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)*
- Email correspondence between the editorial office and the authors*

**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: Jul 17, 2018
To: "Olga Grechukhina" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-18-1220

RE: Manuscript Number ONG-18-1220

Cesarean Scar Pregnancy, Incidence and Recurrence: five-year experience at Yale-New Haven Hospital.

Dear Dr. Grechukhina:

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 Aug 07, 2018, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

1) Precis: The Precis is clearly written and accurately summarizes the main points of this paper.

2) Abstract: The Abstract is succinct and provides a reflective overview of your research.

3) Introduction: In Line 103 - please change "reccur" to either "recur" vs. "reoccur".

4) Materials & Methods: There is mention of IRB approval being obtained in Lines 121-122. Appropriate statistical methods were applied.

5) Results: In general, the results section is well presented & comprehensive. I would suggest in Line 176 adding the word "patients" after "non-Hispanic white" and after "non-Hispanic black."

6) Discussion: The Discussion is well stated and comprehensive.

7) Conclusion: The sentence starting in Line 418 and ending in Line 420 is awkwardly written - recommend rewording.

8) References: List of References appears to be thorough and comprehensive.

9) Tables/Figures: The Tables & Figures appropriately support and further demonstrate the details of your findings.

Reviewer #2:

ONG-18-1220. Cesarean Scar Pregnancy, Incidence and Recurrence: five-year experience at Yale New Haven Hospital.

The authors report their experience with 30 cesarean scar pregnancies (CSPs) in 26 women (one with three CSPs). Their service used multiples diagnostic processes and treatment approaches. While the incidence of this complication increases there are no guidelines for their diagnosis and management.

Forty-six percent of the cases occurred on Hispanic women, a higher proportion than their county population. It will be more appropriate to compare the race/ethnicity of the cases with similar characteristic on their obstetrical -gynecological

services. Hispanics may choose their institution for many other reasons than for this complication.
Considered the best tool for the diagnosis of ectopic pregnancies, transvaginal ultrasound is not adequately mentioned in the report.

I wonder about the best approach for diagnosis and management of this complication. How will the authors proceed with their next case?

The text description appears to repeat the content of the tables.

Reviewer #3:

Abstract - Objective is to describe management, outcomes, and subsequent pregnancy outcomes over a 5 year experience of Cesarean Scar Pregnancy (CSP).

Methods - Retrospective and prospective series - all CSP cases from 5/13-3/18 at Yale, data was included - demographics, PMHx, PSHx, treatment, response, complications, subsequent pregnancies

Results - 30 cases of CSP in 26 patients - 4 recurrences in 2 patients; 46% of CSP in Hispanic women, mean previous c/s number was 2 and average gestational age of 46 days
10 subsequent spontaneous conceptions in 8 patients - 4 recurrent CSPs, 5 IUPs and 1 Sab

Conclusions - There are various treatment modalities, there is a high potential for recurrence, and early and accurate diagnosis with multidisciplinary care is the key to successful treatment.

Introduction - CSP represents 6% of ectopics. The presentation is variable and the gestational age at presentation may vary. Diagnosis is made by TVUS and there is no consensus on optimal treatment. Treatment goals are ending the pregnancy and removing the sac. There is little evidence to guide management decisions and counsel patients.

Materials and Methods - Retrospective and prospective case series of CSP between 5/13-3/18. EMR was reviewed for relevant patient data, treatment, response, and subsequent fertility.
Treatments were systemic MTX, local MTX, local KCL, UAE, hysteroscopy, and compression ballon

Results - 30 cases in 26 patients - 46% were hispanic, 42% were white. There were no differences in regard to demographics, and incidence was associated with obesity.
Presentation and diagnosis - the majority were asymptomatic
Management - all terminated except for 3 that were undergoing spontaneous abortion. The options for treatment were reviewed and selected treatments varied amongst patients - treatments and responses are described

Outcome and follow-up - Of 25 patients, there were 10 conceptions in 8 patients and 4 were recurrent, 1 miscarriage, and 5 viable IUPs

Discussion - This is of concern with the increasing c/s rate. The high rate of hispanic patients raises the question of a racial predisposition. Overweight, obese, and former smokers may be at increased risk as well.

there needs to be a high level of suspicion
Treatment modalities - A recent systematic review discussed 5 treatment modalities and another review failed to identify the leading method of treatment. These results show that systematic MTX can lead to complications but UAE with hysteroscopy and balloon compression are promising.
Follow up needs to consist of serial HCG and u/s
there is a high risk of recurrence and risk of accrete.

Conclusion - diagnosis with ultrasound and referral with close follow-up and multi-disciplinary care are key.

This is a good review of response to various treatment options. Helpful for clinicians facing these cases to see the options and the anticipated response. Though the numbers are small, the information and follow-up is still useful to see.

STATISTICAL EDITOR COMMENTS:

The Statistical Editor makes the following points that need to be addressed:
lines 172-175:Was the incidence of CSP statistically different in 2016 vs others, or was this just within random variation?

lines 177-179: Were the cohorts compared statistically? Were the samples sufficient to have enough power to discern a difference or was the non-difference simply due to low power, based on the small sample sizes (I count n = 12 vs n = 11)

lines 201-202: The hCG levels do not appear to be normally distributed. If so, should cite as median(range or IQR).

lines 304-305, line 50: Need to clarify if there were 3 or two patients with recurrences.

lines 309-315:The confidence interval for 12/26 = 46%(24%-81%), so this small sample is not statistically different from the representation in the city of New Haven. Again, there is insufficient power to make these comparisons.

Table 2: Should state that format is mean±SD. median(range) and n(%) as footnote to table.

Fig 3 could be given as Table.

Fig 4: Since these counts are too small (insufficient power) to compare with larger county cohort, not convinced the comparison is necessary.

