

OBSTETRICS & GYNECOLOGY



NOTICE: This document contains comments from the reviewers and editors generated during peer review of the initial manuscript submission and sent to the author via email.

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

6 May 2020



COLUMBIA UNIVERSITY
MEDICAL CENTER



Dear Dr. Chescheir,

Thank you for your invitation to revise our manuscript, “Symptoms and critical illness among obstetric patients with COVID-19 infection,” for consideration for publication in *Obstetrics and Gynecology*. We have carefully reviewed comments by the reviewers, edited our manuscript substantially, and believe that as a result the study is significantly improved. Attached to this cover letter is a point-by-point response to each of the comments of the reviewers. We include track changes and clean versions of the revised manuscript.

The main/primary study findings have not been published elsewhere and everyone included on the author list contributed in a meaningful way to the manuscript. We note that while smaller subsets of this data were quickly published previously (PMID 32292903, 32283004) this large, full dataset including all cases and characteristics and related statistical comparisons was not.

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 have been explained. STROBE guidelines were followed for this analysis. Thank you for your consideration.

Sincerely,

A handwritten signature in black ink, appearing to read 'A. Friedman'.

Alexander Friedman, MD, MPH
Associate Professor of Obstetrics and Gynecology
Department of Obstetrics and Gynecology, College of Physicians and Surgeons

Responses to Reviewer/Editor Comments made for:

Symptoms and critical illness among obstetric patients with COVID-19 infection

Reviewer 1

Reviewer #1/Comment #1

Reviewer #1: Fantastic report. My comments and suggestions are minor and are made to add to clarity or succinctness.

1) *A literal reading of line 82 would be that those with concerning symptoms were diagnosed based on symptoms alone-this wasn't the case I presume. Don't you mean that symptoms lead to testing?*

Response

This change has been made to the abstract.

Reviewer #1/Comment #2

2) *Line 84: as it is a symptom, dyspnea should come before tachypnea;*

Response

This change was made to the abstract.

Reviewer #1/Comment #3

3) *Line 90: "that" does not belong;*

Response

This change was made to the abstract.

Reviewer #1/Comment #4

4) *Line 91: Please give parenthetical percentages for 124 and 34;*

Response

This change was made to the abstract.

Reviewer #1/Comment #5

5) *Throughout the entire manuscript, tables figures, etc, it would be cleaner, and more reflective of the actual precision that a sample of 158 allows, to report only whole number percentages;*

Response

Thank you – the tables, figures and text have been revised to include whole number percentages.

Reviewer #1/Comment #6

6) *Line 92-93: the nine and ten sum to more than the 15 that the sentence starts with. Please clarify;*

Response

Thank you – these are overlapping categories, however it is understanding that this is confusing. The abstract has been revised for clarity.

Reviewer #1/Comment #7

7) *Line 92: "required" is too strong—how about "received";*

Response

This change has been made.

Reviewer #1/Comment #8

8) *Line 96: Don't need to start with "Evaluating laboratory values" as the rest of the sentence makes it clear that that is what you were doing;*

Response

This has been changed.

Reviewer #1/Comment #9

9) *Line 99: Should be "their" disease course. Also the "Nine women required..." is redundant and should be removed;*

Response

This redundancy has been edited.

Reviewer #1/Comment #10

10) *Line 100: "required" should be "underwent";*

Response

This change has been made.

Reviewer #1/Comment #11

11) *Line 102 should start with "In our cohort: and rather than "will develop" be phrased as "developed";*

Response

This change has been made.

Reviewer #1/Comment #12

12) *Line 103: Sentence beginning on this line is not supported by data in abstract;*

Response

This has been changed.

Reviewer #1/Comment #13

13) *Line 117: Better to say "In one report from China, 8%..."*;

Response

This has been changed.

Reviewer #1/Comment #14

14) *Line 122: After workers might say "to the virus..."*

Response

This edit has been made.

Reviewer #1/Comment #15

15) *Line 136: Same issue as #1 above;*

Response

This is has been updated based on the recommendations from Comment #1.

