

OBSTETRICS & GYNECOLOGY



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- Comments from the reviewers and editors (email to author requesting revisions)
- Response from the author (cover letter submitted with revised manuscript)*

**The corresponding author has opted to make this information publicly available.*

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

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

Date: Jun 02, 2021
To: "Niraj N Mahajan" [REDACTED]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-21-1186

RE: Manuscript Number ONG-21-1186

Impact of the second wave of COVID-19 on pregnancy outcomes and maternal complications in India

Dear Dr. Mahajan:

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 14 days from the date of this letter. If we have not heard from you by Jun 16, 2021, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

The authors described what appears to be an increase in morbidity mortality and poor outcomes in pregnant patients during the "so-called" 2nd wave of COVID-19.

1. This finding has been reported in several publications from England and Spain: (your reference 4 and <https://doi.org/10.1101/2020.12.10.20246959>). How does yours differ? What additional information does your paper provide?
2. Your paper, as well as the ones listed above, have serious flaws. They do not account for the availability of testing, the overall reporting, thus may reflect just an increase in the number of cases. In addition, initially we were unsure on how to respond to COVID positive pregnant patients, thus hospitalizations were more common in the 1st wave, but with experience more outpatient therapy was employed and less need for referral to specialize centers. Thus there were a decrease in number of cases of COVID admitted and only those of higher acuity were omitted or referred to specialized centers. Therefore without knowing the total number of pregnant COVID positive women, as well as their symptom complex, it is difficult to interpret your study.
3. In order to put your COVID complications in pregnancy in prospective it may be helpful to look at the outcomes of non pregnant patients during the 1st and 2nd wave? Did you see a difference in non pregnant COVID-19 patients complication rates?
4. The question is that if this is true then why? In your discussion you mention the possibility of a different variant (B.1.617), however you have no laboratory data to uphold this theory. When was this variant 1st described, and does it chronologically fit your data (first reported in October)? Interestingly, a recent report has shown this virus may be more virulent (<https://doi.org/10.1101/2021.05.04.442663>). This ref would help support your hypothesis.
5. You made a significant amount of comparisons (approaching 50), thus, you should include some control for multiple measurements.
6. Your tables include data that is not necessary and should be more focused.
7. Please list some of the potential weakness and problems with your study.

Reviewer #2:

The manuscript is a research letter which presents data on pregnant and post-partum women infected with COVID-19 in India from the first and second waves of the pandemic. The authors focus on admissions to a single hospital in Mumbai which became a dedicated COVID-19 hospital in mid-April 2020.

1. Introduction, Lines 67-69: Recommend moving this sentence to after line 72.
2. Methods, Lines 80-82: Consider adding graphical representation of the cases in India over time to better delineate cut-points for the first and second waves.
3. Methods, Lines 80-82: From the admission policies in reference 5, the policy changed over time from admitting all pregnant patients with COVID-19 to only those with more moderate to severe disease. Please describe how this policy might have continued to change in the second wave and how this would impact your data. Additionally, while NH is the only dedicated COVID-19 hospital in the area, are COVID patients cared for at other institutions? If so, how is it determined whether the patient is admitted to NH or another facility?
4. Results, Lines 91-94: Recommend adding that these differences did not reach statistical significance.
5. Results, Lines 97-102: Make this a new paragraph dedicated to the comparisons of women who died and reference the appropriate tables for each paragraph individually. Also recommend including some comment that no statistical differences were found, likely due to low N.
6. Results, Line 98: Should be changed to "second wave".
7. Discussion: Though it is possible that the current findings may be due to an increase in B.1.617.1 infection, there are many other potential causes to include higher case rates, changing admission policies, delays in seeking healthcare, etc. Other potential contributors need to be discussed.
8. Table 2: Recommend removing the first line "Total number of pregnant and post-partum women with COVID-19" as this table focuses on those that died and it is confusing to include this here.

