

OBSTETRICS & GYNECOLOGY



NOTICE: This document contains correspondence generated during peer review and subsequent revisions but before transmittal to production for composition and copyediting:

- 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.*

Personal or nonessential information may be redacted at the editor's discretion.

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

Date: Oct 03, 2019
To: "Matthew Nudelman" [REDACTED]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-19-1622

RE: Manuscript Number ONG-19-1622

Effect of delayed cord clamping on umbilical artery blood gas parameters in term infants

Dear Dr. Nudelman:

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 Oct 24, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: This is a systematic review to determine the effect of delayed cord clamping (DCC) on cord blood gas (CBG) in vaginally delivered healthy term deliveries. Eligible studies were randomized control trials (RCT) comparing early cord clamping (ECC) versus DCC. Five studies were included in this review. The studies found only small differences in pH, HCO₃ and base deficit. The authors conclude that DCC had only a minimal effect on cord blood gas and that cord blood gas reference ranges are still applicable to this population. Ways in which this manuscript could be improved include:

1. Lines 92-84: I would give some specifics on the improvement in outcomes with some details of those studies. I also would soften the language that DCC "likely" does not increase maternal morbidities.
2. Line 218: Not sure much can be drawn from 5 studies. Do you really think this warrants a systematic review? It seems many more primary studies need to be performed.
3. Lines 313-314: How would you have determined if a meta-analysis should be performed. Again with such few studies it would be really difficult.
4. Lines 326-328: Again, wouldn't this suggest a systematic review is not warranted with such a small number of included study.
5. Lines 385-386: But are these differences clinically relevant? Neonatal outcomes are improved, so I would think no.
6. Lines 415-416: Why would samples be drawn at different times? What would the benefit be?
7. Lines 425-428: I agree. It seems like we still really do not know the answers given the small number of existing studies.
8. Lines 443-445: Perhaps this is suggesting we don't need further studies, but given you only had 5 studies perhaps we need more studies to be reassured

Reviewer #2: The manuscript describes a systematic review on the topic of delayed cord clamping in term babies and effects on cord blood analysis. The review followed the PRISMA guidelines and was well conducted. Please spell out your PICO question.

The methods section is far too long and contains redundant information. There is some repetition in the text which could be avoided. Overall the text should be shortened. The results section should start with the overview characteristics table of

included studies.

In the discussion the message that delayed cord clamping does not significantly change the cord blood gas analysis needs to be clearer worked out. This systematic review adds to the knowledge about safety of delayed cord clamping.

Reviewer #3: In this manuscript, the authors performed a systematic review to evaluate the effects of delayed cord clamping in vaginally delivered full term infants on umbilical cord vessels blood gas. The rationale for the study is that cord blood gas (CBG) is often used in clinical practice and in medico legal arena to assess the fetal and neonatal conditions and reference values are derived from the newborn population with immediate cord clamping at birth. The authors wish to know whether delayed cord clamping, an increasing trend of cord management at present, will have an effect on the CBG.

The authors performed a search of various data bases (Medline, CINAHL etc.) and identified an initial list of 148 publications for study selection using a set of criteria for eligibility. The ended up with 5 papers (3 observational and 2RCTs) from Sweden, Netherland and Spain. The review was performed by two authors, with a third reviewer performing adjudication if there is a discrepancy. They found no difference in CBG with delayed vs. immediate cord clamping.