Reviewer #1/Comment #16

16) *To avoid text/table redundancy, suggest inserting "(Table 1)" after "factors" in line 156 (thereby pointing readers to all of the factors you evaluated) and eliminating the text from line 158 through "exposures" on line 165;*

Response

We made this edit and eliminated this text.

Reviewer #1/Comment #17

17) *You could similarly reduce text by inserting "(Table 3)" after "values" in line 173 and then cut lines 174 through "Comparisons" on line 177;*

Response

We made this edit and eliminated this text.

Reviewer #1/Comment #18

18) *Line 222: Don't need to start with "Evaluating the clinical course"...*

Response

This change was made – we removed this text.

Reviewer #1/Comment #19

19) *Line 227: Same "requirement" issue;*

Response

Thank you – we changed this to ‘received.’”

Reviewer #1/Comment #20

20) *Line 234: another "required" that should be changed;*

Response

Thank you – we changed this to ‘received.’”

Reviewer #1/Comment #21

21) *Line 234: Why not just say "underwent intubation to receive general anesthesia." and leave it at that?*

Response

We made this edit as recommended.

Reviewer #1/Comment #22

22) *Line 240: "hospitalizations should be "hospitalized";*

Response

This change was made.

Reviewer #1/Comment #23

23) *Line 241 and 244: More "required" that should be changed;*

Response

These changes were made.

Reviewer #1/Comment #24

24) *Line 260: "initiated" would be better than "necessitated";*

Response

This change was made.

Reviewer #1/Comment #25

25) *To reiterate: Table 1 would be cleaner as whole number percentages as would all the tables;*

Response

Percentages are now expressed as whole numbers.

Reviewer #1/Comment #26

26) *Table 4: Would put tachypnea before hypoxia as the latter is a vital sign and should come first in the evaluation;*

Response

This change was made to Table 4.

Reviewer #1/Comment #27

27) *Figure 1 legend: As written, literally means that clinical indication for testing lead to patient symptoms; suggest a comma after "diagnosis, and replace "and" with "as well as"; That's all!!*

Response

Figure 1 was edited as per the recommendations.

Reviewer 2

Reviewer #2/Comment #1

Reviewer #2: the authors have compiled data from 2 NYC sites to describe COVID-positive pregnant patient outcomes. The topic is timely, important and these institutions are at the epicenter.

Intro

1 - The issues are well-presented and important content.

Response

Thank you for the positive response to our manuscript.

Reviewer #2/Comment #2

Methods

2 - Essentially a descriptive study. Overlapping criteria for testing as some were for symptoms, others without symptoms when universal testing was adopted. Complicated structure with primary analysis, and then 3 different types of secondary analyses.

Response

We agree with the reviewer regarding this important point. We have tried to highlight clear, reasonable inferences from the data for the reviewer and have noted this as a limitation in the discussion:

“An additional weakness of this analysis is that women were tested for COVID-19 for multiple indications. It is possible that we overestimated the proportion of women with COVID-19

infection who develop moderate or severe symptoms. For example, there may have been some COVID-19 positive women early in pregnancy who were asymptomatic or mildly symptomatic and were not tested; if women with moderate or severe symptoms in the 1st and 2nd trimester were more likely to be diagnosed this ascertainment could bias our results.

Reviewer #2/Comment #3

3 - How was all this data recorded in a consistent fashion, at both sites, in the middle of the pandemic? One wonders where or why mild symptoms would have been recorded, and where?

Response

This data was recorded for clinical care and it is possible that some conditions may have been under-ascertained as pointed out by the reviewer.

We have added this important point to our discussion:

“An additional weakness of this analysis is that women were tested for COVID-19 for multiple indications. It is possible that we overestimated the proportion of women with COVID-19 infection who develop moderate or severe symptoms. For example, there may have been some COVID-19 positive women early in pregnancy who were asymptomatic or mildly symptomatic and were not tested; if women with moderate or severe symptoms in the 1st and 2nd trimester were more likely to be diagnosed this ascertainment could bias our results. Finally, this data was collected retrospectively from clinical documentation and the presence of some mild COVID-19-associated symptoms could have been under-ascertained if they were not queried for and documented by the provider.”