Reviewer #3:

Lines 91-94: The preterm birth and stillbirth rates were NS different (Table 1). Should explicitly state that or omit from Results, since it is listed in Table 1.

lines 96-102: None of the differences in proportions among those who died during the two time periods were different statistically. The text implies a difference, but none was proven, in part due to low counts and inadequate power. Need to strike or modify this section to conform with Table 2.

Table 2: This Table compares N = 8 vs N = 22, so all %s should be rounded to nearest integer %, not cited to 0.1% precision. Also, none of the statistical comparisons can be generalized, since they were all NS and vastly underpowered. Also, given the size of the samples, should report ranges, not IQR for the maternal age, length of stay, O2 sat, Resp rates, gestational age.

EDITOR COMMENT:

Thank you for submitting your work to Obstetrics and Gynecology. If you opt to submit a revision, please modify the precis to focus on what is demonstrated by your results. Since you do not have data on the variant that these patients contracted, it is okay to speculate about the new variant as a reason for increased disease severity in the discussion, but it cannot be the major conclusion of your work in the precis.

EDITORIAL OFFICE COMMENTS:

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

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

2. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (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. Each of your coauthors received an email from the system, titled "Please verify your authorship for a submission to Obstetrics & Gynecology." Each author should complete the eCTA if they have not yet done so.

3. 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.

4. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric data definitions at <https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-data-definitions> and the gynecology data definitions at <https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions>. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

5. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Research Letters articles should not exceed 600 words. 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:

- * 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).

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

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. 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%).

11. 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.

12. Please review examples of our current reference style at <http://ong.editorialmanager.com> (click on the Home button in the Menu bar and then "Reference Formatting Instructions" document under "Files and Resources"). Include the digital object identifier (DOI) with any journal article references and an accessed date with website references. Unpublished data, in-press items, personal communications, letters to the editor, theses, package inserts, submissions, meeting presentations, and abstracts may be included in the text but not in the reference list.

In addition, the American College of Obstetricians and Gynecologists' (ACOG) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite ACOG documents in your manuscript, be sure the reference you are citing is still current and available. If the reference you are citing has been updated (ie, replaced by a newer version), please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly (exceptions could include manuscripts that address items of historical interest). If the reference you are citing has been withdrawn with no clear replacement, please contact the editorial office for assistance (obgyn@greenjournal.org). In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All ACOG documents (eg, Committee Opinions and Practice Bulletins) may be found at the Clinical Guidance page at <https://www.acog.org/clinical> (click on "Clinical Guidance" at the top).

13. 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 <https://wkauthorservices.editage.com/open-access/hybrid.html>.

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If you choose to revise your manuscript, please submit your revision through Editorial Manager at <http://ong.editorialmanager.com>. Your manuscript should be uploaded in a word processing format such as Microsoft Word. Your revision's cover letter should include the following:

- * A confirmation that you have read the Instructions for Authors (<http://edmgr.ovid.com/ong/accounts/authors.pdf>), and
- * A point-by-point response to each of the received comments in this letter. 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 21 days from the date of this letter. If we have not heard from you by Jun 16, 2021, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Torri D. Metz, MD
Associate Editor, Obstetrics

2019 IMPACT FACTOR: 5.524
2019 IMPACT FACTOR RANKING: 6th out of 82 ob/gyn journals

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: <https://www.editorialmanager.com/ong/login.asp?a=r>). Please contact the publication office if you have any questions.

9th June 2021

Editor in Chief
Obstetrics and Gynecology

Subject: Submission of a revised research letter “Impact of the second wave of COVID-19 on pregnancy outcomes and maternal complications in India” for publication in Obstetrics and Gynecology

Dear Sir,

We sincerely thank the Editors and Reviewers for the critical review of our manuscript letter “Impact of the second wave of COVID-19 on pregnancy outcomes and maternal complications in India”. We have provided point-to-point response to the reviewer's and editor's comments. The manuscript is revised as per the reviewer's and editor's comments.

