aug 2020

Dear EIC,
- The title is not appropriate and doesn't show the purpose of this research.
- Method and material: Because it is not case and control study, authors should mention a study group, not a case and control.
Thanks

REFEREE: EIC | **Revision** (1) 5 Aug 2020

Dear Author,
Thank you very much for the revised manuscript. It is a pleasure to inform you that your manuscript, has been accepted for publication in APID.
Thanks again.