Reviewer #2/Comment #4

Results

4 - Paragraph #1 (line 190-205) has the feel of rambling around and would be better presented by more emphasis on the figures. Towards then end of it, there are a lot of percentages and the reader gets lost wondering what these all refer to.

Response

Thank you for this helpful comment. We have reduced the text in this paragraph to focus on key aspects of how the study population was derived.

Reviewer #2/Comment #5

5 - Sentence line 210-212 appears to blend Results/Discussion. Why even mention this here, as the reader is apt to get the wrong impression - it would be better as a brief mention in Discussion as simply a result of the study 'design' - not at all to be interpreted as relevant to care of pregnant women.

Response

We agree with the editor regarding this important point. We have removed the clause, “secondary to universal testing on asymptomatic patients at term,” as this inference is more appropriately located in the discussion.

Reviewer #2/Comment #6

6 - Table 3 should either be Supplemental, or in the Appendix

Response

We agree with the reviewer – we have relabeled Table 3 as a Supplementary Table 1.

Reviewer #2/Comment #7

Discussion

7 - It feels incorrect here to suggest that the 'large majority' had mild or no symptoms (line 238) - when 40+% were asymptomatic or mild and universally tested. It is a self-fulfilling prophecy. A stronger argument here would be to say this descriptive experience largely mirrors the adult non-pregnant population.

Response

We agree with the reviewer – this framing of our results has been added to the first paragraph of the discussion section.

Reviewer #2/Comment #8

8 - It is suggested that 'processes will need to be in place for outpt surveillance' (line 246), but rather than float this abstract concept, it would be more helpful to know what the authors did, or learned about this, did they come up with something that worked, or not?

Response

Thank you for bringing up this important point. We have added a brief description of how this was handled at our institution. A more expanded discussion of our approach for COVID-19 tracking and telehealth management has been accepted for publication in *NEJM Catalyst*. If the *NEJM Catalyst* e-published prior to proofs being prepared for this manuscript we can add it as a citation.

Reviewer #2/Comment #9

9 - Paragraph beginning with line 255, rather than dwell on one patient here, two there, etc - would like development of why the authors think the China paper had majority decompensating after delivery v NYC report here where they were crashing prior to delivery

Response

We have added a comment to the discussion regarding this important point:

“The cause of this differential is unclear; it is possible that a lower clinical threshold was present in China for delivering women with COVID-19 infection.”

Reviewer #2/Comment #10

10 - Study design does not really allow for statements like (line 269) 'demonstrating increased risk' - when at most these would just be associations. Several causal statements in this paragraph require walking back

Response

Thank you – we have reformatted this statement to better align with the study design:

“Given the large proportion of high-risk patients, we were able to make meaningful comparisons demonstrating increased likelihood of medical comorbidities among patients who developed moderate or severe symptoms.”

Reviewer #2/Comment #11

11 - Limitations are many, to include mixed bag of universal testing/symptomatic testing and then attempting to analyze them all together.

Response

Thank you – we agree with the reviewer regarding this important point. We have modified the discussion to address these issues. We added the following text to the discussion:

“An additional weakness of this analysis is that women were tested for COVID-19 for multiple indications. It is possible that we overestimated the proportion of women with COVID-19 infection who develop moderate or severe symptoms. For example, there may have been some COVID-19 positive women early in pregnancy who were asymptomatic or mildly symptomatic and were not tested; if women with moderate or severe symptoms in the 1st and 2nd trimester were more likely to be diagnosed this ascertainment could bias our results. Finally, this data was collected retrospectively from clinical documentation and the presence of some mild COVID-19-associated symptoms could have been under-ascertained if they were not queried for and documented by the provider.”

Reviewer #2/Comment #12

12 - Concluding paragraph is unnecessary

Response

We have modified the final paragraph based on the comments of the reviewer.

Reviewer #2/Comment #13

Tables

13 - It seems unnecessary to include all of the rows with 0%

Response

We included the rare outcomes with zero counts because we have been frequently asked about risk for these outcomes (thromboembolism, stroke, cardiomyopathy) at our institution. We have left the table as is but defer to the editors regarding whether to remove or include these conditions.

