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OPEN PEER REVIEW

Lung Ultrasonography to Diagnose Bronchopulmonary Dysplasia of Premature Infants

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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

2 comments · 7 Dec 2020 – 21 Dec 2020

Seyed Ali Alamdaran Reviewer

ACCEPT 7 Dec 2020

The manuscript structure is OK.

Referee 1 Reviewer

MAJOR REVISION 21 Dec 2020

Dear authors
I reviewed your manuscript entitled " Lung ultrasonography to diagnose bronchopulmonary dysplasia in premature infants". There were valuable novel findings regarding neonatal lung ultrasound on an interesting topic. I have the following questions and comments:

1- One of the important ultrasound findings was VAS, which you used to refer to echogenic foci within AIS, but in the abstract and figures it is called VIS! Would you clarify if there is any difference? If they are the same, this can cause some ambiguity, and it would be better to use just one name.

2- The PIE-like change was referred to as pulmonary interstitial emphysema-like in the text but as pleural insect erosion-like change in the abstract and figures. Please clarify this and explain whether it is a new name for pleural irregularity given by the authors.

3- In the results, you mentioned " The major LUS findings in BPD infants were as follows: (1) Pleural line abnormalities (coarse, fuzzy or interruption, etc.), which were seen in all early- and late-stage BPD patients (100%) as well as pulmonary interstitial emphysema (PIE)-like changes in 2 early-stage BPD infants (8.0%) and 20 (62.5%) late-stage BPD infants". What do you mean by pulmonary interstitial emphysema change? The pleural irregularity and PIE-like changes are reported in different percentages of patients but are categorized as the number 1 ultrasound finding.

4- Were these findings depicted diffusely in all lung fields, or were local changes also found? If local changes were found, please clarify in which parts of the lungs they were more common and what differential diagnoses could be considered. For example, did you find the VIS sign only locally? Could it be differentiated from air-filled necrotizing pneumonia? What were the statistics for focal findings?

5- Was vesicle formation visualized on the patients' CXR? If so, as is expected in late-BPD, how do you explain this sentence in the conclusion, " for late-stage BPD, LUS has a higher diagnostic value than other methods", given that you mentioned that the sensitivity of VIS was just 52%?

6- Would you please add an explanation of how VIS can be differentiated from an air bronchogram?

7- Please clarify who performed the ultrasound: a radiologist, a neonatologist, or different people?

8- In the results, under general information, there is a typographical error in the patients' ages. Please correct it.
9- In figure 3, please mark just one VIS to make it clearer within the whole box as well.

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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 to reviewer’s comments

Reviewers' Comments:

Reviewer 1:

The manuscript structure is ok.

Reviewer 2:

Dear authors

I reviewed your manuscript as " Lung ultrasonography to diagnose bronchopulmonary dysplasia inpremature infants" There were precious novel findings regarding neonatal lung ultrasound with an intersting topic, I have some questions and comments as following.

1- One of important Ultrasound finding was VAS which you named it in cases of echogene foci within AIS, but in abstract and in figures it us called VIS! Would you clarify if there is any difference? If they are the same it can cause some ambiguity and better to be adjusted to just one name.

Response: We are sorry that it was the clerical error, it should be air vesicle signs (AVS) through the abstract and the text. Please note that we have correcter it in the revised manuscript.

2- PIE- like change was referred as pulmonary interestitial emphysema like in text but as pleural insect erosion like change in abstract and figures, please clarify it and explain whether it is new name for the pleural irregularity named by authors or not.

Response: We are sorry that it was also the clerical error, it should be pleural insect erosion-like change (PIE-like change) ,please note that we have correcter it in the revised manuscript.Thank you very much for your careful review

3- In results you mentioned" The major LUS findings in BPD infants were as follows: (1) Pleural line abnormalities (coarse, fuzzy or interruption, etc.), which were seen in all early- and late-stage BPD patients (100%) as well as pulmonary interstitial emphysema (PIE)-like changes in 2 early-stage BPD infants (8.0%) and 20 (62.5%) late-stage BPD infants" what do you mean by pulmonary interestitial emphysema change? Because the pleural irregularity and PIE like changes are reported in different percentage of patients but are catogorized as number 1 ultrasound finding.

Response: We are sorry that this was also the clerical error, pulmonary interstitial emphysema (PIE)-like changes should be pleural insect erosion (PIE)-like change,please note that we have correcter it in the revised manuscript.Thank you very much for your careful review.