General Comments

The results from this study have significant relevance to the field in that they provide assurance that the cord blood gas reference values can be used irrespective of the timing of cord clamping. This premise is based on the perceived notion that there is an increasing practice trend of delayed cord clamping because of positive recommendations from various professional organizations. The authors need to confirm the notion of increasing trend in practice of delayed cord clamping with a thorough literature review. While the authors have done an exhaustive traditional methodology in conducting the review, there are some issues that need to be addressed as listed below

Specific Comments

Abstract

1. Line 59: Objective the authors' real objective is to compare the cord blood gas in infants with delayed vs. immediate cord clamping
2. Line 85 Conclusion: The last sentence is the conclusion. Consider deleting the first sentence.
3. Line 91-92 Introductions: the authors should expand the discussion to list the benefits of delayed cord clamping for preterm and term infants with appropriate reference citation.
4. Methods: Well done, no comments
5. Results The tables (except table 2) are very crowded and can be remedied by listing some of the items in the text. An example in table 1 is the item on artery vs vein sample validation which were not done in all five studies Table 3 and 4 are also extremely crowded and difficult to read. In assessing the clinical status of infants using cord blood gas, the clinicians rely mostly on arterial or venous pH, bicarbonate and base deficit. To simplify the two tables, the authors might consider listing only those three parameters in the manuscripts and publishing the remaining blood gas parameters on line.
6. Discussion: The authors should make an attempt to do a thorough literature search to document the increasing trend of practice of delayed cord clamping
7. Another point that should be mentioned in the discussion is that the studies involved vaginally delivered term infants. It is not certain whether the results of the review will apply to preterm infants.

STATISTICAL EDITOR'S COMMENTS:

1. Abstract: Need to include the overall number of CBGs (and range per study) included in the review, besides the number of studies.
2. lines 193-194: Need to elaborate on how the difference in means was extracted from other available statistics when a difference in means was not available.
3. lines 198-200, 274-278: How were 95% CI calculated from relatively small samples unless there was information re: whether the data were distributed normally?
- 4: lines 210-211: Need to provide more details regarding what data was evaluated by the two Authors. And specifically,

what were the values and CIs for Cohen's kappa?

Associate Editor's Comments:

We would welcome a revised manuscript but it request that it shortened by 50%. A good deal of what is currently in the text could be moved to appendices.

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. 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.

5. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Review articles should not exceed 25 typed, double-spaced pages (6,250 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.

6. 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).

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

8. Provide a précis on the second page, for use in the Table of Contents. The précis is a single sentence of no more than 25 words that states the conclusion(s) of the report (ie, the bottom line). The précis should be similar to the abstract's conclusion. Do not use commercial names, abbreviations, or acronyms in the précis. Please avoid phrases like "This paper presents" or "This case presents."

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: Reviews, 300 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 to say about the figures in your manuscript:

"Figure 2: Please upload a higher resolution version of this figure. Textures used in the key should be replaced with solid colors, as textures are not easily distinguished in print."

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/ifaauth.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 Oct 24, 2019, 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.

RE: Manuscript Number ONG-19-1622

Effect of delayed cord clamping on umbilical artery blood gas parameters in term infants

Dear Dr. Nudelman:

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 Oct 24, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: This is a systematic review to determine the effect of delayed cord clamping (DCC) on cord blood gas (CBG) in vaginally delivered healthy term deliveries. Eligible studies were randomized control trials (RCT) comparing early cord clamping (ECC) versus DCC. Five studies were included in this review. The studies found only small differences in pH, HCO₃ and base deficit. The authors conclude that DCC had only a minimal effect on cord blood gas and that cord blood gas reference ranges are still applicable to this population. Ways in which this manuscript could be improved include:

1. Lines 92-84: I would give some specifics on the improvement in outcomes with some details of those studies. I also would soften the language that DCC "likely" does not increase maternal morbidities.

Thank you for your comments. We have included the specific benefits of DCC in term infants.

Lines 83-88: "DCC has multiple benefits in term and preterm infants⁷⁻¹¹ In term infants DCC has been shown to increase blood volume,¹² hematocrit,^{9,10} hemoglobin,^{9,10,11} ferritin,^{9,10} and iron stores.^{9,10} It decreases anemia,^{9,10} and improves long-term neurodevelopmental outcomes.^{13,14} DCC likely does not increase maternal postpartum hemorrhage, nor interventions for neonatal hyperbilirubinemia or polycythemia.^{9,11,15}"

We have added the word "likely" in the final sentence. Line 86

2. Line 218: Not sure much can be drawn from 5 studies. Do you really think this warrants a systematic review? It seems many more primary studies need to be performed.