Statistical editor

Comment 1

Table 1: The mild or asymptomatic and the moderate or severe columns should have N = 124 and N = 34 in the column headings. The moderate or severe column should format the n(%) to the nearest integer %, not to 0.1% precision, based on the size of the denominator. Also, the main text and Abstract should conform to that format.

Response

Thank you – these changes have been made.

Comment 2

Table 2: The problem with these comparisons is that some of these women were tested based on symptoms while others were part of a protocol of universal testing. Thus the combined mild and asymptomatic category may not be representative of all mild or asymptomatic women in labor with covid-19. The proportions for that column may not be representative. Should instead compare mild vs moderate of severe and omit the asymptomatic inclusion.

Response

Thank you for this suggestion – we changed the comparison to mild vs moderate/severe per the recommendations of the editor.

Comment 3

Table 3: Again, should only compare the mild vs the moderate/severe patients. The n(%) should be formatted with % rounded to the nearest integer %, not to 0.1% level of precision.

Response

Thank you for this suggestion – we have included a sensitivity analysis comparing mild to moderate or severe patients.

Comment 4

Table 4: The n(%) should be formatted with % rounded to the nearest integer %, not to 0.1% level of precision.

Response

Thank you – this change has been made.

Editor comments

Comment 1

Thank you for submitting your work to O&G. We no longer require that authors adhere to the Green Journal format with the first submission of their papers. However, any revisions must do so. I strongly encourage you to read the instructions for authors (the general bits as well as those specific to the feature-type you are submitting). The instructions provide guidance regarding formatting, word and reference limits, authorship issues and other relevant topics. Adherence to these requirements with your revision will avoid delays during the revision process by avoiding re-revisions on your part in order to comply with formatting.

Response

Thank you – we believe that the manuscript is formatted appropriately for the Green Journal.

Comment 2

PRESENTATION OF STATS INFORMATION (P Values vs Effect Size and Confidence Intervals)
While P values are a central part of inference testing in statistics, when cited alone, often the strength of the conclusion can be misunderstood. Whenever possible, 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. This is true for the abstract as well as the manuscript, tables and figures.

Response

We believe that statistics are presented appropriately.

Comment 3

Please provide absolute values for variables, in addition to assessment of statistical significance.

Response

We believe that absolute values are consistently presented

Comment 4

We ask that you provide crude OR's followed by adjusted OR's for all relevant variables.

Response

We provide crude ORs as estimates.

Comment 5

91. $34/158=22\%$. True, it's a minority who developed mod/sev symptoms but it is about 1/5—perhaps “significant minority”?

Response

We have made the recommended change to the précis and abstract conclusion.

Comment 6

92: *Its women who are hospitalized not cases. Can you edit for this change please? Something like “Fifteen women with moderate or severe symptoms were hospitalized,....” Please be aware of this throughout your abstract and paper (for instance, line 94)*

Response

This has been changed.

Comment 7

Did any require intubation? Proning? HFNC?

Response

Thank you for pointing out this information would be helpful. We have added it to **Table 4**.

Comment 8

Spell out AST here.

Response

This change was made.

Comment 9

you mentioned on line 92 that 9 women required ICU/Stepdown—can delete here

Response

This change was made.

Comment 10

Agree with reviewer that “required” is perhaps not the best term here. Perhaps “Two women were delivered preterm because....”.

Response

This was changed per the recommendation of the reviewer.

Comment 11

You've not mentioned length of illness in the abstract results so probably should not be included in discussion of abstract.

Response

We added length of length of illness to the results.

Comment 12

Do you have data on test characteristics for the PCR test you were using (Sens/spec, etc)?

Response

Thank you for bringing up this important point. This was discussed in our study group and with a pathologist leading COVID-19 testing. There is data being developed from our center regarding validity of COVID-19 testing (<https://www.biorxiv.org/content/10.1101/2020.04.22.055327v1>). Unfortunately, the calculation of these test characteristics is relatively complex and contingent on viral load. For that reason we did not add this data.

Comment 13

154: were women with dyspnea managed as outpatients considered to have mild or mod/severe symptoms?

