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- Comments from the reviewers and editors (email to author requesting revisions)
- Response from the author (cover letter submitted with revised manuscript)\*

\*The corresponding author has opted to make this information publicly available.

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Questions about these materials may be directed to the *Obstetrics & Gynecology* editorial office: obgyn@greenjournal.org.

Date:	Feb 14, 2020
То:	"Craig V. Towers"
From:	"The Green Journal" em@greenjournal.org
Subject:	Your Submission ONG-20-94

### RE: Manuscript Number ONG-20-94

Fetal bradycardia in response to maternal hypothermia: a case series and literature review

Dear Dr. Towers:

Your manuscript has been reviewed by the Editorial Board and by special expert referees. Although it is judged not acceptable for publication in Obstetrics & Gynecology in its present form, we would be willing to give further consideration to a revised version.

If you wish to consider revising your manuscript, you will first need to study carefully the enclosed reports submitted by the referees and editors. Each point raised requires a response, by either revising your manuscript or making a clear and convincing argument as to why no revision is needed. To facilitate our review, we prefer that the cover letter include the comments made by the reviewers and the editor followed by your response. The revised manuscript should indicate the position of all changes made. We suggest that you use the "track changes" feature in your word processing software to do so (rather than strikethrough or underline formatting).

Your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Mar 06, 2020, we will assume you wish to withdraw the manuscript from further consideration.

### **REVIEWER COMMENTS:**

#### REVIEWER #1:

The authors present a case series of maternal hypothermia associated with fetal bradycardia. The manuscript is a good review of the differential of fetal bradycardia baseline including considerations for maternal hypothermia. The series is consistent with previously published cases as cited. I don't know if there is anything this series adds to the existing literature. The noted association of opioid abuse disorder and fetal bradycardia is interesting and is important to consider. The remaining cases of infection pyelonephritis I presume are sepsis related.

#### Teaching Points:

1. Line 40 I would suggest adding a change in baseline fetal bradycardia is not an indication for delivery. As written it leaves the question wide open including other bradycardias unrelated to baseline which I don't think was the intent after reading the manuscript.

2. Line 49-51 My suggestions would be to wrap in the physiology of core body temperature is not independent to fetal FHR. The findings are consistent with postnatal responses to temperature change. Decreased depolarization of cardiac pacemaker cells, causing bradycardia.

3. Line 69-70 The distinction between fetal heart block and baseline is very important. Unless this is diagnosed prenatally it can cause a clinical dilemma in decision for delivery.

Case:

4. Line 81 During the admission for pyelonephritis what were the rest of the vital signs during the hypothermia episode ie BP, HR and O2 sats? These could confound the FHR tracing. Also with each tracing was there clear separate rates?

5. Line 102-103 What was the physiology of over corrected DKA and hypothermia. The tracing in DKA would be expected to be abnormal with possible late decelerations associated with maternal acidosis.

6. Line 118 The use of ultrasound addresses the above concerns about distinguishing maternal from fetal HR.

Figures:

7. Although discussed above usually the maternal HR is superimposed on the strip. Where was maternal HR recorded?

Discussion:

8. The findings were consistent with other studies. I would suggest discussing some of the adult physiology regarding depolarization etc that can cause bradycardia

REVIEWER #2:

1. Teaching Points - Would consider adding a qualifier to #3, such as , "with coincident reassuring features as noted in point 2". The point almost reads like all bradycardias with hypothermia are fine.

2. Precis: Would soften this. Should not be absolute with 6 cases. Something like 'usually' or 'often'.

3. Abstract. Compromise is a little vague. Maybe consider hypoxia or acidosis? Isnt that really the difference in these cases? Hypothermic events aren't necessarily hypoxic ones?

4. Introduction. Wouldn't a normal variant also be a possible explanation for a low baseline? Ive had many patients present 100-105 without fetal compromise.

Recommend that the authors expound on the physiology of bradycardia with hypothermia. I wouldn't assume that all readers are familiar with mechanisms.

5. Cases. How long was the maternal temperature hypothermic for each case?

The authors refer to normal 'milestones' for the children. Was this a formal evaluation? A standardized test for which readers would be familiar? Or more a general sense of no gross CNS abnormalities?

Were any cord gases or pH data available at birth?

6. Discussion.

Same recommendation about 'compromise'

How long does it take to correct during maternal warming?

