OBSTETRICS & GYNECOLOGY

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

Date: Oct 04, 2018
To: "Najoua . EL HELALI" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-18-1667

RE: Manuscript Number ONG-18-1667

Efficacy and cost of 6 years of point-of-care intrapartum Group B Streptococcus molecular screening

Dear Dr. EL HELALI:

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 25, 2018, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

REVIEWER #1:

El Helali and colleagues examined the efficacy of point of care testing for GBS. Comments for the authors:

Abstract:

1. May be better to phrase the study design as pre- and post-intervention as opposed to before and after.

2. Is EOGBSD a standard abbreviation? This should be defined in the Methods, is this maternal and neonatal?

3. Some description of compliance with antenatal GBS testing should be reported in the Results.

4. P-values for reduction in antibiotic days and hospital days should be reported.

5. New results (cost to avoid one case of EOGBSD) should not be in the Conclusion, this belongs in the Results.

Introduction:

6. Well written overall Introduction.

7. Further description of poor PPV of antenatal culture screening should be included.

Methods:

8. IRB approval and consent should be included.

9. Some description of the population characteristics should be included.

10. Much greater detail is needed on the intrapartum protocol. Performance characteristics of the test, exact protocol, turn around time, compliance.

11. Similarly, greater data on the cost analysis is needed. Did everyone have insurance so it was reimbursement? Did you adjust for inflation, etc?

Results

12. Need to report how many women did not undergo antnatal culture during the pre-test period.

13. Similarly, how often was point of care testing not performed, not back in time, uninterpretable results? This is important for a new quality initiative.

14. Methodology to calculate extra cost to prevent a case of GBS needs to be described in the Methods.

15. Last paragraph of the Results is unclear. Would be clearer to state the absolute number of cases of GBS that would need to be prevented to make point of care testing cost effective.

Discussion

16. One sentence paragraphs should be avoided (lines 192-194).

17. Greater discussion of limitations should be included.

REVIEWER #2:

The authors are to be congratulated for this study which expands on prior work demonstrating the value of PCR for diagnosis of GBS carriage.

Although not an RCT, the authors have convincingly showed a significantly lowering in the rate of early onset GBS sepsis in a large population at a single institution during the time period after change to universal GBS screening on L&D. Specific comments are as follows:

1. Will the authors briefly describe the hospital staff in terms of size and how the new program was implemented? Translational research is difficult to do in many settings. The reader will be interested in the specific steps the authors used to implement the new screening program when the staff were accustomed to the antenatal cultures at 35-37 weeks.

2. Rapid labor is always a problem on L&D even if an antenatal culture was performed. Would the authors please describe the timeline required for acquisition of the result and proximetry of the laboratory to L&D?

3. Are urine cultures done routinely? If positive, how were these treated at the time of diagnosis and during the PCR study period.

4. Why was only 4 years prior to the study chosen and 6 years after? Was a sample size calculation done?

5. Would the authors offer suggestions on how to improve compliance with the PCR guideline due to the 8-9% of positive for whom IAP could not be given?

REVIEWER #3:

This manuscript examines intrapartum PCR was compared with antenatal culture screening in an uncontrolled, single institution, before after study for the outcome of EOGBSD. The study periods included fours year before and six years after the intervention, starting in 2006 and concluding in 2015. Overall, the paper is clearly written with clinically useful data regarding GBS screening. The following comments should be addressed in the paper:

1- In the Précis EOGBS should be spelled out

2- The authors should make it clear that during the period 2010 - 2015 that no antepartum screening was carried out and that all the screening was performed intrapartum exclusively

3- As an OB reviewer, it would be helpful to explain in the probable EOGBSD the underlying process for why the blood and CSF cultures are negative, i.e. false negatives. This could be added to the discussion section to the end of the paragraph at the top of page 11.

4- Page 8, lines 149-150, Please provide a statistical test for whether the following percentages are significantly different: "91.80% women who were screened positive received IAP compared to 89% during the antenatal culture period."

5- It would be informative to provide the timing of antibiotic initiation prior to delivery in both groups. One concern with intrapartum testing is that the time to screen and receive the results in a real time setting may lead to delayed initiation of antibiotic in GBS positive women.

6- The results section is well written overall. It would be helpful to add statistical testing for the differences in Probable + proven EOGBSD in both time periods, i.e. 0.86% vs. 0.38% to the results section.