Response

Thank you for pointing that this requires further clarification. These women were classified as having moderate symptoms. We have revised the manuscript to state the following in the methods:

“Patients with dyspnea but no evidence of hypoxia or clinical decompensation were classified as having moderate disease but could be managed as outpatients with close follow up and regular surveillance of symptoms by a clinician. This follow up included enrollment in a COVID telehealth follow-up program with video visits with a physician every 24 to 48 hours depending on the severity of symptoms. Patients were instructed to monitor their symptoms, and to take their temperature and heart rate twice per day. Symptoms and findings were reviewed with a doctor at each video visit. Patients with concerning symptoms, such as worsening dyspnea, difficulty completing full sentences, or increased work of breathing were instructed to present to the triage for evaluation. Outpatients with two or more weeks of surveillance who had their symptoms resolve or improve substantially were discontinued from the program.”

To describe their disease course at the end of the results section we now state:

“Nineteen women with moderate disease severity (based on the presence of dyspnea but no other concern findings) were managed at home with regular telehealth visits, close monitoring of symptoms, vital sign surveillance, and triage evaluation as needed but did not require hospitalization during their infection course.”

Comment 14

160: was this BMI as calculated based on admission's data or prepregnancy BMI?

Response

Body mass index was calculated on admission data. This information has been added to the table.

Comment 15

169-172 I'm unclear what you mean by symptoms were compared between groups. You've listed all the symptoms that defined mild symptoms (repeated from lines 147-149. Could you just reference back to that symptom list rather than repeating it?)

Are you saying you wanted to see which of the mild symptoms those women with mod/sev disease also had? Why? It makes sense that they would have some of these and how is that clinically helpful?

Response

Thank you for requiring that this needs further clarification. We wanted to see if women with moderate or severe infection were more likely to have other symptoms including whether they had more symptoms on presentation. We agree that this does not have major clinical utility but we do believe it is important descriptively in terms of characterizing the epidemiology of the infections. We have edited this portion of the methods to make it clearer and easier to read. We have also abbreviated the reporting of these results.

Comment 16

185: best not to include data (# of mod/sev) in the method section

Response

Thank you – we have made this change.

Comment 17

190. Do not begin a sentence with a numeral. Either spell out or edit your sentence to avoid the need to start w/ a number.

Response

This change has been made.

Comment 18

Somewhere in the results describe the clinical course of all 34 women w/ mod or severe disease. In your discussion, you say only 10% required hospitalization, (19): why were the other 15 not hospitalized? It seems that dyspnea alone may be the deciding symptom for you—this needs some explanation perhaps in the methods section. If dyspnea was considered a defining symptom for mod/severe category, its unclear to me why it wasn't a reason for admission. Just needs a better explanation.

Response

Thank you for pointing that this requires further clarification. We have revised the manuscript to state the following in the methods:

“Patients with dyspnea but no evidence of hypoxia or clinical decompensation were classified as having moderate disease but could be managed as outpatients with close follow up and regular surveillance of symptoms by a clinician. This follow up included enrollment in a COVID telehealth follow-up program with video visits with a physician every 24 to 48 hours depending on the severity of symptoms. Patients were instructed to monitor their symptoms, and to take their temperature and heart rate twice per day. Symptoms and findings were reviewed with a doctor at each video visit. Patients with concerning symptoms, such as worsening dyspnea, difficulty completing full sentences, or increased work of breathing were instructed to present to the triage for evaluation. Outpatients with two or more weeks of surveillance who had their symptoms resolve or improve substantially were discontinued from the program.”