Line 148 - this sentence is long and structurally confusing. Recommend editing

Could the authors recommend the most effective warming techniques? Several are mentioned.

- 7. References no comments
- 8. Figures. No comments. They are easy to read

#### ASSOCIATE EDITOR'S COMMENTS:

Please in your revision do not use the term "fetal heart rate bradycardia" but simply "fetal bradycardia"

Line 102-103 What was the physiology of over corrected DKA and hypothermia. The tracing in DKA would be expected to be abnormal with possible late decelerations associated with maternal acidosis.

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Figures:

Although discussed above usually the maternal HR is superimposed on the strip. Where was maternal HR recorded?

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EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:

- A. OPT-IN: Yes, please publish my point-by-point response letter.
- B. OPT-OUT: No, please do not publish my point-by-point response letter.

2. As of December 17, 2018, Obstetrics & Gynecology has implemented an "electronic Copyright Transfer Agreement" (eCTA) and will no longer be collecting author agreement forms. When you are ready to revise your manuscript, you will be prompted in Editorial Manager (EM) to click on "Revise Submission." Doing so will launch the resubmission process, and you will be walked through the various questions that comprise the eCTA. Each of your coauthors will receive an email from the system requesting that they review and electronically sign the eCTA.

Please check with your coauthors to confirm that the disclosures listed in their eCTA forms are correctly disclosed on the manuscript's title page.

3. Our journal requires that all evidence-based research submissions be accompanied by a transparency declaration statement from the manuscript's lead author. The statement is as follows: "The lead author\* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained." \*The manuscript's guarantor.

If you are the lead author, please include this statement in your cover letter. If the lead author is a different person, please ask him/her to submit the signed transparency declaration to you. This document may be uploaded with your submission in Editorial Manager.

4. Tables, figures, and supplemental digital content should be original. The use of borrowed material (eg, lengthy direct quotations, tables, figures, or videos) is discouraged, but should it be considered essential, written permission of the copyright holder must be obtained. Permission is also required for material that has been adapted or modified from another source.

Both print and electronic (online) rights must be obtained from the holder of the copyright (often the publisher, not the author), and credit to the original source must be included in your manuscript. Many publishers now have online systems for submitting permissions request; please consult the publisher directly for more information.

When you submit your revised manuscript, please upload 1) the permissions license and 2) a copy of the original source from which the material was reprinted, adapted, or modified (eg, scan of book page(s), PDF of journal article, etc.).

5. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric and gynecology data definitions at https://www.acog.org/About-ACOG/ACOG-Departments/Patient-Safety-and-Quality-Improvement/reVITALize. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Case Reports should not exceed 8 typed, double-spaced pages (2,000 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.

7. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:

\* All financial support of the study must be acknowledged.

\* Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.

\* All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your response in the journal's electronic author form verifies that permission has been obtained from all named persons.

\* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).

8. Provide a short title of no more than 45 characters (40 characters for case reports), including spaces, for use as a running foot.

9. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

In addition, the abstract length should follow journal guidelines. The word limits for different article types are as follows: Case Reports, 125 words. Please provide a word count.

10. Only standard abbreviations and acronyms are allowed. A selected list is available online at http://edmgr.ovid.com /ong/accounts/abbreviations.pdf. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

11. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

12. In your Abstract, manuscript Results sections, and tables, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone.

If appropriate, please include number needed to treat for benefits (NNTb) or harm (NNTh). When comparing two procedures, please express the outcome of the comparison in U.S. dollar amounts.

Please standardize the presentation of your data throughout the manuscript submission. For P values, do not exceed three decimal places (for example, "P = .001"). For percentages, do not exceed one decimal place (for example, 11.1%").

13. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: http://edmgr.ovid.com/ong/accounts/table\_checklist.pdf.

14. The American College of Obstetricians and Gynecologists' (ACOG) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite ACOG documents in your manuscript, be sure the reference you are citing is still current and available. If the reference you are citing has been updated (ie, replaced by a newer version), please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly (exceptions could include manuscripts that address items of historical interest). If the reference you are citing has been withdrawn with no clear replacement, please contact the editorial office for assistance (obgyn@greenjournal.org). In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All ACOG documents (eg, Committee Opinions and Practice Bulletins) may be found via the Clinical Guidance & Publications page at https://www.acog.org/Clinical-Guidance-and-Publications/Search-Clinical-Guidance.