Fig 5: Could be easily incorporated into table 2.

EDITOR'S NOTE:

Thank you for sending this manuscript to the Green Journal. Please note, that should you decide to revise this for potential publication, it needs to be rewritten as a case series, with descriptive statistics only. While 30 cases of CSP is a relatively large number, it is still too small to make meaningful comparisons.

Your paper requires significant editing. I recommend that you consult the Green Journal's Guide to Writing, available on the landing page of this website. You will receive a PDF with my own suggestions for some editing for your manuscript to improve clarity, succinctness, and organization. I did not provide comments for the entire article but enough to give you the gist of what sort of work needs to be done. These sorts of massive edits can be quite painful, I recognize but I encourage you to undertake them in order for the paper to be considered for publication in the Green Journal. You have a significant case series, with some follow up, that will help inform our readers about this growing problem.

EDITOR'S NOTES:

1. Thank you for your submission to Obstetrics & Gynecology. In addition to the comments from the reviewers above, you are being sent a notated PDF that contains the Editor's specific comments. Please review and consider the comments in this file prior to submitting your revised manuscript. These comments should be included in your point-by-point response cover letter.

The notated PDF is uploaded to this submission's record in Editorial Manager. If you cannot locate the file, contact Katie McDermott and she will send it by email – kmcdermott@greenjournal.org.

2. 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, as well as subsequent author queries. 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:
1. OPT-IN: Yes, please publish my response letter and subsequent email correspondence related to author queries.
2. OPT-OUT: No, please do not publish my response letter and subsequent email correspondence related to author queries.

3. Each author on this manuscript must submit a completed copy of our revised author agreement form (updated in the August 2014 issue). Please submit forms for the following authors:

Uma Deshmukh, M.D.
Linda Fan, M.D.
Katherine Kohari, M.D.
Sonya Abdel-Razeq Abdel-Razeq, M.D.
Anna K. Sfakianaki, M.D.

Please note:

a) Any material included in your submission that is not original or that you are not able to transfer copyright for must be listed under I.B on the first page of the author agreement form.

b) All authors must disclose any financial involvement that could represent potential conflicts of interest in an attachment to the author agreement form.

c) All authors must indicate their contributions to the submission by checking the applicable boxes on the author agreement form.

d) The role of authorship in Obstetrics & Gynecology is reserved for those individuals who meet the criteria recommended by the International Committee of Medical Journal Editors (ICMJE; http://www.icmje.org):

* Substantial contributions to the conception or design of the work;
OR
the acquisition, analysis, or interpretation of data for the work;
AND
* Drafting the work or revising it critically for important intellectual content;
AND
* Final approval of the version to be published;
AND
* Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

The author agreement form is available online at http://edmgr.ovid.com/ong/accounts/agreementform.pdf. Signed forms should be scanned and uploaded into Editorial Manager with your other manuscript files. Any forms collected after your revision is submitted may be e-mailed to obgyn@greenjournal.org.

4. 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.

5. All studies should follow the principles set forth in the Helsinki Declaration of 1975, as revised in 2013, and manuscripts should be approved by the necessary authority before submission. Applicable original research studies should be reviewed by an institutional review board (IRB) or ethics committee. This review should be documented in your cover letter as well in the Materials and Methods section, with an explanation if the study was considered exempt. If your research is based on a publicly available data set approved by your IRB for exemption, please provide documentation of this in your cover letter by submitting the URL of the IRB web site outlining the exempt data sets or a letter from a representative of the IRB. In addition, insert a sentence in the Materials and Methods section stating that the study was approved or exempt from approval. In all cases, the complete name of the IRB should be provided in the manuscript.

6. 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 will be transitioning as much as possible to use of the reVITALize definitions, and we encourage authors to familiarize themselves with them. The obstetric data definitions are available at http://links.lww.com/AOG/A515, and the gynecology data definitions are available at http://links.lww.com/AOG/A935.

7. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 22 typed, double-spaced pages (5,500 words); Case Reports should not exceed 8 typed, double-spaced pages (2,000 words); Review articles should not exceed 25 typed, double-spaced pages (6,250 words); Current Commentary articles should not exceed 12 typed, double-spaced pages (3,000 words); Clinical Practice and Quality articles should not exceed 22 typed, double-spaced pages (5,500 words); Procedures and Instruments articles should not exceed 8 typed, double-spaced pages (2,000 words); Personal Perspectives essays should not exceed 12 typed, double-spaced pages (3,000 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and appendixes).

Please limit your Introduction to 250 words and your Discussion to 750 words.

8. Specific rules govern the use of acknowledgments in the journal. Please edit your acknowledgments or provide more information in accordance with 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 signature on the journal's author agreement 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).

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: Original Research articles, 300 words; Reviews, 300 words; Case Reports, 125 words; Current Commentary articles, 250 words; Clinical Practice and Quality, 300 words; Procedures and Instruments, 200 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. Our readers are clinicians and a detailed review of the literature is not necessary. Please shorten the Discussion and focus on how your results affect or change actual patient care. Do not repeat the Results in the Discussion section.

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. (Line 200) The American College of Obstetricians and Gynecologists' (College) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite College 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. 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 a College document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All College documents (eg, Committee Opinions and Practice Bulletins) may be found via the Resources and Publications page at http://www.acog.org/Resources-And-Publications.

15. 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.

Figure 1: Please upload a second version without arrows. These will be added back per journal style.
Figure 2: Please provide an information letter of permission for print and electronic use from the illustrator (can be an email).
Figure 3: Okay
Figure 4: Please provide a non-3D version of this figure. Per journal style, we try to avoid using 3D when possible.
Figure 5: okay

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.