We appreciate this important comment. DCC as the standard of care is recommended by multiple international organizations and is adopted by growing number of clinicians. The effect of DCC on CBG is an important issue that needs to be addressed. Existing literature seems inconsistent regarding the effect of DCC on CBG, which causes confusion for clinicians. The goal of this review was to systematically identify the existing publications on this subject, critically assess the quality of each study, and provide a comprehensive summary of the findings. We screened 148 unique records and identified 23 eligible studies. We ultimately identified five publications that adequately addressed this issue. Based dichotomously on statistical significance, some studies showed an effect on CBG while others did not. However, the magnitude of these changes is minimal and the resulting values are still within the normal limits of current reference ranges. Hence a consistent conclusion is that DCC has minimal clinical impact on CBG.

This review identified limited number of studies on this topic, highlighting the need for future large studies. We state in our discussion section that “Larger studies, similar to those originally used to describe CBG reference ranges,^{23-25,27,32} are needed to more accurately describe the effect of DCC on blood acid-base balance in term singleton vaginal deliveries.” Lines 261-263

3. Lines 313-314: How would you have determined if a meta-analysis should be performed. Again with such few studies it would be really difficult.

In general, a meta-analysis can be performed even with a limited number of studies if they have homogeneous designs and use similar descriptive statistics to describe their summary effect estimates (i.e. difference in means and standard deviations). In our case, we did not perform a meta-analysis because the five studies did not have the comparable descriptive statistics. Furthermore, we could not calculate these descriptive statistics based on the provided information without making gross assumptions about each study original data distributions.

4. Lines 326-328: Again, wouldn't this suggest a systematic review is not warranted with such a small number of included study.

Thank you for your comment. This is the first systematic review that critically evaluated of the effect of DCC on cord blood acid-base status. Even though there are small number of studies, a comprehensive summary of the findings is helpful for clinical practitioners. This review provides the background information and guidance on appropriate study methods for future research and meta-analysis on this topic.

5. Lines 385-386: But are these differences clinically relevant? Neonatal outcomes are improved, so I would think no.

Thank you for your comment. We agree that these small changes in blood gas values are not clinically relevant. In our manuscript we state that “the magnitude of this effect may not be clinically significant in healthy term vaginally delivered newborns.” Lines 274-275

6. Lines 415-416: Why would samples be drawn at different times? What would the benefit be? Although there are multiple benefits to DCC, the ideal duration has not yet been established. Drawing samples at different times before cord clamping allows the researchers to evaluate the effect of different duration of DCC on infant blood gas.

7. Lines 425-428: I agree. It seems like we still really do not know the answers given the small number of existing studies.

Thank you for your comment. We agree and have revised the Discussion section to include clinical and research implications to acknowledge that “Larger studies, similar to those originally used to describe CBG reference ranges, are needed to more accurately describe the effect of DCC on blood acid-base balance in term singleton vaginal deliveries.” Lines 261-263

8. Lines 443-445: Perhaps this is suggesting we don't need further studies, but given you only had 5 studies perhaps we need more studies to be reassured

Thank you for your comment. We agree and in the following sentence we emphasize that additional larger studies would be helpful in more accurately describing the effect DCC.

“Larger studies, similar to those originally used to describe CBG reference ranges, are needed to more accurately describe the effect of DCC on blood acid-base balance in term singleton vaginal deliveries.” Lines 261-263

Reviewer #2: The manuscript describes a systematic review on the topic of delayed cord clamping in term babies and effects on cord blood analysis. The review followed the PRISMA guidelines and was well conducted. Please spell out your PICO question.

Thank you for your comment. We have revised the statement about objective of this study to ensure all the PICO information were included.