15. The Journal's Production Editor had the following queries about the figures in your manuscript:

"Figures 1-3: Please confirm that these figures are original to the manuscript. "

When you submit your revision, art saved in a digital format should accompany it. If your figure was created in Microsoft Word, Microsoft Excel, or Microsoft PowerPoint formats, please submit your original source file. Image files should not be copied and pasted into Microsoft Word or Microsoft PowerPoint.

When you submit your revision, art saved in a digital format should accompany it. Please upload each figure as a separate file to Editorial Manager (do not embed the figure in your manuscript file).

If the figures were created using a statistical program (eg, STATA, SPSS, SAS), please submit PDF or EPS files generated directly from the statistical program.

Figures should be saved as high-resolution TIFF files. The minimum requirements for resolution are 300 dpi for color or black and white photographs, and 600 dpi for images containing a photograph with text labeling or thin lines.

Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce.

16. Authors whose manuscripts have been accepted for publication have the option to pay an article processing charge and publish open access. With this choice, articles are made freely available online immediately upon publication. An information sheet is available at http://links.lww.com/LWW-ES/A48. The cost for publishing an article as open access can be found at http://edmgr.ovid.com/acd/accounts/ifauth.htm.

Please note that if your article is accepted, you will receive an email from the editorial office asking you to choose a publication route (traditional or open access). Please keep an eye out for that future email and be sure to respond to it

promptly.

\* \* \*

If you choose to revise your manuscript, please submit your revision through Editorial Manager at http://ong.editorialmanager.com. Your manuscript should be uploaded in a word processing format such as Microsoft Word. Your revision's cover letter should include the following:

\* A confirmation that you have read the Instructions for Authors (http://edmgr.ovid.com/ong/accounts/authors.pdf),

and

\* A point-by-point response to each of the received comments in this letter.

If you submit a revision, we will assume that it has been developed in consultation with your co-authors and that each author has given approval to the final form of the revision.

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Mar 06, 2020, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

2018 IMPACT FACTOR: 4.965 2018 IMPACT FACTOR RANKING: 7th out of 83 ob/gyn journals

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: https://www.editorialmanager.com/ong/login.asp?a=r). Please contact the publication office if you have any questions.

February 28, 2020

To the Editors' of the Journal:

We would like to thank *Obstetrics and Gynecology* for the review of our manuscript entitled "Fetal bradycardia in response to maternal hypothermia: a case series and literature review" for publication. Below we have answered all the queries and created a tracked changes copy along with a clean version of the manuscript. Again, this study is original, the authors of this manuscript have no conflicts of interest or financial disclosures, and this manuscript has not been previously published or submitted to any other journal for consideration. Both authors had a substantial contribution to the study. In addition, we have written informed consent from the 5 patients. None of the provided information on the 5 presented patients has any identifiable material presented in the manuscript.

As requested in the queries, the corresponding author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

For the Journal Production Editor, the submitted figures are original to the manuscript.

Lastly, it states that a case report cannot exceed 2000 words (ours is 1333 words) and that it cannot be more than 8 pages. If I read this correctly, the 8 pages includes all the pages except the references. Our manuscript excluding the references is 11 pages. The body of the paper (excluding the title page, precis, and abstract) is 5 pages with 2 tables and 1 page with all the figure legends. If this is too large, please advise us on how to cut back on the manuscript.

Respectively,

Craig V. Towers M.D. Department of Obstetrics & Gynecology Division of Maternal-Fetal Medicine University of Tennessee Medical Center, Knoxville

RE: Manuscript Number ONG-20-94

Fetal bradycardia in response to maternal hypothermia: a case series and literature review

**REVIEWER COMMENTS:** 

### REVIEWER #1:

The authors present a case series of maternal hypothermia associated with fetal bradycardia. The manuscript is a good review of the differential of fetal bradycardia baseline including considerations for maternal hypothermia. The series is consistent with previously published cases as cited. I don't know if there is anything this series adds to the existing literature. The noted association of opioid abuse disorder and fetal bradycardia is interesting and is important to consider. The remaining cases of infection pyelonephritis I presume are sepsis related. ---- we concur

**Teaching Points:** 

1. Line 40 I would suggest adding a change in baseline fetal bradycardia is not an indication for delivery. As written it leaves the question wide open including other bradycardias unrelated to baseline which I don't think was the intent after reading the manuscript. --- concur see Reviewer #2 Comment number 1

2. Line 49-51 My suggestions would be to wrap in the physiology of core body temperature is not independent to fetal FHR. The findings are consistent with postnatal responses to temperature change. Decreased depolarization of cardiac pacemaker cells, causing bradycardia. --- this was brought up in several places and was added to the Discussion Section (full paragraph at the bottom of page 7

3. Line 69-70 The distinction between fetal heart block and baseline is very important. Unless this is diagnosed prenatally it can cause a clinical dilemma in decision for delivery. --- concur and further discussed (seen in red) middle of page 4 line 70 of the Introduction.