Figures should be no smaller than the journal column size of 3 1/4 inches. Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce. Refer to the journal printer's web site (http://cjs.cadmus.com/da/index.asp) for more direction on digital art preparation.

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If you choose to revise your manuscript, please submit your revision via Editorial Manager for Obstetrics & Gynecology at http://ong.editorialmanager.com. It is essential that your cover letter list point-by-point the changes made in response to each criticism. Also, please save and submit your manuscript in a word processing format such as Microsoft Word.

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

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 Aug 07, 2018, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

2017 IMPACT FACTOR: 4.982
2017 IMPACT FACTOR RANKING: 5th out of 82 ob/gyn journals

If you would like your personal information to be removed from the database, please contact the publication office.

Cover Letter for Manuscript Submission

To:

Nancy Chescheir, M.D.

Editor-in-Chief

Obstetrics and Gynecology

Dear Dr. Chescheir,

Enclosed is the revised manuscript entitled "Cesarean Scar Pregnancy, Incidence and Recurrence: five-year experience at Yale-New Haven Hospital" to be considered for publication in Obstetrics and Gynecology.

The authors appreciate the constructive feedback and suggestions for improvement on our initial submission. The manuscript was revised substantially in response to those comments, and we appreciate the opportunity to have our manuscript be reconsidered.

This study was approved by Yale Institutional Review Board. With this letter I affirm 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. There is no funding or conflict of interests to disclose by any of the authors. This manuscript has not been previously submitted for publication.

Part of this data was previously presented by Uma Deschmikh at the ACOG Annual Clinical and Scientific Meeting, in 2017 in the form of a poster presentation.

We appreciate your time and consideration and look forward to hearing back from you.

Sincerely,

Olga Grechukhina, M.D.

Yale University, School of Medicine

On behalf of the authors of the manuscript

Uma Deshmukh, M.D.

Linda Fan, M.D.

Katherine Kohari, M.D.

Sonya Abdel-Razeq, M.D.

Ozan Mert Bahtiyar M.D.

Anna K. Sfakianaki M.D.

Dear Editors and Reviewers,

Thank you so much for reviewing our manuscript for possible publication in Obstetrics & Gynecology. The constructive comments and suggestions were extremely valuable for making this manuscript better and were very appreciated. We addressed all of the points to the best of our abilities and we appreciate the opportunity to be considered for publication again.

Below, please find a point-by-point response to the reviewers' and editors' comments. Also, the revision of the manuscript was performed in the "track changes" mode per editor's recommendation.

Sincerely,

The authors

REVIEWER COMMENTS:

Reviewer #1:

1) Precis: The Precis is clearly written and accurately summarizes the main points of this paper.

2) Abstract: The Abstract is succinct and provides a reflective overview of your research.

3) Introduction: In Line 103 - please change "reccur" to either "recur" vs. "reoccur".

Change for "recur" was made.

4) Materials & Methods: There is mention of IRB approval being obtained in Lines 121-122. Appropriate statistical methods were applied.

5) Results: In general, the results section is well presented & comprehensive. I would suggest in Line 176 adding the word "patients" after "non-Hispanic white" and after "non-Hispanic black." .

The word "patients" was added as suggested.

6) Discussion: The Discussion is well stated and comprehensive.

7) Conclusion: The sentence starting in Line 418 and ending in Line 420 is awkwardly written - recommend rewording.

This sentence was re-written per reviewer suggestion.

8) References: List of References appears to be thorough and comprehensive.

9) Tables/Figures: The Tables & Figures appropriately support and further demonstrate the details of your findings.

Reviewer #2:

ONG-18-1220. Cesarean Scar Pregnancy, Incidence and Recurrence: five-year experience at Yale New Haven Hospital.

The authors report their experience with 30 cesarean scar pregnancies (CSPs) in 26 women (one with three CSPs). Their service used multiples diagnostic processes and treatment approaches. While the incidence of this complication increases there are no guidelines for their diagnosis and management.

> Thank you for this comment. Over the years a team of providers in Maternal-Fetal Medicine Unit as well as General Gynecology division emerged as experts in diagnosing, counseling, managing and following up patients with the diagnosis of CSP. This team developed institutional guidelines for initial diagnosis, counseling and management of CSPas well as provided a list of Maternal-Fetal Medicine subspecialists and gynecologist with a special expertise in CSP to who the patients with CSP should be referred. These guidelines are currently in use ay Yale-new haven Hospital. A paragraph to this was added to the manuscript (last paragraph in discussion).

Forty-six percent of the cases occurred on Hispanic women, a higher proportion than their county population. It will be more appropriate to compare the race/ethnicity of the cases with similar characteristic on their obstetrical -gynecological services. Hispanics may choose their institution for many other reasons than for this complication.

> Thank you for this suggestion. Indeed, it would be interesting to compare our CSP cohort with our MFM Unit population. The authors encountered several problems upon attempt to collect this data. The major issue was that a very large number of patients in the MFM ultrasound unit either deferred answering the question on race/ethnicity or answered "other" to this question. Having said that, our MFM Unit is a referral center from all of the Southern Connecticut and the served area represents a large diverse population from race/ethnic and socioeconomic stand points, thus in our Unit we expect to see a more or less equal representation or the area population. We are not limited by any insurance type and take bother private and State insurance as well as uninsured patients.
>
> To further address this question, since it is a case series we tried to avoid any statistical comparisons (this is also in line with Obstetrics & Gynecology Editor's recommendation of avoiding comparative statistics and describing our cohort instead) and provided the information from Census Bureau more for a background description of the served population, rather than to have a control group. Having said this, we believe further studies are needed to provide better description of the racial distribution of CSP and possible racial predisposition to CSP.

Considered the best tool for the diagnosis of ectopic pregnancies, transvaginal ultrasound is not adequately mentioned in the report.