We hereby confirm that all authors have seen and approved the revised manuscript, contributed significantly to the work, and also that the manuscript has not been previously published nor is not being considered for publication elsewhere. We also declare that all the authors don't have any conflict of interest to disclose and intent to publish solely to Obstetrics and Gynecology.

The study is registered with the Clinical Trial Registry of India (Registration no: CTRI/2020/05/025423). The study was approved by the Ethics Committees of all participating Institutes and ICMR-NIRRH (IEC no. D/ICEC/Sci-53/55/2020 dated 04.06.2020).

As a corresponding author, 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.

We are looking forward publication of our manuscript in your journal.

Thanking you

Yours Sincerely,

Dr. Rahul Gajbhiye

Principal Investigator PregCovid Registry (www.pregcovid.com)

Scientist D (Assistant Director)

DBT Wellcome India Alliance Clinical & Public Health Intermediate Fellow

ICMR-National Institute for Research in Reproductive Health



Response to Reviewer's and Editor's Comments

Reviewer #1:

The authors described what appears to be an increase in morbidity mortality and poor outcomes in pregnant patients during the "so-called" 2nd wave of COVID-19.

1. This finding has been reported in several publications from England and Spain: (your reference 4 and <https://doi.org/10.1101/2020.12.10.20246959>). How does yours differ? What additional information does your paper provide?

Response: We thank the reviewer for providing valuable comments and suggestions. We agree with the comment that there are publications from the U.K. and Spain comparing the impact of the first and second waves of COVID-19. However, these studies have provided limited information. Iftimie S et al., 2021 carried out a comparison of first and second waves for all hospitalized cases of SARS-CoV-2 infection in Reus, Spain. They observed a significantly higher number of admissions to Gynecology, Pediatrics, and Emergency Departments and fewer to Internal Medicine and ICU during the second wave. Pregnant and postpartum women (13 and 17 cases, respectively) were asymptomatic in the second wave. Also, the sample size of pregnant and postpartum women in the study from Spain was smaller.

In our study, a total of 1530 pregnant and postpartum women with COVID-19 were compared for the impact of first and second waves of COVID-19. We observed significantly higher numbers of symptomatic pregnant and postpartum women in the second wave in our study. There were no deaths observed among pregnant or postpartum women in the study reported from Spain thus indicating low severity of the disease

during the second wave. This is also in contrast to our observations. We reported higher severe COVID-19 cases and higher mortality in pregnant and postpartum women during the second wave. So, the observations of the impact of the second wave in the Spanish population are totally in contrast to our study.

Another study by Kadiwar et al. 2021 reported the increased numbers of critical COVID-19 cases amongst pregnant and peripartum women during the second wave requiring extracorporeal membrane oxygenation (ECMO) at the Royal Brompton Hospital in London, U.K. Their observations were mainly based on the ECMO referrals during the second wave than the first wave. This study was conducted in a referral centre in the UK for severe acute respiratory failure that offers ECMO. Our study was conducted in a dedicated COVID-19 hospital in pregnant and post-partum women admitted during the first and second wave of COVID-19 with asymptomatic, mild, moderate, severe, and COVID-19.

Our study provided additional information on clinical presentations in pregnant and postpartum with COVID-19 during both waves of COVID-19. We reported a higher frequency of dyspnea (96%) and fever (82%) on admission in women who died during the second wave of the pandemic. We reported that anemia and gestational hypertension were significantly higher during the second wave. We also reported information on pregnancy complications, obstetrics outcomes, case fatality rate, the cause of death in pregnant and postpartum women during the first and second waves of COVID-19. This information was not reported in studies from UK and Spain.

2. Your paper, as well as the ones listed above, have serious flaws. They do not account for the availability of testing, the overall reporting, thus may reflect just an increase in the number of cases. In addition, initially we were unsure on how to respond to COVID positive pregnant patients, thus hospitalizations were more common in the 1st wave, but with experience more outpatient therapy was employed and less need for referral to specialized centers. Thus there was a decrease in number of cases of COVID admitted and only those of higher acuity were omitted or referred to specialized centers. Therefore, without knowing the total number of pregnant COVID positive women, as well as their symptom complex, it is difficult to interpret your study.