Case:

4. Line 81 During the admission for pyelonephritis what were the rest of the vital signs during the hypothermia episode ie BP, HR and O2 sats? These could confound the FHR tracing. Also, with each tracing was there clear separate rates? --- the information was added seen at the bottom of page 4 and top of page 5 lines 82 & 83.

5. Line 102-103 What was the physiology of over corrected DKA and hypothermia. The tracing in DKA would be expected to be abnormal with possible late decelerations associated with maternal acidosis. ------ we agree, the tracing during the DKA was abnormal but when it was overcorrected producing hypoglycemia, the tracing described in this manuscript was seen; therefore, we did not add this but we can if desired.

6. Line 118 The use of ultrasound addresses the above concerns about distinguishing maternal from fetal HR. ---- the authors concur

# Figures:

7. Although discussed above usually the maternal HR is superimposed on the strip. Where was maternal HR recorded? ---- the monitors for most of these cases (that were collected over a period of years) did not have the capability of printing the maternal heart rate simultaneously on the strip --- the maternal heart rates were recorded in the patient flow sheets during the admission.

Discussion:

8. The findings were consistent with other studies. I would suggest discussing some of the adult physiology regarding depolarization etc. that can cause bradycardia ---- done as stated in #2 above

## **REVIEWER #2:**

1. Teaching Points - Would consider adding a qualifier to #3, such as , "with coincident reassuring features as noted in point 2". The point almost reads like all bradycardias with hypothermia are fine. ---- we concurred with this statement and added the phrase to Teaching Point number 3 seen on page 1

3. Abstract. Compromise is a little vague. Maybe consider hypoxia or acidosis? Isnt that really the difference in these cases? Hypothermic events aren't necessarily hypoxic ones? ---- this was done as seen in red in the Conclusion part of the Abstract

4. Introduction. Wouldn't a normal variant also be a possible explanation for a low baseline? Ive had many patients present 100-105 without fetal compromise. ---- we concur, and this was clarified in the first paragraph of the Introduction seen at the top of page 4

Recommend that the authors expound on the physiology of bradycardia with hypothermia. I wouldn't assume that all readers are familiar with mechanisms. ---- done as stated for Reviewer Number 1 Comment #2 above

5. Cases. How long was the maternal temperature hypothermic for each case? ---- This ranged from 1 hour to 36 hours, but we did not add this unless the Editors feel it is needed (see below)

The authors refer to normal 'milestones' for the children. Was this a formal evaluation? A standardized test for which readers would be familiar? Or more a general sense of no gross CNS abnormalities? ---- this was clarified for all five cases by removing a sentence from Cases 1, 2 & 3 and making a blanket statement seen on page 6 lines 113 and 114

Were any cord gases or pH data available at birth? -- this was added to the Cases section page 6 line 118

6. Discussion.

Same recommendation about 'compromise' ---- fixed as seen on line 122 under Discussion page 6

How long does it take to correct during maternal warming? ---- this was similar to number 5 above

Line 148 - this sentence is long and structurally confusing. Recommend editing --- we agreed and rewrote this part of the manuscript as seen in the last paragraph of the Discussion page 8

Could the authors recommend the most effective warming techniques? Several are mentioned. --- we added a sentence to address this seen on lines 125-127 at the bottom of page 6

- 7. References no comments
- 8. Figures. No comments. They are easy to read

# ASSOCIATE EDITOR'S COMMENTS:

Please in your revision do not use the term "fetal heart rate bradycardia" but simply "fetal bradycardia" ---- this was corrected throughout, and we believe we found them all

Line 118 The use of ultrasound addresses the above concerns about distinguishing maternal from fetal HR. ----- this was answered above under Reviewer number 1

## Figures:

Although discussed above usually the maternal HR is superimposed on the strip. Where was maternal HR recorded? ------ this was answered above under Reviewer number 1