> This was added to the Methods section. Indeed, all patients had both transabdominal and transvaginal ultrasound for diagnosis confirmation.

I wonder about the best approach for diagnosis and management of this complication. How will the authors proceed with their next case?

> Unfortunately, the limitation of this study is that we are unable to identify the "ideal" method of CSP treatment (in part due to relatively small number of cases, in part due to each patient being unique in its presentation and setting). Thus, every subsequent case will continue to require an extensive discussion between the provider and the patient that will allow to tailor the treatment to specific patient's situation and desires. Having said this, we did come up with Institutional guidelines, outlining general diagnosis, counseling and treatment options and providing a list of practitioners with expertise in providing care to patients w CSP. This was discussed in the discussion (line 321)/conclusion section and another sentence was added to the Limitations section.

The text description appears to repeat the content of the tables.

> We removed the text that was concisely outlined in the tables.

Reviewer #3:

Abstract - Objective is to describe management, outcomes, and subsequent pregnancy outcomes over a 5 year experience of Cesarean Scar Pregnancy (CSP).

Methods - Retrospective and prospective series - all CSP cases from 5/13-3/18 at Yale, data was included - demographics, PMHx, PSHx, treatment, response, complications, subsequent pregnancies

Results - 30 cases of CSP in 26 patients - 4 recurrences in 2 patients; 46% of CSP in Hispanic women, mean previous c/s number was 2 and average gestational age of 46 days
10 subsequent spontaneous conceptions in 8 patients - 4 recurrent CSPs, 5 IUPs and 1 Sab

Conclusions - There are various treatment modalities, there is a high potential for recurrence, and early and accurate diagnosis with multidisciplinary care is the key to successful treatment.

Introduction - CSP represents 6% of ectopics. The presentation is variable and the gestational age at presentation may vary. Diagnosis is made by TVUS and there is no consensus on optimal treatment. Treatment goals are ending the pregnancy and removing the sac. There is little evidence to guide management decisions and counsel patients.

Materials and Methods - Retrospective and prospective case series of CSP between 5/13-3/18. EMR was reviewed for relevant patient data, treatment, response, and subsequent fertility.
Treatments were systemic MTX, local MTX, local KCL, UAE, hysteroscopy, and compression ballon

Results - 30 cases in 26 patients - 46% were hispanic, 42% were white. There were no differences in regard to demographics, and incidence was associated with obesity.

Presentation and diagnosis - the majority were asymptomatic
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Outcome and follow-up - Of 25 patients, there were 10 conceptions in 8 patients and 4 were recurrent, 1 miscarriage, and 5 viable IUPs

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there needs to be a high level of suspicion
Treatment modalities - A recent systematic review discussed 5 treatment modalities and another review failed to identify the leading method of treatment. These results show that systematic MTX can lead to complications but UAE with hysteroscopy and balloon compression are promising.
Follow up needs to consist of serial HCG and u/s
there is a high risk of recurrence and risk of accrete.

Conclusion - diagnosis with ultrasound and referral with close follow-up and multi-disciplinary care are key.

This is a good review of response to various treatment options. Helpful for clinicians facing these cases to see the options and the anticipated response. Though the numbers are small, the information and follow-up is still useful to see.

STATISTICAL EDITOR COMMENTS:

The Statistical Editor makes the following points that need to be addressed:
lines 172-175: Was the incidence of CSP statistically different in 2016 vs others, or was this just within random variation?

> This is an interesting question. Although there was an uptrend in the number of CSP diagnoses at YNHH over the years, we are unable to determine if this uptrend reflects a truly increasing incidence of the condition or higher awareness of the providers of the diagnosis and improving diagnostic skills of the sonographers. In this case series (in line with editor's recommendation) the authors would like to avoid making any statements on statistical significance. We are planning further studies that would address the questions of "true" incidence, racial predisposition, incidence of obesity, diabetes and smoking in women with CSP in comparison to a control group which will need to be created.

lines 177-179: Were the cohorts compared statistically? Were the samples sufficient to have enough power to discern a difference or was the non-difference simply due to low power, based on the small sample sizes (I count n = 12 vs n = 11).

> This case series does not have enough power to discern any difference within the group. Thus we are using only descriptive statistics and avoiding statements like "(no) significant difference" and changed the wording regarding obesity, race and smoking in the discussion to reflect that (lines 272-279).

lines 201-202: The hCG levels do not appear to be normally distributed. If so, should cite as median(range or IQR).

Corrected per recommendation.

lines 304-305, line 50: Need to clarify if there were 3 or two patients with recurrences.

There were two recurrences during the study period. The discrepancy was corrected. One patient with CSP included in the study was a recurrence, however the authors did not have any information on the initial episode (which occurred prior to the study period) and this case was not included in the analysis of the "subsequent conceptions".

lines 309-315:The confidence interval for 12/26 = 46%(24%-81%), so this small sample is not statistically different from the representation in the city of New Haven. Again, there is insufficient power to make these comparisons.

A note is added to line 131 that there is not enough power to make conclusion on racial predisposition, however there is a trend and further research is needed.

Table 2: Should state that format is mean±SD. median(range) and n(%) as footnote to table.

Corrected

Fig 3 could be given as Table.

Reformatted into a table (Table 3)

Fig 4: Since these counts are too small (insufficient power) to compare with larger county cohort, not convinced the comparison is necessary.

The figure #4 was removed per recommendations

Fig 5: Could be easily incorporated into table 2.

Fig 5 was removed from the manuscript.

EDITOR'S NOTE:

Thank you for sending this manuscript to the Green Journal. Please note, that should you decide to revise this for potential publication, it needs to be rewritten as a case series, with descriptive statistics only. While 30 cases of CSP is a relatively large number, it is still too small to make meaningful comparisons.