Response: We wish to inform the reviewer that Kasturba Hospital for Infectious Diseases, Mumbai, which is a part of BYL Nair Charitable Hospital (NH) was the first laboratory in Mumbai Metropolitan Region (MMR) established for the diagnosis of COVID-19. After this, several laboratories (public and private) were established in the MMR for diagnosis of COVID-19 immediately after the cases of SARS-CoV-2 were identified in the early phase of a pandemic. Since then, there had never been any issues with the availability of testing for COVID-19 right in the MMR region. We do agree that hospitalizations were more common in the first wave for general populations as well as pregnant women in other parts of India. However, this was not the case for NH. In mid-April 2020, NH was declared as a dedicated COVID-19 hospital. In April 2020, all pregnant women were admitted irrespective of labor or symptoms (n = 30). From May 2020, the policy was changed. As per the admission policy of NH, pregnant women with COVID-19 who are near-term or those who needed obstetric interventions or Moderate or severe symptomatic cases were admitted. Our admission policy is uniform during both

the waves of COVID-19. All patients are screened at a special screening outpatient department and only eligible patients are admitted at NH. There are various levels of COVID-19 care centers (CCCs) in MMR, where women who are not in labor, or not requiring obstetric interventions, or those asymptomatic or mild symptomatic are referred to CCCs or advised home quarantine.

The study population included a wide spectrum of COVID-19 in pregnant and post-partum women. Our admission policy was uniform during both waves of a pandemic. Our study population included women in the first, second, the third trimester of pregnancy, and the postpartum period. Out of a total of 1530 patients admitted at BYL Nair Hospital, Mumbai in both the waves of COVID-19, 1027 women delivered. Spontaneous abortion (n=42), Medical Termination of Pregnancy (MTP) (n=7), Ectopic pregnancy (n=6), postpartum admission (n=36), and 30 maternal deaths were reported in our study population. There were 273 symptomatic patients with moderate and severe disease in 72 patients. Thus, our study population covers a comparatively larger sample size with all spectrum of COVID-19 in pregnant and postpartum women during both the waves of COVID-19 representative of the majority of the pregnant women with COVID-19.

3. In order to put your COVID complications in pregnancy in prospective it may be helpful to look at the outcomes of non-pregnant patients during the 1st and 2nd wave? Did you see a difference in non-pregnant COVID-19 patients complication rates?

Response: We agree with the reviewer that it would be helpful to look at the outcomes of non-pregnant patients during the first and second waves of COVID-19. NH is 1043 bedded dedicated COVID-19 Hospital for all the COVID-19 patients including pregnant and non-pregnant women. There was a difference noted in the case fatality rate among non-pregnant patients also when the data were compared between two waves of COVID-19. However, details of non-pregnant patients are outside the purview of our project and therefore it is not possible to provide the details of complications amongst the non-pregnant group. Moreover, the admission policy for non-pregnant patients with COVID-19 was different than the pregnant women with COVID-19. As per the admission policy for non-pregnant patients at NH, only moderate and severe cases were admitted. Therefore, the non-pregnant patients and pregnant patients groups cannot be compared. Also, the data is single-center data and hence cannot be generalized. The case fatality rate amongst the non-pregnant patients with COVID-19 (age group 18-45 years) was higher during the second wave compared to the first wave. The comparison of complications amongst non-pregnant patients with COVID-19 in both waves of a pandemic is beyond the scope of this study.

