OBSTETRICS & GYNECOLOGY

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

Date: Jan 24, 2022
To: "Joe Eid" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-22-97

RE: Manuscript Number ONG-22-97

Early administration of Remdesivir and clinical outcomes in hospitalized pregnant individuals with COVID-19.

Dear Dr. Eid:

Thank you for your submission to Obstetrics & Gynecology. The Reviewers and Editors have evaluated your work. Given the significant public health importance of your study and findings we are interested in advancing your manuscript as a fast-track publication if you can adequately address the comments raised by the Reviewers. As such, we would ask that you return your revisions within 7 days or sooner. Again, thank you for your submission to Obstetrics & Gynecology and please let me know if I can be of any further assistance.

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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).

Please be sure to address all comments in your point-by-point response.

Your paper will be maintained in active status for 7 days from the date of this letter. If we have not heard from you by Jan 31, 2022, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

Obstetrics and Gynecology
Manuscript # ONG-22-97

"Early administration of remdesivir and clinical outcomes in hospitalized pregnancy individuals with COVID-19"

GENERAL

The submitted manuscript is a retrospective cohort study describing clinical outcomes in two cohorts of pregnant patients admitted with COVID-19 infection and administered remdesivir therapy, stratified with relation to symptom onset.

1. What criteria were utilized to determine administration of remdesivir therapy (i.e. was it initiated immediately for all patients at time of admission)? Did this change over the 19-month study interval?

2. Consider revising the manuscript title to "…requirement for ICU admission" in place of "…and clinical outcomes" as this is the focus of the study.

3. Did any patients with COVID-19 who were admitted not receive remdesivir? If so, this could serve as a third "control" group.

4. Presumably onset of symptoms was based on patient (or caregiver) report, but this should be explicitly stated.

5. The sentence in Lines 41-43 is confusing, stating that patients qualified for remdesivir therapy if hospitalization or oxygen supplementation was required or risk factors for progression of disease were present. Were not all included patients admitted (Line 39), and per the NIH pregnancy represents an intrinsic clinical risk factor?

6. Did any of the patients receive any other therapies (monoclonal antibodies, dexamethasone, etc.) either prior to or

during admission? If so, was this treatment approach standardized such that both groups (early/late-remdesivir) would have been otherwise therapeutically identical? Additionally, were any of the N=41 patients included in the analysis transferred already mechanically ventilated (i.e. escalation of therapy, if performed, may not have been per the authors' institutional practices)?

7. Recognizing that decisions for ICU admission/intubation is based on clinical judgement, given that this represents the primary outcome variable for the study consider stating if some basic criteria existed (i.e. requirement for high-flow nasal cannula, refractory hypoxemia, hemodynamic instability, etc.); in our institution this has evolved considerably due to limited availability of ICU facilities.

8. In Table 2, does "receipt of corticosteroids" include both fetal lung maturity courses or an extended dexamethasone course for COVID treatment? If the latter, I would suggest clarifying and if the former, consider including as a separate line in the table.

9. Also, in Table 2, are the authors able to distinguish "spontaneous" from "indicated" preterm deliveries? (as the latter would imply deteriorating maternal status) Given the conclusion suggests that early administration of remdesivir improves maternal outcome, potential avoidance of "indicated" preterm delivery could represent an independent obstetrical outcome variable of interest.

10. The Discussion section should be expanded substantially; consider commenting on a pathophysiologic rationale to explain their observations and perhaps proposing a revised strategy for remdesivir utilization based on their findings.

Reviewer #2: This research letter is an observational study of outcomes of two groups of pregnant people hospitalized with COVID-19 infection: one who received remdesivir prior to 7 days and one who received it at or beyond 7 days. The authors make a strong argument for the need for data on remdesivir for treatment of COVID-19 in pregnant people. The results are compelling, but would be strengthened by additional details with regards to the group disease characteristics and the timing of remdesivir.

Introduction, lines 32: perhaps would be useful to transparently state something such as, "because the efficacy of remdesivir in the non pregnant population has been established, it became standard of care in the pregnant population" to explain why your objective cannot be to compare remdesivir vs no remdesivir in the hospitalized population.

Methods, lines 41-43: it is relevant to note that pregnancy itself is an NIH risk factor for progression to severe/critical disease (thus all pregnant people who are hospitalized are eligible).

Results, line 55: Please state your n for the early and late groups here.

Results: Please describe the timing of remdesivir receipt in each group (mean, mode, range).

Results: please describe the pre-remdesivir disease category (mild/moderate) for each group and whether or not they required supplemental O2 prior to initiation of remdesivir.

Discussion, line 74-75: do you mean for hospitalized individuals, or do you mean for outpatient treatment of mild disease as well? Would you include only unvaccinated? If you do not want to state either of these, perhaps list them as questions that still need to be answered.

STATISTICAL EDITOR COMMENTS:

The Statistical Editor makes the following points that need to be addressed:

Table 1: Should indicate in footnote the stats tests used to compare the groups.

Table 2: Should include a stats test (Fisher's) for comparison of maternal deaths. While the counts are small and there is little stats power, other infrequent outcomes (e.g., PPH) are already included in the Table.

General: While these are very important and useful data, many of the baseline characteristics or adverse outcomes had low frequency, so those comparisons that had NS conclusions cannot be generalized from these samples. Should include a concise sentence stating those limitations. Equally important, these groups were not randomly allocated, so there may be unmeasured differences between the groups that could account for different outcomes. Need to also include that among limitations.

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology have increased 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.
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* Funding information (ie, grant numbers or industry support statements) should be disclosed on the title page and in the body text. For industry-sponsored studies, the Role of the Funding Source section should be included in the body text of the manuscript.
* Include clinical trial registration numbers, PROSPERO registration numbers, or URLs at the end of the abstract (if applicable).
* Name the IRB or Ethics Committee institution in the Methods section (if applicable).
* Add any information about the specific location of the study (ie, city, state, or country), if necessary for context.

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4. Please submit a completed STROBE checklist with the submission.

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), observational studies using ICD-10 data (ie, RECORD), 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), quality improvement in health care studies (ie, SQUIRE 2.0), and studies reporting results of Internet e-surveys (CHERRIES). 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, RECORD, CHEERS, SQUIRE 2.0, or CHERRIES guidelines, as appropriate.

5. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Research Letters should not exceed 600 words and may include no more than two figures and/or tables (2 items total). Stated word limits include the title page, précis, abstract, text, tables, boxes, and figure legends, but exclude references.

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

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* 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).

* If your manuscript was uploaded to a preprint server prior to submitting your manuscript to Obstetrics & Gynecology, add the following statement to your title page: "Before submission to Obstetrics & Gynecology, this article was posted to a preprint server at: [URL]."

7. 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 limit for Research Letters is 125 words. Please provide a word count.

8. 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.

9. 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.

10. ACOG avoids using "provider." Please replace "provider" throughout your paper with either a specific term that defines the group to which are referring (for example, "physicians," "nurses," etc.), or use "health care professional" if a specific term is not applicable.

11. In your submission, 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.

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%").

12. 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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* 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. Do not omit your responses to the Editorial Office or Editors' comments.

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 7 days from the date of this letter. If we have not heard from you by Jan 31, 2022, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Jason D. Wright, MD
Editor-in-Chief

The Editors of Obstetrics & Gynecology
2020 IMPACT FACTOR: 7.661
2020 IMPACT FACTOR RANKING: 3rd out of 83 ob/gyn journals

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