“Our objective is to compare the effect of ECC and DCC on arterial and venous CBG in term singleton infants born vaginally.” Lines 99-100

The methods section is far too long and contains redundant information. There is some repetition in the text which could be avoided. Overall the text should be shortened. The results section should start with the overview characteristics table of included studies.

Thank you for your comment. We have shortened the text throughout the paper. We have revised the results section to start with the overview characteristics of the included studies.

In the discussion the message that delayed cord clamping does not significantly change the cord blood gas analysis needs to be clearer worked out. This systematic review adds to the knowledge about safety of delayed cord clamping.

Thank you for this comment. We added this comment to our clinical implication section.

“Limited existing evidence suggests that DCC up to 120 s has minimal clinical impact in healthy term newborns. Our findings also support the safety of DCC, specifically with regard to fetal-newborn acid-base status. However, our review was limited to healthy term newborns and may not be applicable to medically complex infants.” Lines 256 - 259

Reviewer #3: In this manuscript, the authors performed a systematic review to evaluate the effects of delayed cord clamping in vaginally delivered full term infants on umbilical cord vessels blood gas. The rationale for the study is that cord blood gas (CBG) is often used in clinical practice and in medico legal arena to assess the fetal and neonatal conditions and reference values are derived from the newborn population with immediate cord clamping at birth. The authors wish to know whether delayed cord clamping, an increasing trend of cord management at present, will have an effect on the CBG.

The authors performed a search of various data bases (Medline, CINAHL etc.) and identified an initial list of 148 publications for study selection using a set of criteria for eligibility. The ended up with 5 papers (3 observational and 2RCTs) from Sweden, Netherland and Spain. The review was performed by two authors, with a third reviewer performing adjudication if there is a discrepancy. They found no difference in CBG with delayed vs. immediate cord clamping.

General Comments

The results from this study have significant relevance to the field in that they provide assurance that the cord blood gas reference values can be used irrespective of the timing of cord clamping. This premise is based on the perceived notion that there is an increasing practice trend of delayed cord clamping because of positive recommendations from various professional organizations. The authors need to confirm the notion of increasing trend in practice of delayed cord clamping with a thorough literature review. While the authors have done an exhaustive traditional methodology in conducting the review, there are some issues that need to be addressed as listed below

Specific Comments

Abstract

1. Line 59: Objective the authors' real objective is to compare the cord blood gas in infants with delayed vs. immediate cord clamping

Thank you for your comment. We have revised our objective “Our objective is to compare the effect of ECC and DCC on arterial and venous CBG in term singleton infants born vaginally .” Lines 99-100

2. Line 85 Conclusion: The last sentence is the conclusion. Consider deleting the first sentence. Thank you. We have deleted that sentence.

3. Line 91-92 Introductions: the authors should expand the discussion to list the benefits of delayed cord clamping for preterm and term infants with appropriate reference citation.

Thank you for the comment. We have expanded this section and included the appropriate references.

“Delayed cord clamping (DCC), 30 to 60 s after delivery recommended by international and national organizations,¹⁻⁶ is a recent change to management of the third stage of labor. DCC has multiple benefits in term and preterm infants⁷⁻¹¹ In term infants DCC has been shown to increase blood volume,¹² hematocrit,^{9,10} hemoglobin,^{9,10,11} ferritin,^{9,10} and iron stores.^{9,10} It decreases anemia,^{9,10} and improves long-term neurodevelopmental outcomes.^{13,14} DCC likely does not increase maternal postpartum hemorrhage, nor interventions for neonatal hyperbilirubinemia or polycythemia.^{9,11,15}” Lines 82-88

4. Methods: Well done, no comments

5. Results The tables (except table 2) are very crowded and can be remedied by listing some of the items in the text. An example in table 1 is the item on artery vs vein sample validation which were not done in all five studies Table 3 and 4 are also extremely crowded and difficult to read. In assessing the clinical status of infants using cord blood gas, the clinicians rely mostly on arterial or venous pH, bicarbonate and base deficit. To simplify the two tables, the authors might consider listing only those three parameters in the manuscripts and publishing the remaining blood gas parameters on line.