In response to the comment, we are providing the details of non-pregnant patients with COVID-19 admitted at NH during both the waves of COVID-19:

BYL Nair Charitable Hospital, Mumbai (Dedicated COVID-19, Hospital)	First wave of COVID-19	Second wave of COVID-19
Total number of patients with COVID-19 admitted at NH (<i>all males and non-pregnant females</i>)	6613	1884
The case fatality rate amongst patients with COVID-19	1681 (25.4%)	632 (33.5%)
Non-Pregnant Women with COVID-19 in the age group 18-45 years admitted at NH	645	186
The case fatality rate amongst non-pregnant women with COVID-19 in the age group 18-45 years	73 (11.3%)	31 (16.7%)

4. The question is that if this is true then why? In your discussion you mention the possibility of a different variant (B.1.617), however you have no laboratory data to uphold this theory. When was this variant 1st described, and does it chronologically fit your data (first reported in October)? Interestingly, a recent report has shown this virus may be more virulent (<https://doi.org/10.1101/2021.05.04.442663>). This ref would help support your hypothesis.

Response: We agree with the reviewer that we do not have the laboratory data on SARS CoV-2 variant B.1.617 in our study population. We also thank you for providing the link to a recent report on the high virulence of SARS CoV-2 variant B.1.617

The B.1.617 variant was first detected in October 2020 in India and was divided into three lineages - B.1.617.1, B.1.617.2, and B.1.617.3. Despite its name, B.1.617.3 was the first sub-lineage of this variant to be detected, in October 2020 in India. The two other sub lineages [B.1.617.1](#) (variant Kappa) and B.1.617.2 (variant Delta) were first detected in December 2020 in the Vidarbha region of Maharashtra state which then spread to the other regions in Maharashtra including the Mumbai Metropolitan Region. This chronology very well fits into our data. The COVID-19 cases in the Mumbai region started declining from October 2020 and the epidemic curve touched the baseline for the Mumbai region in December 2020 - January 2021. In early February, there was a rise in COVID-19 cases and that was the beginning of the second wave in the Mumbai Metropolitan Region. The B.1.617 variant was detected mainly in Amravati, Nagpur, Akola, Wardha, Pune, Thane, Aurangabad, and Chandrapur districts till January 2021 which was, later on, spread to Mumbai and other regions. Therefore, the duration of the second wave in our study (Mumbai region) is from February 2021 till 14th May 2021. The duration of the first wave is from April 2020 to 31st January 2021. For more clarity and suggestion from the Reviewer 2, we have added a figure 1 (graph depicting timelines of the 1st and 2nd wave and patients admitted month-wise in NH). Page no. 4, Line no. 76.

High lung viral load and more severe lung histopathological changes were seen in hamsters with B.1.617.1 infection suggesting a highly pathogenic variant [Yadav et al., <https://www.biorxiv.org/content/10.1101/2021.05.05.442760v1>]. WHO declared the

SARS CoV-2 variant B.1.617 as a variant of concern (VOC) on 11th May 2021. A recent study by Hoffmann et al. reported that SARS-CoV-2 variant B.1.617 is resistant to Bamlanivimab and evades antibodies induced by infection and vaccination. Based on these observations, we speculate that the increased frequency of symptomatic cases, severe COVID-19 disease, and increased maternal mortality could be due to the new variant of concern B.1.617.

We have added the reference suggested by the reviewer as well as other references indicating the high virulence of B.1.617. Page no. 5, line no. 102

5. You made a significant amount of comparisons (approaching 50), thus, you should include some control for multiple measurements.

Response: We have compared the data of 1st and 2nd waves of the pandemic with pre-pandemic data of the NH and added it as a supplementary Table 1. Following sentence is added in the revised manuscript, Page no. 4 Line no.84-85.

The maternal mortality rate was significantly higher in the COVID-19 pandemic compared to the pre-pandemic period (Supplementary Table 2).

6. Your tables include data that is not necessary and should be more focused.

Resposne: As per the comment, we have revised the Table 1and Table 2. Table 2 is now submitted as supplementary Table 1.

7. Please list some of the potential weakness and problems with your study.

Response: We have added the potential weakness and problems with our study in the revised manuscript. Page no. 5, line no. 104-105.