Your paper requires significant editing. I recommend that you consult the Green Journal's Guide to Writing, available on the landing page of this

website. You will receive a PDF with my own suggestions for some editing for your manuscript to improve clarity, succinctness, and organization. I did not provide comments for the entire article but enough to give you the gist of what sort of work needs to be done. These sorts of massive edits can be quite painful, I recognize but I encourage you to undertake them in order for the paper to be considered for publication in the Green Journal. You have a significant case series, with some follow up, that will help inform our readers about this growing problem.

EDITOR'S NOTES:

1. Thank you for your submission to Obstetrics & Gynecology. In addition to the comments from the reviewers above, you are being sent a notated PDF that contains the Editor's specific comments. Please review and consider the comments in this file prior to submitting your revised manuscript. These comments should be included in your point-by-point response cover letter.

The notated PDF is uploaded to this submission's record in Editorial Manager. If you cannot locate the file, contact Katie McDermott and she will send it by email – kmcdermott@greenjournal.org.

Comment 1. the address was changed to the departmental address.

Comment 2. Line 45 – "case series" was added to substitute "retrospective and prospective"; Line 114-119. Material and methods section was edited to reflect how the patients were identified and enrolled.

Comment 3. Material and Methods – the use of electronic medical record review was reflected as recommended.

Comment 4. Virgules were substituted with commas and "and". Virgules removed from the text completely except for numeric expressions.

Comment 5. Sentences that started with a number were rephrased to start with a word.

Comment 6. The conclusion in the abstract was reworded as recommended

Comment 7. Introduction was rewritten as recommended. It was condensed and the extra information on mechanism was removed completely

Comment 8. The objective (last sentence of the introduction) was rewritten to reflect specific goals of the paper.

Comment 9. the study period was edited to represent "from 5/2013 to 3/2018" per recommendations.

Comment 10. description of therapeutic interventions was completely removed from the methods section and added to the results section.

Comment 11. Statistics section was edited to reflect that only descriptive statistics was used in this case series.

2. 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, as well as subsequent author queries. 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:

OPT-IN: Yes, please publish my response letter and subsequent email correspondence related to author queries.

3. Each author on this manuscript must submit a completed copy of our revised author agreement form (updated in the August 2014 issue). Please submit forms for the following authors:

Uma Deshmukh, M.D.
Linda Fan, M.D.
Katherine Kohari, M.D.
Sonya Abdel-Razeq Abdel-Razeq, M.D.
Anna K. Sfakianaki, M.D.

The author agreement form was provided by all authors.

Please note:

a) Any material included in your submission that is not original or that you are not able to transfer copyright for must be listed under I.B on the first page of the author agreement form.

There is no such material in the manuscript which the authors are unable to transfer.

b) All authors must disclose any financial involvement that could represent potential conflicts of interest in an attachment to the author agreement form.

c) All authors must indicate their contributions to the submission by checking the applicable boxes on the author agreement form.

d) The role of authorship in Obstetrics & Gynecology is reserved for those individuals who meet the criteria recommended by the International Committee of Medical Journal Editors (ICMJE; https://na01.safelinks.protection.outlook.com/?url=http%3A%2F%2Fwww.icmje.org&data=02%7C01%7Colga.grechukhina%40yale.edu%7Ca7d24a8170614b2960b308d5ec129a9d%7Cdd8cbebb21394df8b4114e3e87abeb5c%7C0%7C0%7C636674487011102847&sdata=seojyX0YAvOiH%2BDSKQQOs%2B%2BBiiZOvA9JX0%2BEBguTDfs%3D&reserved=0):

* Substantial contributions to the conception or design of the work;
OR
the acquisition, analysis, or interpretation of data for the work;
AND
* Drafting the work or revising it critically for important intellectual content;
AND
* Final approval of the version to be published;
AND
* Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

The author agreement form is available online at https://na01.safelinks.protection.outlook.com/?url=http%3A%2F%2Fedmgr.ovid.com%2Fong%2Faccounts%2Fagreementform.pdf&data=02%7C01%7Colga.grechukhina%40yale.edu%7Ca7d24a8170614b2960b308d5ec129a9d%7Cdd8cbebb21394df8b4114e3e87abeb5c%7C0%7C0%7C636674487011102847&sdata=tlcOHKa7sUg6%2BPK8mlPbZeZDMv0lBy2yVB1gCTuSbEw%3D&reserved=0. Signed forms should be scanned and uploaded into Editorial Manager with your other manuscript files. Any forms collected after your revision is submitted may be e-mailed to obgyn@greenjournal.org.

4. 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.

This statement was included in the cover letter.

5. All studies should follow the principles set forth in the Helsinki Declaration of 1975, as revised in 2013, and manuscripts should be approved by the necessary authority before submission. Applicable original research studies should be reviewed by an institutional review board (IRB) or ethics committee. This review should be documented in your cover letter as well in the Materials and Methods section, with an explanation if the study was considered exempt. If your research is based on a publicly available data set approved by your IRB for exemption, please provide documentation of this in your cover letter by submitting the URL of the IRB web site outlining the exempt data sets or a letter from a representative of the IRB. In addition, insert a sentence in the Materials and Methods section stating that the study was approved or exempt from approval. In all cases, the complete name of the IRB should be provided in the manuscript.

This statement was included in the cover letter.