Thank you for your comments. We followed your suggestions by editing tables 1, 3(now 4), and 4(now 5) to improve readability and by transferring parts of tables 3 and 4 to two supplementary tables (S1 and S2).

6. Discussion: The authors should make an attempt to do a thorough literature search to document the increasing trend of practice of delayed cord clamping

Thank you for your comments. We have conducted a literature search on implementation of DCC in clinical practice. We have added the following sentence in the discussion: “ DCC is quickly becoming standard practice in the delivery room as demonstrated by the recent quality improvement papers showing DCC implementation in preterm and term newborns ” Lines 254-255

7. Another point that should be mentioned in the discussion is that the studies involved vaginally delivered term infants. It is not certain whether the results of the review will apply to preterm infants.

Thank you for your comment. We have clarified this in the following sentence under discussion: research implication.

“ . DCC is increasingly performed in other newborn populations (preterm infants, twins, cesarean section deliveries) and the effect of DCC on CBG needs to be determined .” Lines 263 - 265

STATISTICAL EDITOR'S COMMENTS:

1. Abstract: Need to include the overall number of CBGs (and range per study) included in the review, besides the number of studies.

Thank you for your comment. We have included the following sentence in our abstract “Five studies with a total of 234 ECC and 218 DCC arterial CBG samples were included in this review.”

2. lines 193-194: Need to elaborate on how the difference in means was extracted from other available statistics when a difference in means was not available.

Thank you for your comment. We provided additional information on how difference of means and 95% CIs were calculated when not originally provided by a study.

“When a difference in means in CBG parameters between DCC and ECC groups was unavailable, we extracted other available descriptive statistics such as M , SD , median, and range for each group. Tables and figures were created to summarize each study’s methodological details, CBG parameters, and comparison between ECC and DCC. The 95% CIs for the mean and the difference in means were calculated using the following equations: $Mean (95\% CI) = M \pm 1.96 (SD/\sqrt{n})$, $Difference in means (95\% CI) = M_1 - M_2 \pm 1.96 \sqrt{(SD_1^2/n_1 + SD_2^2/n_2)}$, when sufficient information was available and gross assumptions about a study’s original data was not required.” Lines 147-154

3. lines 198-200, 274-278: How were 95% CI calculated from relatively small samples unless there was information re: whether the data were distributed normally?

Thank you for your comment. In the footnotes of tables 4 and 5 we reported the exact equations we used to calculate the difference in mean and 95% CIs. We also added the following sentence to the data synthesis section.

“When a difference in means in CBG parameters between DCC and ECC groups was unavailable, we extracted other available descriptive statistics such as M , SD , median, and range for each group. Tables and figures were created to summarize each study’s methodological details, CBG parameters, and comparison between ECC and DCC. The 95% CIs for the mean and the difference in means were calculated using the following equations: $Mean (95\% CI) = M \pm 1.96 (SD/\sqrt{n})$, $Difference in means (95\% CI) = M_1 - M_2 \pm 1.96 \sqrt{(SD_1^2/n_1 + SD_2^2/n_2)}$, when sufficient information was available and gross assumptions about a study’s original data was not required.” Lines 147-154

We did not attempt to calculate similar statistics from the Wiberg 2008 and Lievaart 1984 studies because they specifically noted skewed distributions.

4: lines 210-211: Need to provide more details regarding what data was evaluated by the two Authors. And specifically, what were the values and CIs for Cohen's kappa?

Thank you for your comment. We have additional information to the following sentences:

“During initial record screening, MN and EB classified each article as either “include, exclude, or unsure” and then evaluated full texts of screened records for eligibility. MN and EB independently extracted data using an excel-based data extraction form.” Lines 125-128

“Inter-reviewer agreement was 97% ($k = .89$ [95% CI: .81, .91], $p < .001$) for the initial record screening and 100% during the eligibility assessment.” Lines 159-161.