7- The authors should add that a limitation is the study design. With use of a historical study population in which women were screened antepartum, there is a possibility that women in the later period could have received both antepartum and intrapartum screening.

STATISTICAL EDITOR'S COMMENTS:

1. lines 130-132: Need to state how proportions were statistically tested.

2. lines 134-135: Since the study period was from 2006-2015, was the exchange rate from Euros to dollars assumed constant over that time period and were the costs of either bacterial culture or PCR testing also constant? If not, how were those adjusted in computing costs?

3. lines 137-139: How many refused during each time period?

4. Table 1: The difference in proportion of CD is not NS, p = .02 by Chi-square. The comparison of % (+) screening and % unknown GBS status are each significantly different by Chi-square (both p < .0001).

5. Table 2: Suggest including n with %, formatted as n(%) for subsets of cases.

6. Table 3: Were LOS normally distributed? If not, should cite as median (IQR or range) and test non-parametrically. If one assumes normality, then given the stated means, SD and samples, the difference in LOS is significant (p < .001). For comparing the proven GBS cases (n = 12 vs 4), should use Fisher's test, which has p = 0.026. The comparison of probable cases (n = 33 vs 14), the p < .0001 by Chi-square. LOS for GBS cases and average duration of Ab therapy: If non-normally distributed, should cite as median (IQR or range) and test non-parametrically. Many readers will not be familiar with the formatting of EOGBS rates (proven and probable); should cite as cases per 1,000 (3.8 vs 0.9). Should also include CIs for each rate. (The incident rate ratio = 4.0 (95% CI = 2.3-7.4))

7. lines 231-238: Again, this formatting for incidence may be confusing for many readers, would be better to cite throughout as rates per 1000.

8. Table 4: Should expand the analysis of cost per preventing one case to include more of the variability implied by these data. That is, the counts of EOGBS are relatively few (45 vs 18 total cases) and the CIs for difference varied plausibly from a reduction by a factor of 2.3 to 7.4 from an estimated risk rate ratio of 4. Therefore one should not give the estimate of cost per case, but use the CIs to construct plausible bounds on the future cost savings of applying this to other populations. Also, if indeed the rate of GBS were varying among pregnant women, then one could also construct a model of cost per case prevented assuming various population rates of GBS.

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, 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.

2. Based on the forms that have been submitted, Drs. Fakher Habibi, Yves Giovangrandi, and Autret have not met the criteria for authorship. On the third page of the form, under the section labeled "Authorship," items #2-4, in addition to either 1a or 1b, MUST be checked off in order to quality for authorship. Theey should be moved to the acknowledgments, or they could resubmit a revised author agreement form if they filled it out erroneously the first time. All updated and missing forms should be uploaded with the revision in Editorial Manager.

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. Responsible reporting of research studies, which includes a complete, transparent, accurate and timely account of what was done and what was found during a research study, is an integral part of good research and publication practice and not an optional extra. Obstetrics & Gynecology supports initiatives aimed at improving the reporting of health research, and we ask authors to follow specific guidelines for reporting randomized controlled trials (ie, CONSORT), observational studies (ie, STROBE), meta-analyses and systematic reviews of randomized controlled trials (ie, PRISMA), harms in systematic reviews (ie, PRISMA for harms), studies of diagnostic accuracy (ie, STARD), meta-analyses and systematic reviews of observational studies (ie, MOOSE), economic evaluations of health interventions (ie, CHEERS), and quality improvement in health care (ie, SQUIRE 2.0). Include the appropriate checklist for your manuscript type upon submission. Please write or insert the page numbers where each item appears in the margin of the checklist. Further information and links to the checklists are available at http://ong.editorialmanager.com. In your cover letter, be sure to indicate that you have followed the CONSORT, MOOSE, PRISMA, PRISMA for harms, STARD, STROBE, CHEERS, or SQUIRE 2.0 guidelines, as appropriate.

5. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology 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.

6. 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). 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.

7. 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).

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In addition, the abstract length should follow journal guidelines. The word limits for different article types are as follows: Original Research articles, 300 words. Please provide a word count.

9. 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.

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11. We discourage claims of first reports since they are often difficult to prove. How do you know this is the first report? If this is based on a systematic search of the literature, that search should be described in the text (search engine, search terms, date range of search, and languages encompassed by the search). If on the other hand, it is not based on a systematic search but only on your level of awareness, it is not a claim we permit.

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.

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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 Oct 25, 2018, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

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