6. 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 will be transitioning as much as possible to use of the reVITALize definitions, and we encourage authors to familiarize themselves with them. The obstetric data definitions are available at https://na01.safelinks.protection.outlook.com/?url=http%3A%2F%2Flinks.lww.com%2FAOG%2FA515&data=02%7C01%7Colga.grechukhina%40yale.edu%7Ca7d24a8170614b2960b308d5ec129a9d%7Cdd8cbebb21394df8b4114e3e87abeb5c%7C0%7C0%7C636674487011102847&sdata=4TAF3yPq0YWgiOQo%2B9vPpw3LqdMunmFSXVrKvNr%2FFpw%3D&reserved=0, and the gynecology data definitions are available at https://na01.safelinks.protection.outlook.com/?url=http%3A%2F%2Flinks.lww.com%2FAOG%2FA935&data=02%7C01%7Colga.grechukhina%40yale.edu%7Ca7d24a8170614b2960b308d5ec129a9d%7Cdd8cbebb21394df8b4114e3e87abeb5c%7C0%7C0%7C636674487011102847&sdata=AWM2DmJrEjRAC2vrvmIG%2FHIDAl82xckhaKCaAMJrX5E%3D&reserved=0.

7. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 22 typed, double-spaced pages (5,500 words); Case Reports should not exceed 8 typed, double-spaced pages (2,000 words); Review articles should not exceed 25 typed, double-spaced pages (6,250 words); Current Commentary articles should not exceed 12 typed, double-spaced pages (3,000 words); Clinical Practice and Quality articles should not exceed 22 typed, double-spaced pages (5,500 words); Procedures and Instruments articles should not exceed 8 typed, double-spaced pages (2,000 words); Personal Perspectives essays should not exceed 12 typed, double-spaced pages (3,000 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and appendixes).

Please limit your Introduction to 250 words and your Discussion to 750 words.

Introduction and discussion were edited and compressed substantially. The current word counts are 250 and 750 for introduction and discussion respectively.

8. Specific rules govern the use of acknowledgments in the journal. Please edit your acknowledgments or provide more information in accordance with 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 signature on the journal's author agreement 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).

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: Original Research articles, 300 words; Reviews, 300 words; Case Reports, 125 words; Current Commentary articles, 250 words; Clinical Practice and Quality, 300 words; Procedures and Instruments, 200 words. Please provide a word count.

The abstract was edited and compressed substantially. the current word count is 297.

10. Only standard abbreviations and acronyms are allowed. A selected list is available online at https://na01.safelinks.protection.outlook.com/?url=http%3A%2F%2Fedmgr.ovid.com%2Fong%2Faccounts%2Fabbreviations.pdf&data=02%7C01%7Colga.grechukhina%40yale.edu%7Ca7d24a8170614b2960b308d5ec129a9d%7Cdd8cbebb21394df8b4114e3e87abeb5c%7C0%7C0%7C636674487011102847&sdata=RMH1%2FiVBnLmLB2CEI0u5ZnKJF2u1TkaL9Pz3ZYqF6pk%3D&reserved=0. 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.

All virgule symbols were removed from the text.

12. Our readers are clinicians and a detailed review of the literature is not necessary. Please shorten the Discussion and focus on how your results affect or change actual patient care. Do not repeat the Results in the Discussion section.

Discussion section was rewritten and is now shorter and more concise.

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://na01.safelinks.protection.outlook.com/?url=http%3A%2F%2Fedmgr.ovid.com%2Fong%2Faccounts%2Ftable_checklist.pdf&data=02%7C01%7Colga.grechukhina%40yale.edu%7Ca7d24a8170614b2960b308d5ec129a9d%7Cdd8cbebb21394df8b4114e3e87abeb5c%7C0%7C0%7C636674487011102847&sdata=jvvMXRNQl%2BjOKgC4ypolGFXzMja66SmkRAax%2BUXDjkE%3D&reserved=0.

All tables were reformatted to conform to the journal style.

14. (Line 200) The American College of Obstetricians and Gynecologists' (College) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite College 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. 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 a College document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All College documents (eg, Committee Opinions and Practice Bulletins) may be found via the Resources and Publications page at https://na01.safelinks.protection.outlook.com/?url=http%3A%2F%2Fwww.acog.org%2FResources-And-Publications&data=02%7C01%7Colga.grechukhina%40yale.edu%7Ca7d24a8170614b2960b308d5ec129a9d%7Cdd8cbebb21394df8b4114e3e87abeb5c%7C0%7C0%7C636674487011102847&sdata=rYdn%2BOgIifEB7MuQLPOfxJ%2BlyaRm0C5p5O4gv%2F9VXfc%3D&reserved=0.

This citation was removed from the manuscript.

15. 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.

Figure 1: Please upload a second version without arrows. These will be added back per journal style. Submitted in a requested format
Figure 2: Please provide an information letter of permission for print and electronic use from the illustrator (can be an email). Permission was included in the email.
Figure 3: Okay
Figure 4: Please provide a non-3D version of this figure. Per journal style, we try to avoid using 3D when possible. This Figure was completely removed from the manuscript, since this data was described in the text with a sentence.

Figure 5: okay

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.

All figures comply to the requirements.

Figures should be no smaller than the journal column size of 3 1/4 inches. Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce. Refer to the journal printer's web site (https://na01.safelinks.protection.outlook.com/?url=http%3A%2F%2Fcjs.cadmus.com%2Fda%2Findex.asp&data=02%7C01%7Colga.grechukhina%40yale.edu%7Ca7d24a8170614b2960b308d5ec129a9d%7Cdd8cbebb21394df8b4114e3e87abeb5c%7C0%7C0%7C636674487011102847&sdata=vC6PiCME%2BtCV9kwKs9RwJenGNF8X6qjShweDvXWwyW4%3D&reserved=0) for more direction on digital art preparation.