We have revised the final paragraph of the results to focus on care of women with moderate and severe symptoms. We believe that this improved over the initial version:

“Of 15 women with moderate or severe infection who were hospitalized, nine received step-down or ICU-level care. Eleven of the 15 women with moderate or severe infection were hypoxic of whom ten received respiratory support short of intubation (including oxygen via nasal canula, high flow nasal canula, non-rebreather mask, and Venturi mask) with one patient undergoing intubation to receive general anesthesia in a cesarean complicated by postpartum hemorrhage (**Table 4**). The mean duration of time from onset of symptoms to ICU or step-down care was 3.7 days (SD 4.0). The mean total length of stay for the 15 hospitalized women with moderate or severe infection was 6.4 days (SD 6.1). The duration of ICU-level or step-down care varied significantly: 5 women received 3 days or less of ICU or step-down while the remaining four women received 9, 10, 10, and 16 days (**Figure 4**). Two women underwent preterm delivery – at 31 and 36 weeks – for maternal decompensation. One woman was readmitted postpartum four days after discharge from delivery and received six days of supplemental oxygen for hypoxia. Overall, 14 of the 15 women had abnormal chest x-ray findings, two women had sepsis, and one woman had acute renal failure. No women developed stroke, thromboembolism, or cardiomyopathy (**Table 4**). Nineteen women with moderate disease severity (based on the presence of dyspnea but no other concern findings) were managed at home with regular telehealth visits, close monitoring of symptoms, vital sign surveillance, and triage evaluation as needed but did not require hospitalization during their infection course.”

Comment 19

It would be useful to see data presented as something like the following:

158 total

X asymptomatic: How many remained asymptomatic? Did any advance to mod/sev?

Y: Initial mild: How many remained so? How long were they symptomatic?

Z: Mod/sev initially: What was their course? How did you decide which to hospitalize and which to keep at home?

Response

Thank you – we have added a new **Figure 3** with this information. We have simplified Figure 1 and Figure 2. We believe that this information is now more interpretable. We have revised the methods and the final paragraph of the results to better describe the clinical course of the moderate/severe cases. For the mild patients unfortunately we do not have data on exactly how much time was required for cessation of symptoms.

Comment 20

210. I am not understanding why universal testing on asymptomatic patients is related to earlier EGA for those with mod or severe disease? Testing of asymptomatic patients shouldn't influence the EGA for when those with mod/sev disease manifest.

Response

Apologies for this being confusing. We have edited the text to clarify this point. We wanted to point out that there may have been some patients who had mild symptoms or were asymptomatic whose diagnosis was not ascertained. Thus, the proportion of patients with severe symptoms (as opposed to absolute number) may be overestimated. We have revised the text to make this point more clearly:

“An additional weakness of this analysis is that women were tested for COVID-19 both symptoms and for admission screening. It is possible that we overestimated the proportion of women with COVID-19 infection who develop moderate or severe symptoms. For example, there may have been some COVID-19 positive women early in pregnancy who were asymptomatic or mildly symptomatic and were not tested; if women with moderate or severe symptoms in the 1st and 2nd trimester were more likely to be diagnosed this ascertainment could bias our results.”

Comment 21

238. Again, while I agree its important to emphasize that a “large majority” had mild or no symptoms, I think its equally important to emphasize that even in the setting of universal testing for the majority of your reporting period, 22% had mod-severe disease. By only emphasizing the majority relatively benign course, it seems to me you risk underemphasizing how significant this can be for many. Your call, but that’s how this strikes me.

Response

Thank you – we have changed the language to support that a significant minority of women had severe symptoms.

Comment 22

240: Perhaps “About 10% of women with COVID-19 were hospitalized with moderate or severe disease and 6% required.....ICU or step-down level of care. Of the patient who were treated in the ICU or step-down units, several had prolonged inpatient courses and one was delivered at 31 weeks gestational secondary to maternal decompensation. Half of the patients who developed moderate or severe symptoms had an underlying medical condition. In addition, xx% of those with moderate or severe symptoms initially were diagnosed without symptoms or with mild symptoms”.

Response

Thank you – we removed the numbers from the discussion and discussed the actual results in the results section in more detail as per recommendations above. The first paragraph of the discussion now reads:

“In this descriptive study of obstetric patients with COVID-19 infection, the large majority of women had mild or no symptoms, and a majority of patients with mild dyspnea and no other concerning findings were safely managed as outpatients. A significant minority had hypoxia requiring respiratory support and ICU or step-down level care. This experience largely mirrors findings in the adult non-pregnant population.”