Associate Editor's Comments:

We would welcome a revised manuscript but it request that it shortened by 50%. A good deal of what is currently in the text could be moved to appendices.

Thank you for your suggestion. We have moved most of the results for the “Risk of Bias Within Studies” and “Risk of Bias Across Studies” sections to a supplementary text file. The methods section has also been shortened.

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.

Yes, please 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.

We will confirm their eCTA forms are 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.

We have confirmed this sentence is on our cover letter

4. 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://urldefense.proofpoint.com/v2/url?u=https-3A-www.acog.org-About-2DACOG-ACOG-2DDepartments-Patient-2DSafety-2Dand-2DQuality-2DImprovement-reVITALize&d=DwIGaQ&c=jIuf2QGe13CVwCCNhnnHSyGX0TfHadH8sr2VwRkl7n8&r=hyXavTc0BIqjITFqNmdO6MWrLp2r688KDEs_iNDTLTo&m=rxFuNJAVMPP-E5Cm7quw4JEt2hoOZxJkfVq-Ef2TPkY&s=YasFhQ3SZ7JKAA8VQ9H1TpcItnPhY0m9Q_dqNs5IW5k&e= . If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

5. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Review articles should not exceed 25 typed, double-spaced pages (6,250 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.

6. 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).

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

We have changed our short title to “Delayed cord clamping and cord blood gas”

8. Provide a **précis** on the second page, for use in the Table of Contents. The précis is a single sentence of no more than 25 words that states the conclusion(s) of the report (ie, the bottom line). The précis should be similar to the abstract's conclusion. Do not use commercial names, abbreviations, or acronyms in the précis. Please avoid phrases like "This paper presents" or "This case presents."

“DCC up-to 120 s may have a small effect on cord blood gas, which are not clinically significant in vaginally delivered healthy term singletons.”

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: Reviews, 300 words; Please provide a word count.

10. Only standard abbreviations and acronyms are allowed. A selected list is available online at https://urldefense.proofpoint.com/v2/url?u=http-3A_edmgr.ovid.com_ong_accounts_abbreviations.pdf&d=DwIGaQ&c=jIuf2QGe13CVwCCNhnnHSyGX0TfHadH8sr2VwRkl7n8&r=hyXavTc0BIqjITFqNmdO6MWrLp2r688KDEs_iNDTLTo&m=rxAFuNJaVMPPE5Cm7quw4JEt2hoOZxJkfVq-Ef2TPkY&s=PIIToB1VlfyEjoS4ytVwJNrb0slKu96jBcfyQCfkFk4&e=. 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:

https://urldefense.proofpoint.com/v2/url?u=http-3A_edmgr.ovid.com_ong_accounts_table-5Fchecklist.pdf&d=DwIGaQ&c=jIuf2QGe13CVwCCNhnnHSyGX0TfHadH8sr2VwRkl7n8&r=hyXavTc0BIqjITFqNmdO6MWrLp2r688KDEs_iNDTLTo&m=rxFuNJaVMPPE5Cm7quw4JEt2hoOZxJkfVq-Ef2TPkY&s=hwGoSOvX4adOfDs3vPZ2ih3Zv8eZbFtWmi05YovwBE8&e= .

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://urldefense.proofpoint.com/v2/url?u=https-3A_www.acog.org_Clinical-2DGuidance-2Dand-2DPublications_Search-2DClinical-2DGuidance&d=DwIGaQ&c=jIuf2QGe13CVwCCNhnnHSyGX0TfHadH8sr2VwRkl7n8&r=hyXavTc0BIqjITFqNmdO6MWrLp2r688KDEs_iNDTLTo&m=rxFuNJaVMPPE5Cm7quw4JET2hoOZxJkfVq-Ef2TPkY&s=DaFRiaZLFJ2qytrJ9ZI1rXHi3IKIFuPZyDJQVcLO6J8&e= .