4- Where these findings depicted diffusely in all lung's fields, or local changes were also found? If the answer is yes, please clarify in which part of lungs were more common and what differential diagnoses could be considered? For example did you found just local VIS sign? Could it be differentiated from air filled necrotizing pneumonia? What was the statistics of focal findings?

Response: Generally, these findings diffusely in all lung's fields, but they are easy to be found at the back of chest, which may be related to more severe lesions in the back.

But we did not compare it with necrotizingpneumonia,which is also relatively rare in newborns. However,they should have different medical histories and clinical manifestations,and their differences in ultrasound imagine should be studied later.This is one of the limitations of this paper,which has been mentioned in the revised manuscript.Please seen the last part of the discussion.

5- Where the vesicle formation visualized on patients CXR? And if yes as is expected in late-BPD, how do you explain about this sentence brought in conclusion" for late-stage BPD, LUS has a higher diagnostic

value than other methods" as you mentioned that sensitivity of VAS was just 52%!
Response: In fact that vesicle formation can also be found on patients CXR in the late-stage of BPD. The sentense"for late-stage BPD,LUS has a higher diagnostic value than other methods" is not very accurate, we have revised it as "Compared with the diagnosis of early-stage BPD, ultrasound has a higher value in the diagnosis of late-stage BPD".Although the detection rate of VAS is relatively low (only 52%), the diagnosis of BPD can be generally confirmed once the VAS is found. Therefore, we say that this sign has a high diagnostic value for BPD.

6- Would you please add this explanation that how the VAS can be differentiated from air bronchogram?
Response: According to my study and my knowledge,VAS existed within vesicle-forming lung field, while air bronchogram existed within consolidated lung tissue.

7- please clarify who has performed ultrasound, Radiologist? Neonatalogist? Different persons?
Response: LUS examination was performed by systematically trained neonatologists. We have mentioned this in the revised edition.

8- In result, the general information, there is writing mistake in patients age, please correct it.
Response: Thank you very much, we have corrected it.

9- In figure 3, please mark just one of VIS to make it more clear whitin the whole box as well.
Response: we have revised the picture according to the suggestion.

Associate Editor's Comments:
Associate Editor 1:
The reviewers and editors were very interested in your work,which they found timely,novel,and important.They however had a few minor concerns regarding your manuscript, as detailed in their attached reviews.
Addressing these concerns will require a major revision of your manuscript before it can be reconsidered for publication in the Journal. If you are willing to revise your manuscript in accordance with these comments, we will be happy to reconsider it.
When preparing your revised manuscript,you must carefully consider the reviewers' comments,and submit a "point by point" reply to all of them. You should also show in red the changes made in the body of the revised manuscript.Your reply should be uploaded as a file in addition to your revised manuscript.
EIC Decision:
Thank you for submitting your manuscript to Iran J Pediatr.Your manuscript has now been reviewed by two reviewers and an Associate Editor.I now have the reports of the Referees,which suggest that your manuscript might be suitable for publication following a number of revisions.I attach some reviewer comments and invite you to submit a revised version of your manuscript addressing the points made.
Response: Dear Editor and EIC,
Many thanks for giving me the opportunity to revise my paper. Please note that I have r3evised it according to the reviewer's comments one by one. I hope now it may meet the requirements of the Journal, but if still has any problems, I can also revise it again!
Stay in health and happy new year!
Best Regards,
Dr.Jing Liu

2 Revision 1

1 comment · 3 Apr 2021

Neda Pak Reviewer

MINOR REVISION 3 Apr 2021

Dear authors
Thank you for the revision, but there are still a few questions and comments:

1- Please describe what is called “pleural insect erosion (PIE)-like change” in ultrasound imaging, as no definition is available for this sign, just a name. Pleural insect erosion (PIE)-like change seems to be one type of pleural line abnormality; please explain exactly which type.
2- In the results, you mentioned that pleural line abnormalities (coarse, fuzzy or interrupted, etc.) were seen in all patients with early- and late-stage BPD, but pleural insect erosion (PIE)-like change was seen in fewer patients. If we consider (PIE)-like change to be one of the pleural abnormalities, there would be a discrepancy between your findings unless you mention other types of pleural abnormalities besides (PIE)-like change. In that case, you should provide an exact definition of (PIE)-like change, distinct from pleural thickening, fuzziness, interruption, etc.!
3- The incorrect term (VIS) is still in the abstract and should be changed to AVS!
4- There are a few writing mistakes to be corrected as follows: in the limitations, the word “ultrasound imaginge ” and, in the figure legends, the word “thickenin” should be corrected.
5- In line 160, the word “ specific ” is extra.
6- Regarding this question and your answer: “ Would you please add this explanation that how the AVS can be differentiated from air bronchogram? Response: According to my study and my knowledge,VAS existed within vesicle-forming lung field, while air bronchogram existed within consolidated lung tissue.” I believe this should be added to the text to make it easier for readers to differentiate them, considering that there may be some similarities. Please also briefly explain the difference between ultrasound images of a vesicle-forming lung field and consolidation with an air-bronchogram.