Non-availability of genome sequencing data to show the direct association of B.1.617 leading to adverse outcomes, and single-center study are the limitations of our study.

Reviewer #2:

The manuscript is a research letter which presents data on pregnant and post-partum women infected with COVID-19 in India from the first and second waves of the pandemic. The authors focus on admissions to a single hospital in Mumbai which became a dedicated COVID-19 hospital in mid-April 2020.

1. Introduction, Lines 67-69: Recommend moving this sentence to after line 72.

Response: Necessary changes have been made in the revised manuscript. Page no. 4, line no. 66-68

2. Methods, Lines 80-82: Consider adding graphical representation of the cases in India over time to better delineate cut-points for the first and second waves.

Response: Thank you for the suggestion. We have added a graph showing the pregnant and postpartum women with COVID-19 admitted at BYL Nair Hospital, Mumbai from the beginning of the 1st wave of pandemic till 14th June 2021 to better delineate cut-points for the first and second wave (Figure 1), Page no. 4, Line no. 76.

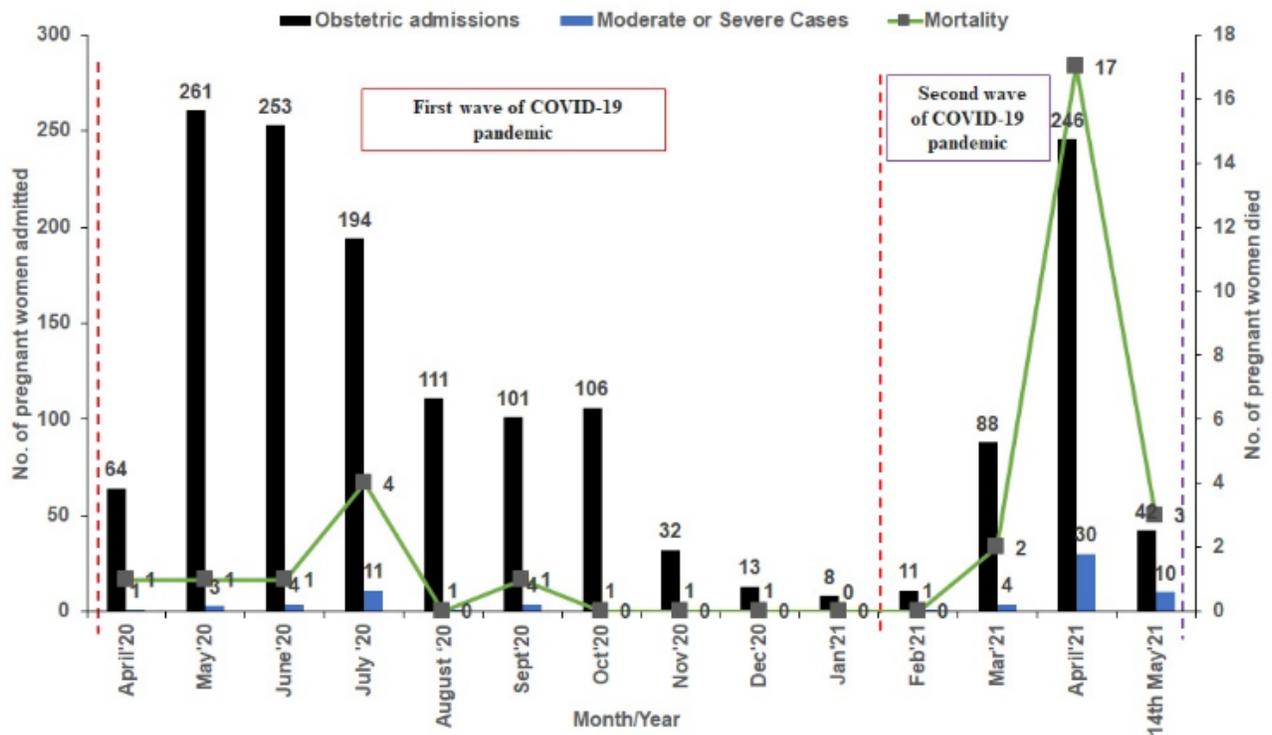


Figure 1: Timelines of the first and second waves of COVID-19 in India

3. Methods, Lines 80-82: From the admission policies in reference 5, the policy changed over time from admitting all pregnant patients with COVID-19 to only those with more moderate to severe disease. Please describe how this policy might have continued to change in the second wave and how this would impact your data. Additionally, while NH is the only dedicated COVID-19 hospital in the area, are COVID patients cared for at other institutions? If so, how is it determined whether the patient is admitted to NH or another facility?

Reply: In mid-April 2020, BYL Nair Hospital, Mumbai was declared as a dedicated COVID-19 hospital. In April, 2020, all pregnant women were admitted irrespective of labor

or symptoms (n =30). From May 2020, the policy was changed. As per the admission policy of NH, pregnant women with COVID-19 who are near-term or need obstetric interventions or symptomatic were admitted. The details are mentioned in reference 5. For more clarity, we are reproducing the text from our published article reference 5 (Mahajan et al.,2020).

“ As the pandemic evolved, the admission policy needed to be updated regularly, taking into consideration the increased inflow of patients. Therefore, the initial policy of admitting all pregnant patients with confirmed COVID-19 was changed to admitting only those with moderate to severe symptoms and those with high-risk pregnancies or requiring active obstetric management. This approach was endorsed by MoHFW in their home isolation guidelines, that mild cases can be managed at COVID Care Centers (CCCs), First Referral Units, Community Health Centers, sub-district and district hospitals, or at home.