Comment 23

250. Purely an interest question on my part and no change in the paper is suggested, but do you have any idea if the women with asthma who got really sick differed from those who did not? Thinking about the medications used, degree of control of symptoms and wondering if one should proactively contact asthmatic pregnant women in their practice and try to maximize their baseline asthma control in order to minimize their risk should they become infected}

Response

Thank you for this interesting question. In general the asthmatics in this study that had mild to no symptoms and were well controlled. Among the women with moderate/severe disease, one patient had a history of poorly controlled asthma and 2 women had asthma exacerbation while having a COVID-19 infection. While we aren't able to make any statistical inferences given the 'n' it appeared that asthma was a general risk factor absent factors related to asthma control not being optimized.

Comment 24

256: Did they define severe disease the same way? You lumped mod/severe and had 22% in that category. I'm not convinced that this aligns with Chinese data.

Response

Thank you for bringing up this point. They defined severity based on hypoxia. We have clarified that when evaluating risk for hypoxia, our study and the Chinese study aligns.

Comment 25

256-260: :You use in “that cohort” and in “This cohort” . For clarity could you state instead “in the Chinese cohort” and “in our cohort”?

Response

This change has been made.

Comment 26

262 Spell out COPD

Response

This change has been made.

EDITORIAL OFFICE

Comment 1

1. Please add the following text to your Financial Disclosure:

“Cynthia Gyamfi-Bannerman disclosed receiving money paid to her institution from SMFM/AMAG. She also received funding from Sera Prognostics and various funds for medicolegal work. She also disclosed receiving NIH grants. Russell Miller disclosed receiving honorarium for writing a chapter on TRAP sequence for UpToDate. He received funds for medicolegal consulting (cases entirely unrelated to the topic of this study). “

We will need the disclosures for Timothy Wen and Caitlin Baptiste as well.

Response

We have made these edits.

Comment 2

2. Provide a running title.

Response

This has been added to the title page.

Comment 3

3. Renumber your tables from “2a,” 2b,” “3,” and “4” to “2,” “3,” “4,”and “5.” Make sure you edit the manuscript text as well.

Response

This change has been made.

Comment 4

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

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

Response

We elect A. OPT-OUT.

Comment 5

5. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (eCTA). When you are ready to revise your manuscript, you will be prompted in Editorial Manager (EM) to click on "Revise Submission." Doing so will launch the resubmission process, and you will be walked through the various questions that comprise the eCTA. Each of your coauthors will receive an email from the system requesting that they review and electronically sign the eCTA.

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

Response

The coauthors confirm their disclosures are accurately represented on the manuscript.

Comment 6

6. 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.

Response

This statement is included on the cover letter.

Comment 7

7. 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://onq.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.

Response

This study confirms to STROBE guidelines. This information is present on the cover letter.

Comment 8

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

Response

We believe this study confirms with the revitalize initiative.

Comment 9

9. 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 print appendixes) but exclude references.

Response

We believe this manuscript adheres to space limitations.

Comment 10

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

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

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

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

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

Response

We include no acknowledgements for this study.

Comment 11

11. Provide a short title of no more than 45 characters, including spaces, for use as a running foot.

Running Title: COVID-19 symptoms among obstetric patients

Comment 12

12. 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 Original Research articles is 300 words. Please provide a word count.

Response

The word count is 288 words.

Comment 13

13. Only standard abbreviations and acronyms are allowed. A selected list is available online at <http://edmqr.ovid.com/onq/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.

Response

We believe all acronyms are appropriate.

Comment 14

14. 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.

Response

We do not use the virgule symbol with words.

Comment 15

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

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

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

Response

We believe that our manuscript conforms to this formatting.

Comment 16

16. 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 it is not based on a systematic search but only on your level of awareness, it is not a claim we permit.

Response

We not believe that we claim that this is a 'first report' in the manuscript.

Comment 17

17. 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://edmqr.ovid.com/ong/accounts/table_checklist.pdf.

Response

We believe that the tables conform to journal style.

Comment 18

18. Figures 1-3 may be resubmitted as-is with the revision.

Response

We have resubmitted the figures as is.

Comment 19

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

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

Response

We decline open access.