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

"Figure 2: Please upload a higher resolution version of this figure. Textures used in the key should be replaced with solid colors, as textures are not easily distinguished in print."

Thank you for your comment. We have adjusted our textures and colors.

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.

Thank you for your comment. We uploaded the original source files

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 https://urldefense.proofpoint.com/v2/url?u=http-3A__links.lww.com_LWW-2DES_A48&d=DwIGaQ&c=jIuf2QGe13CVwCCNhnnHSyGX0TfHadH8sr2VwRkl7n8&r=hyXavTc0BIqjITFqNmdO6MWrLp2r688KDEs_iNDTLTo&m=rxAFuNJJaVMPPE5Cm7quw4JEt2hoOZxJkfVq-Ef2TPkY&s=GgQ7_qDWh3w256pvLC3Mb4vtX01WdDzf7mcBdirWHxM&e= .

The cost for publishing an article as open access can be found at https://urldefense.proofpoint.com/v2/url?u=http-3A__edmgr.ovid.com_acd_accounts_ifauth.htm&d=DwIGaQ&c=jIuf2QGe13CVwCCNhnnHSyGX0TfHadH8sr2VwRkl7n8&r=hyXavTc0BIqjITFqNmdO6MWrLp2r688KDEs_iNDTLTo&m=rxAFuNJJaVMPPE5Cm7quw4JEt2hoOZxJkfVq-Ef2TPkY&s=Lzf3DqPvjS4iIL_WmE51i011TxSYoet5jZag2kDTskc&e= .

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 https://urldefense.proofpoint.com/v2/url?u=http-3A__ong.editorialmanager.com&d=DwIGaQ&c=jIuf2QGe13CVwCCNhnnHSyGX0TfHadH8sr2VwRkl7n8&r=hyXavTc0BIqjITFqNmdO6MWrLp2r688KDEs_iNDTLTo&m=rxAFuNJJaVMPPE5Cm7quw4JEt2hoOZxJkfVq-Ef2TPkY&s=J4s0uAoIiqqFdwsVg6E8ElsKNn-Jlo7OA0bWHr7r8Rw&e= . 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 (https://urldefense.proofpoint.com/v2/url?u=http-3A__edmgr.ovid.com_ong_accounts_authors.pdf&d=DwIGaQ&c=jIuf2QGe13CVwCCNhnnHSyGX0TfHadH8sr2VwRkl7n8&r=hyXavTc0BIqjITFqNmdO6MWrLp2r688KDEs_iNDTLTo&m=

https://urldefense.proofpoint.com/v2/url?u=https-3A_www.editorialmanager.com_ong_login.asp-3Fa-3Dr&d=DwIGaQ&c=jIuf2QGe13CVwCCNhnnHSyGX0TfHadH8sr2VwRkl7n8&r=hyXavTc0BIqjITFqNmdO6MWrLp2r688KDEs_iNDTLTo&m=rxAFuNJAVMPPE5Cm7quw4JEt2hoOZxJkfVq-Ef2TPkY&s=NluLVK5jOx1yWvcYHCTI8J5spLo09rUTWskxX5e1pvM&e=), 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 Oct 24, 2019, 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://urldefense.proofpoint.com/v2/url?u=https-3A_www.editorialmanager.com_ong_login.asp-3Fa-3Dr&d=DwIGaQ&c=jIuf2QGe13CVwCCNhnnHSyGX0TfHadH8sr2VwRkl7n8&r=hyXavTc0BIqjITFqNmdO6MWrLp2r688KDEs_iNDTLTo&m=rxAFuNJAVMPPE5Cm7quw4JEt2hoOZxJkfVq-Ef2TPkY&s=NluLVK5jOx1yWvcYHCTI8J5spLo09rUTWskxX5e1pvM&e=). Please

contact the publication office if you have any questions.