Severity-based stratification of inpatients was done on detailed history and clinical examination. With the help of a multidisciplinary approach, patients with moderate to severe disease were moved to the high dependency unit/ICU, while those with mild disease were managed in the wards”.

Our admission policy is uniform during both the waves of COVID-19 (from May 2020 till date). All patients are screened at a special screening outpatient department and only eligible patients are admitted at NH. There are various levels of COVID-19 care centers (CCCs) in MMR, where women who are not in labor, or not requiring obstetric

interventions, or those asymptomatic or mild symptomatic are referred to CCCs or advised home quarantine.

4. Results, Lines 91-94: Recommend adding that these differences did not reach statistical significance.

Response: Necessary changes have been made in the revised manuscript. Page no. 4, line no. 84.

5. Results, Lines 97-102: Make this a new paragraph dedicated to the comparisons of women who died and reference the appropriate tables for each paragraph individually. Also recommend including some comment that no statistical differences were found, likely due to low N.

Response: Necessary changes have been made in the revised manuscript. Page no. 4, line no. 78-94.

6. Results, Line 98: Should be changed to "second wave".

Response: Necessary changes have been made in the revised manuscript. Page no. 4 line no. 87.

7. Discussion: Though it is possible that the current findings may be due to an increase in B.1.617.1 infection, there are many other potential causes to include higher case rates,

changing admission policies, delays in seeking healthcare, etc. Other potential contributors need to be discussed.

Response: As per the suggestion, we have added other potential contributors in the discussion section Page no. 5, line no. 105-108.

8. Table 2: Recommend removing the first line "Total number of pregnant and post-partum women with COVID-19" as this table focuses on those that died and it is confusing to include this here.

Response: Necessary changes have been made in the revised supplementary Table 1.

Reviewer #3:

Lines 91-94: The preterm birth and stillbirth rates were NS different (Table 1). Should explicitly state that or omit from Results, since it is listed in Table 1.

Response: We have added the following sentence in the revised manuscript, page no. 4-line no. 84-85.

However, these differences did not reach statistical significance.

lines 96-102: None of the differences in proportions among those who died during the two time periods were different statistically. The text implies a difference, but none was proven, in part due to low counts and inadequate power. Need to strike or modify this section to conform with Table 2.