***

If you choose to revise your manuscript, please submit your revision via Editorial Manager for Obstetrics & Gynecology at https://na01.safelinks.protection.outlook.com/?url=http%3A%2F%2Fong.editorialmanager.com&data=02%7C01%7Colga.grechukhina%40yale.edu%7Ca7d24a8170614b2960b308d5ec129a9d%7Cdd8cbebb21394df8b4114e3e87abeb5c%7C0%7C0%7C636674487011102847&sdata=Ww50oP2jbUZoroM4CQMhowp9PFNgq4W%2Fx%2FgSBoH%2BCOw%3D&reserved=0. It is essential that your cover letter list point-by-point the changes made in response to each criticism. Also, please save and submit your manuscript in a word processing format such as Microsoft Word.

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

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 Aug 07, 2018, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

2017 IMPACT FACTOR: 4.982
2017 IMPACT FACTOR RANKING: 5th out of 82 ob/gyn journals

If you would like your personal information to be removed from the database, please contact the publication office.

From: Stephanie Casway
To: Denise Shields
Subject: FW: O&G Author Queries: 18-1220
Date: Friday, August 17, 2018 8:13:02 AM
Attachments: 8.16.18 Revisions ncc - OG responses.docx

Hi Denise,

These revisions were in response to a request from Rebecca. If you need more info, just let me know. Thanks!

From: Grechukhina, Olga [redacted]
Sent: Thursday, August 16, 2018 9:11 PM
To: Stephanie Casway <SCasway@greenjournal.org>
Subject: Re: O&G Author Queries: 18-1220

Hi Ms. Casway,

Thank you for the email! Please see the responses below. The manuscript attached reflects the edits in the track changes mode.

I am sure you saw, but just to double check - the draft that you send me in your last email contains the old tables. The updated tables were attached in my previous email.

Thank you!

Have a lovely weekend!

Olga

1. On line 209 you indicated that there were 3 patients in this circumstance described on lines 249-252 where you say this was "The patient".....please clarify. (line 204). *This was rephrased: "Notably, t~~T~~his ~~was the~~ patient [NCC1] [GO2] ~~who~~was initially erroneously diagnosed..."*

---

2. This seems like a high volume for a first trimester reduction (line 209). *The volume of KCl used was reviewed again and was reported correctly (consistent with documentation in the charts). However, the concentration was noted to be different from the reported and changed to 2 mEq/mL.*
3. Safety is really difficult to define and for interventions with unusual complications, small numbers of cases cannot be used to describe "safety". Could you please rephrase something like "The use of an intrauterine double balloon catheter has emerged as an effective

conservative method, with no identified major complications associated with it use". (line 349) *This was rephrased per recommendation.*

4. Additionally, there was a comment in Table 2 about the number of smokers. You may have addressed this earlier in the manuscript, but would you mind replying to the comment here about any changes you made. *We agree that since the numbers are small and we are unable to perform any meaningful statistical comparison, we decided to remove that statement completely from the discussion.*

From: Stephanie Casway <SCasway@greenjournal.org>
Sent: Thursday, August 16, 2018 10:54:14 AM
To: Grechukhina, Olga
Subject: FW: O&G Author Queries: 18-1220

Hi again Olga,

Dr. Chescheir has reviewed your edits and has 3 additional queries. Hopefully these will be the last queries. Thanks so much for your help!

1. On line 209 you indicated that there were 3 patients in this circumstance described on lines 249-252 where you say this was "The patient".....please clarify. (line 204)
2. This seems like a high volume for a first trimester reduction (line 209)
3. Safety is really difficult to define and for interventions with unusual complications, small numbers of cases cannot be used to describe "safety". Could you please rephrase something like "The use of an intrauterine double balloon catheter has emerged as an effective conservative method, with no identified major complications associated with it use". (line 349)
4. Additionally, there was a comment in Table 2 about the number of smokers. You may have addressed this earlier in the manuscript, but would you mind replying to the comment here about any changes you made.

From: Grechukhina, Olga [redacted]
Sent: Monday, August 13, 2018 8:20 PM
To: Stephanie Casway <SCasway@greenjournal.org>
Subject: Re: O&G Author Queries: 18-1220

Dear Ms. Casway,

Please find attached the revised Word document in track changes format as well as our

responses to the comments and tables. I am also attaching the new author Agreement form from Dr. Abdel-Razeq.

On behalf of all authors we wanted to thank the editors team for constructive feedback and interesting questions!

Please let me know if there are any further questions or suggestions! We will be looking forward to hearing back from you!

Thank you!

Sincerely,

Olga

From: Stephanie Casway <SCasway@greenjournal.org>
Sent: Friday, August 10, 2018 8:26:53 AM
To: Grechukhina, Olga
Subject: RE: O&G Author Queries: 18-1220

Hi Olga,

Monday would be great. If you need additional time, just let us know. Thanks!

From: Grechukhina, Olga [redacted]
Sent: Friday, August 10, 2018 8:24 AM
To: Stephanie Casway <SCasway@greenjournal.org>
Subject: Re: O&G Author Queries: 18-1220

Dear Ms. Casway,
Thank you for the update!
We are working on revisions. When is the manuscript due?
Thank you!
Olga

Sent from my iPhone

On Aug 10, 2018, at 8:16 AM, Stephanie Casway <SCasway@greenjournal.org> wrote:

Good Morning Olga,

Following our editor's conference call yesterday, we have two additional queries to add. Please see below and let me know if you have any questions. Thanks!

1. Please omit "Yale New-Haven Hospital" from the title.
2. Please change your precis to deemphasize the role of an experienced team. Key findings of your series should be emphasized. You may want to comment on multiple possible approaches possibly leading to the need for individualization of care; need for close follow-up after treatment due to significant risk of persistence; or relatively high recurrence risks--others you think to be important. The precis is the single-sentence "hook" in the table of contents for the reader to see, to help pull them in to read the article.