## Discussion:

The findings were consistent with other studies. I would suggest discussing some of the adult physiology regarding depolarization etc that can cause bradycardia ----- this was answered above under Reviewer number 1

# EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:

A. OPT-IN: Yes, please publish my point-by-point response letter. --- the authors agree with this

B. OPT-OUT: No, please do not publish my point-by-point response letter.

2. As of December 17, 2018, Obstetrics & Gynecology has implemented an "electronic Copyright Transfer Agreement" (eCTA) and will no longer be collecting author agreement forms. When you are ready to revise your manuscript, you will be prompted in Editorial Manager (EM) to click on "Revise Submission." Doing so will launch the resubmission process, and you will be walked through the various questions that comprise the eCTA. Each of your coauthors will receive an email from the system requesting that they review and electronically sign the eCTA. --- we will verify this is correct

Please check with your coauthors to confirm that the disclosures listed in their eCTA forms are correctly disclosed on the manuscript's title page. --- we will verify this is correct

3. Our journal requires that all evidence-based research submissions be accompanied by a transparency declaration statement from the manuscript's lead author. The statement is as follows: "The lead author\* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported;

that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained." \*The manuscript's guarantor.

If you are the lead author, please include this statement in your cover letter. If the lead author is a different person, please ask him/her to submit the signed transparency declaration to you. This document may be uploaded with your submission in Editorial Manager. --- in the letter

4. Tables, figures, and supplemental digital content should be original. The use of borrowed material (eg, lengthy direct quotations, tables, figures, or videos) is discouraged, but should it be considered essential, written permission of the copyright holder must be obtained. Permission is also required for material that has been adapted or modified from another source. ---- N/A

Both print and electronic (online) rights must be obtained from the holder of the copyright (often the publisher, not the author), and credit to the original source must be included in your manuscript. Many publishers now have online systems for submitting permissions request; please consult the publisher directly for more information.

When you submit your revised manuscript, please upload 1) the permissions license and 2) a copy of the original source from which the material was reprinted, adapted, or modified (eg, scan of book page(s), PDF of journal article, etc.).

5. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. --- we believe all is correct (if not please let us know and we will correct this)

7. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:

\* All financial support of the study must be acknowledged. --- there was none

\* Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly. --- none

\* All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your response in the journal's electronic author form verifies that permission has been obtained from all named persons. --- N/A

\* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting). ----- E-Poster at the 2020 ACOG Annual Clinical & Scientific Meeting, Seattle, Washington, April 24<sup>th</sup>-27<sup>th</sup>.

8. Provide a short title of no more than 45 characters (40 characters for case reports), including spaces, for use as a running foot. ---- done

9. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully. ---- we reviewed this and believe all is correct

In addition, the abstract length should follow journal guidelines. The word limits for different article types are as follows: Case Reports, 125 words. Please provide a word count. --- word count is 125

10. Only standard abbreviations and acronyms are allowed. A selected list is available online at Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript. --- we believe this is all correct

11. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement. ---- these were all corrected and removed (hopefully we did not miss any)

12. In your Abstract, manuscript Results sections, and tables, the preferred citation should be in terms of an effect size, such as odds ratio or relative risk or the mean difference of a variable between two groups, expressed with appropriate confidence intervals. When such syntax is used, the P value has only secondary importance and often can be omitted or noted as footnotes in a Table format. Putting the results in the form of an effect size makes the result of the statistical test more clinically relevant and gives better context than citing P values alone. ---- N/A for this manuscript (no statistics)

13. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: ---- we believe we have these correct (if not please let us know)

15. The Journal's Production Editor had the following queries about the figures in your manuscript:

"Figures 1–3: Please confirm that these figures are original to the manuscript. " --- yes, and stated in the cover letter portion

When you submit your revision, art saved in a digital format should accompany it. If your figure was created in Microsoft Word, Microsoft Excel, or Microsoft PowerPoint formats, please submit your original source file. Image files should not be copied and pasted into Microsoft Word or Microsoft PowerPoint.

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Figures should be saved as high-resolution TIFF files. The minimum requirements for resolution are 300 dpi for color or black and white photographs, and 600 dpi for images containing a photograph with text labeling or thin lines.

Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce. --- we believe we have all of this correct

Please note that if your article is accepted, you will receive an email from the editorial office asking you to choose a publication route (traditional or open access). Please keep an eye out for that future email and be sure to respond to it promptly. --- due to funding we will probably not be able to do open access

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