Response: We have added the sentence 'No statistical differences were found possibly due to the low sample size' in revised manuscript. Page no. 5, line no. 91-92.

Table 2: This Table compares N = 8 vs N = 22, so all %s should be rounded to nearest integer %, not cited to 0.1% precision. Also, none of the statistical comparisons can be generalized, since they were all NS and vastly underpowered. Also, given the size of the samples, should report ranges, not IQR for the maternal age, length of stay, O2 sat, Resp rates, gestational age.

Response : We have edited table 2 based on the comment and included the revised Table as supplementary Table 1 in revised submission.

EDITOR COMMENT:

Thank you for submitting your work to Obstetrics and Gynecology. If you opt to submit a revision, please modify the precis to focus on what is demonstrated by your results. Since you do not have data on the variant that these patients contracted, it is okay to speculate about the new variant as a reason for increased disease severity in the discussion, but it cannot be the major conclusion of your work in the precis.

Response : We agree with editor and reviewers comments. We have revised the precis as follows:

Precis

Significant increase in symptomatic cases, severe COVID-19 disease, adverse pregnancy outcomes, and high maternal mortality in the second wave of COVID-19 in India

EDITORIAL OFFICE COMMENTS:

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

Please reply to this letter with one of two responses:

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

[Response : OPT-IN: Yes, please publish my point-by-point response letter.](#)

2. Obstetrics & Gynecology uses an "electronic Copyright Transfer Agreement" (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. Each of your coauthors received an email from the system, titled "Please verify your authorship for a submission to Obstetrics & Gynecology." Each author should complete the eCTA if they have not yet done so.

[Response : All authors have verified the authorship for a submission to Obstetrics & Gynaecology](#)

3. 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 : [We have submitted the STROBE check list.](#)

4. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric data definitions at <https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-data-definitions> and the gynecology data

definitions at <https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions>. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

Response : We have used the reVITALize definitions.

5. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Research Letters articles should not exceed 600 words. Stated word limits include the title page, précis, abstract, text, tables, boxes, and figure legends, but exclude references.

Response: The revised manuscript adheres to the word limit of 600 words.

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

- * All financial support of the study must be acknowledged.
- * Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
- * All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your response in the journal's electronic author form verifies that permission has been obtained from all named persons.
- * If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of

the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).

* 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]."

Response : We have revised the manuscript as per the guidelines.

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

Response : Short title 'Pregnancy and second wave of COVID-19' is added in the revised manuscript. page no. 1 line no. 25

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.

Response : We have used the standard abbreviations and acronyms as per the guidelines.

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.

Response : we have not used the virgule symbol (/) in sentences with words.

10. 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 (NNT_h). 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 have revised the manuscript and tables as per the guidelines.

11. 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.

Response : Tables are prepared as per the checklist

12. Please review examples of our current reference style at <http://ong.editorialmanager.com> (click on the Home button in the Menu bar and then

"Reference Formatting Instructions" document under "Files and Resources). Include the digital object identifier (DOI) with any journal article references and an accessed date with website references. Unpublished data, in-press items, personal communications, letters to the editor, theses, package inserts, submissions, meeting presentations, and abstracts may be included in the text but not in the reference list.

In addition, the American College of Obstetricians and Gynecologists' (ACOG) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite ACOG documents in your manuscript, be sure the reference you are citing is still current and available. If the reference you are citing has been updated (ie, replaced by a newer version), please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly (exceptions could include manuscripts that address items of historical interest). If the reference you are citing has been withdrawn with no clear replacement, please contact the editorial office for assistance (obgyn@greenjournal.org). In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All ACOG documents (eg, Committee Opinions and Practice Bulletins) may be found at the Clinical Guidance page at <https://www.acog.org/clinical> (click on "Clinical Guidance" at the top).

Response : References are formatted as per the journal style.

13. 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 <https://wkauthorservices.editage.com/open-access/hybrid.html>.

Response: Not applicable