From: Stephanie Casway
Sent: Wednesday, August 8, 2018 1:19 PM
To: 'Grechukhina, Olga' [redacted]
Subject: O&G Author Queries: 18-1220

Re: "Cesarean Scar Pregnancy, Incidence, and Recurrence: Five-Year Experience at Yale-New Haven Hospital"

Hi again Olga,

Thank you for revising your manuscript. There are remaining issues that must be addressed before we can consider your manuscript further for publication. Each of these points are marked in the track changes in the attached manuscript. When revising, please leave the track changes on, and do not use the "Accept all Changes" function in Microsoft Word. Please respond to the comments in the track changes and address each of the queries below in a point-by-point response. For your reference, I have copied the author queries below:

1. AQ: Each author must meet four criteria to be an author. On the Author Agreement form, Dr. Abdel-Razeq did not indicate that she agrees to be held accountable for all aspects of the work. If this was an error, submit a new form with the appropriate boxes checked. If this was not an error, remove the author's name from the byline and add it to the

acknowledgment ("The authors thank...).

2. Do you mean she had a recurrence after the pregnancy you just described or that this pregnancy was a recurrence? (line 217)
3. Do you have a reference for this statement? How much has it increased? (line 296)
4. If these women had their cesarean births out of the country could it also be related to technical differences (Suture type? Number of layers? Use of bovie?) Antibiotic use? Healing differences perhaps related to nutrition?) instead of biological differences? (line 302)
5. Where do you report that data? Also, CSP is not "abnormal placentation"—its implantation in the wrong place. (line 304)
6. Change recommended: The diagnosis of an IUIP didn't cause (result in) medical termination. (line 308)
7. Given 3 systematic reviews, please clearly state what your case series adds. What is the knowledge gap that needs to be filled? (line 318)
8. This array of individual factors listed on line 380-381 would suggest that it would be quite difficult to do an RCT. (line 322)
9. How do your cases align with a 13% rate of severe complications? (line 328)
10. Did you have severe bleeding in the 28 women not treated with UAE? If not, why would one consider this prophylactically? (line 335)
11. You used it twice. Not able to comment on safety. (line 336)
12. What is the biological plausibility of detached trophoblast as a cause of a complication? It shouldn't be producing hCG and even if it could, wouldn't it be connected to maternal blood supply to result in measurable maternal hCG levels? I'm totally unconvinced by what you've written so far that detached trophoblast can cause any sort of problem. Also, it's unclear why a CSP with a negative quantitative hCG could be considered anything other than "resolved." A normal hCG is negative. Not sure what you mean by normalizing hCG? Important in case descriptions to mention why you intervened in women with falling hCGs. (line 341)
13. How do you define resolution? (line 342)
14. How was "special expertise" defined? Was it related to success in prior treatments? Number of prior patients without considering patient outcomes? (line 355)
15. What do you mean by "remote" here and in line 437? (line 366)
16. Is this a known process? Cesarean scar pregnancy developing into morbidly adherent placenta? Please provide a reference. (line 383)
17. Earlier you called for an RCT, although I'm skeptical that given the individualized care and planning you note are necessary that such a study could be done. (line 387)
18. Your comment on the high risk of smoking in women with CSP and the rate

was around 33%. In 2011 according to the CDC, about 23% of women in Connecticut smoked in the 3 months before pregnancy. Given your small N, not sure you could conclude that the numbers are really different. (table 2)

19. Please provide data for how many were without symptoms. (table 2)
20. I don't really see much of a difference in the CS rates here. (32.6-33.5 in the two extremes of included years> Also, your provision of the CS rate suggests that most of the women were delivered at Yale-New Haven Hospital in their prior pregnancies. I would guess, that since almost ½ were Hispanic women who tend to be more transient than some populations, and that many people living in the area are likely transient related to education, that many of your patients did NOT have their prior deliveries there. As such, not convinced that the Yale New Haven CS rate is terribly relevant. (table 3)

In order to keep your manuscript moving through our process, please respond within 48 hours.

Regards,

Stephanie Casway, MA
Production Editor
Obstetrics & Gynecology
American College of Obstetricians and Gynecologists
409 12th St, SW
Washington, DC 20024
Ph: (202) 314-2339
Fax: (202) 479-0830
scasway@greenjournal.org

<18-1220R1 ms (8-8-18v2).docx>

From: [redacted]
To: Stephanie Casway
Subject: Re: O&G Figure Revision: 18-1220
Date: Tuesday, August 7, 2018 4:55:52 PM

Dear Ms. Casway,

Thank you for your email. Th figures look great, I do not see any mistakes.

Regarding the figure, with this email, I am granting Obstetrics & Gynecology permission to use this illustration (Fig. 2B) in print and online formats.

Thank you so much!

Sincerely,
Olga

From: Stephanie Casway <SCasway@greenjournal.org>
Sent: Tuesday, August 7, 2018 3:13:10 PM
To: Grechukhina, Olga
Subject: O&G Figure Revision: 18-1220

Good Afternoon Dr. Grechukhina,

Your figures and legend have been edited, and PDFs of the figures and legend are attached for your review. Please review the figures CAREFULLY for any mistakes. In addition, please see our query below.

AQ1: In order to use Figure 2B we just need an email from you granting us permission to use the illustration in print and online formats. Would you mind including this in your reply?

PLEASE NOTE: Any changes to the figures must be made now. Changes at later stages are expensive and time-consuming and may result in the delay of your article's publication.

To avoid a delay, I would be grateful to receive a reply no later than Thursday, 8/7. Thank you for your help.

Best wishes,

Stephanie Casway, MA
Production Editor
Obstetrics & Gynecology
American College of Obstetricians and Gynecologists
409 12th St, SW
Washington, DC 20024

Ph: (202) 314-2339
Fax: (202) 479-0830
scasway@greenjournal.org