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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.

Response to reviewer’s comments

Dear Jing Liu,

Thank you for submitting your valuable manuscript to the journal. We would like to inform you that the peer review of your manuscript is now completed and despite several useful points, it needs "**Minor Revision**". Below you may find the peer review comments. Please reply to them one-by-one and re-submit it again.

Dear Editor and EIC,
Many thanks for giving me the opportunity again.to revise my paper. Please note we have revised it according to the reviewer’s comments one by one. I hope now it may meet the requirements of the Journal, but if still has any problems, we can also revise it again!
Stay in health!
Best Regards,

Reviewers' Comments:

Reviewer 1:

Dear authors

Thank you for revision, but there are still few questions and comments:

1- Please describe what is named “pleural insect erosion (PIE)-like change” in ultrasound imaging. As no definition is available for this sign but just a name. pleural insect erosion (PIE)-like change seems to be one type of pleural line abnormality that should be explained exactly which type.

Response:Dear reviewer, you are right.PIE-like change is a kind of specific pleural line abnormalities,that is mild consolidation and nonconsolidated lesions alternate at the pleural line,resulting in the discontinuity of the thickened pleural line, which looks like was bited by insects on ultrasound. We have revised this part in the second revised manuscript. Please see the red part in the results section.

2- In result you mentioned that Pleural line abnormalities (coarse, fuzzy or interruption, etc.), were seen in all early- and late-stage BPD but pleural insect erosion (PIE)-like change in less patients, if we consider (PIE)-like change as one of pleural abnormalities, so there would be a discrepancy between your findings unless you mention other type of pleural abnormaility except (PIE)-like change, which in that case you should have exact definition for (PIE)-like change, apart from pleural thickening, fuzzy, or interruption, etc.!

Response:Dear reviewer, thank you very much for the constructive comment. Please note we have reclassified the pleural line abnormalities, that are nonspecific pleural line abnormalities(including coarse, fuzzy or interruption) and specific pleural line abnormality(that is PIE-like change). Please see the red part in the results section.

3- There is still wrong (VIS) word in the abstract which should be changed to AVS!

This error has been corrected.

3- There are few writing mistakes to be corrected as following: in limitation the word “ultrasound imaginge “, in figures legend the word “thickenin” should be corrected.

This error has been corrected.

4- In line 160, the word “ specific “ is extra.

This error has been corrected.

6- Regarding this question and your answer” Would you please add this explanation that how the AVS can be differentiated from air bronchogram? Response: According to my study and my knowledge,VAS existed within vesicle-forming lung field, while air bronchogram existed within consolidated lung tissue.” I believe this should be added to text to make it easier for readers to differentiate them, considering this fact that may be some similarities. and explain briefly about difference between ultrasound of vesicle forming lung field and consolidation with air-bronchogram.

We have done this according to the comment. Please see the red part in the discussion section.

3 Revision 2

1 comment · 3 May 2021

Referee 1 Reviewer

MINOR REVISION 3 May 2021

Dear Authors

Thank you for the requested revision. I believe the word (interruption) should be omitted from the definition of nonspecific pleural changes, because pleural interruption is actually seen in PIE-like change as discontinuity of the thickened pleural line and is a specific pleural change. So the manuscript needs just a minor change.

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.

Response to Reviewers' Comments

Reviewer 1:
Dear Authors

Thank you for requested revision, I believe the word (interruption) should be omitted from definition of non specific pleural changes, because actually pleural interruption is seen in PIE -like change as discontinuity of the thickened pleural line, s a specific pleural change. so the manuscript needs just minor change.

Response: I agree with this suggestion, please note we have deleted the word of interruption in the revised manuscript.

4 Revision 3

0 comments

No public comments in this round.