NOTICE: This document contains correspondence generated during peer review and subsequent revisions but before transmittal to production for composition and copyediting:

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

*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.
RE: Manuscript Number ONG-19-1695

Diffuse large B-cell lymphoma during third-trimester pregnancy and lactation

Dear Dr. Hersey:

Your manuscript has been reviewed by the Editorial Board and by special expert referees. Although it is judged not acceptable for publication in Obstetrics & Gynecology in its present form, we would be willing to give further consideration to a revised version.

If you wish to consider revising your manuscript, you will first need to study carefully the enclosed reports submitted by the referees and editors. Each point raised requires a response, by either revising your manuscript or making a clear and convincing argument as to why no revision is needed. To facilitate our review, we prefer that the cover letter include the comments made by the reviewers and the editor followed by your response. The revised manuscript should indicate the position of all changes made. We suggest that you use the "track changes" feature in your word processing software to do so (rather than strikethrough or underline formatting).

Your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Oct 31, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

GENERAL

The submitted case report describes clinical management of a patient following diagnosis of diffuse lymphatic B-cell lymphoma (DLBCL) at 27 weeks gestation.

* Focusing on the raison d'être of this report: in the authors' opinion, what distinguishes this manuscript from previous publications describing antepartum management of non-Hodgkin's lymphoma? (perhaps synchronization of lactation during postpartum chemotherapy and/or potential precipitation of tumor lysis syndrome by antenatal corticosteroids?) At present the report reads as a descriptive narrative, and this should be explicit in the text.

* The case section can be substantially condensed; as an example: for intended publication in an obstetrical journal, the section on immunohistochemical staining may be reduced to notation of positive pan-B cell antigen immunophenotyping confirming the diagnosis of DLBCL.

* What was this patient's clinical stage? (staging evaluation is mentioned in multiple sections, but the actual stage is not provided).

* Lines 172-174: Were teratogenic effects a concern during imaging evaluation at 27 weeks gestation?

* As antepartum chemotherapy was deferred, was any surveillance maternal or fetal imaging performed between diagnosis and delivery?

ABSTRACT

* Line 40: Syntax of "...is rare with limited research" is awkward. Consider omitting the first two sentences and beginning the manuscript with the third sentence.

* Line 42: I infer the authors intend "intervention" in reference to Oncologic therapy, but this should be clarified.

* Line 48: Consider revising this sentence to reflect the chronologic order of occurrence: i.e. staging - timing of delivery - lactation.

* Line 52: "Teaching point #1" is not a teaching point; consider revision to state "antenatal corticosteroids may have the
potential consequence of precipitating tumor lysis syndrome".

* Line 55: Consider "MRI can substitute for other imaging modalities during pregnancy"

* Line 57: Consider "Pharmacokinetics can be utilized to determine a lactation schedule to minimize neonatal chemotherapy exposure".

INTRODUCTION:
* The first sentence may be omitted.
* Line 66: "usually occurs later in life".
* The last sentence may be relocated to the conclusion of the discussion section.

CASE:
* As noted above, this section should be edited for brevity.
* Line 102: What specialties were represented in the multidisciplinary team? This would be instructional to readers in constructing a team during a similar clinical scenario.
* Line 113: "Under close surveillance" is a colloquial expression; in a formal submission specifics should be stated (i.e. "weekly prenatal visits, etc.").
* The description of the postpartum lactation protocol (Lines 188-192) should be included in this section.
* Lines 167-177: Consider briefly describing standard evaluation, with modifications for pregnancy (see above ACOG committee opinion reference).

DISCUSSION:
* Line 143: Caution should be exercised in concluding chemotherapy is associated with spontaneous preterm delivery: in the citation listed (Lee, 2014), only 2 of the 4 preterm deliveries (50%) resulted from spontaneous preterm labor (Table 1); in further reviewing the source citations, 1 of the patients underwent indicated induction of labor and the other is unspecified.
* (as above) Antenatal corticosteroids precipitating tumor lysis syndrome is an interesting concept (I was unable to locate any case reports), and together with coordination of chemotherapy and lactation constitute the unique aspects of the current manuscript.

TABLE/FIGURE:
* Figure 1 (histopathologic images) may be omitted for publication in an obstetrical journal

Reviewer #2: The authors submit a case report of diffuse large B cell lymphoma in pregnancy. I have the following comments regarding the manuscript:

Teaching Points
1. Point 1: The consideration in this case seemed more related to tumor lysis syndrome in the setting of antenatal corticosteroid administration for fetal lung development. This seems like a better teaching point than what is currently written.

2. Point 2: To say that MRI is the preferred staging method in pregnancy seems to go beyond what can be demonstrated in this case report. Perhaps something more like: Although suboptimal, MRI can be used for initial staging during pregnancy. The patient still needed a postpartum PET scan for staging to be completed.

3. Point 3: Change "there is data" to "there are data" since the word data is plural.

Case
1. Line 164. I am not sure that one can argue that the benefit of one dose of late preterm steroids "greatly outweighed" the risk of tumor lysis syndrome. In the ALPS trial, there was a small benefit related to short term respiratory morbidity. Would be cautious in making a statement like this and favor just taking it out or significantly revising it.

2. Line 116. Change APGARS to Apgar scores. It is not an acronym (named after Virginia Apgar).

3. Line 184. Can the authors provide a reference for the idea that the half-life of drug in the breastmilk is the same as the half-life of the drug? This is often not the case.
Discussion

1. In my opinion, the discussion needs to clarify that in the vast majority of cases, chemotherapy should not be withheld during pregnancy. I realize that this patient had a favorable risk profile, but I do not want the course in this case to be extrapolated inappropriately to women in early pregnancy or with more advanced or aggressive cancer.

EDITOR COMMENTS:

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

***The notated PDF is uploaded to this submission's record in Editorial Manager. If you cannot locate the file, contact Randi Zung and she will send it by email - rzung@greenjournal.org.***

- please amend the "multidisciplinary approach" aspect here. It goes without saying that such care of such a patient requires many disciplines.

- what is the denominator here? Live births? Or is that 1/1000 people with lymphoma are pregnant?

- underwent labor induction

- this is an OB journal and none of us will know what the standard R-CHOP protocol is. Perhaps just say "a standard chemotherapeutic protocol" in the abstract.

- again, please modify the "multidisciplinary approach" comment,

- If other staging is the standard method, you may wish to say something like "MRI may be substituted for standard staging using CT scans with contrast if adequate imaging is obtained" [I made that up--I don't know the standard imaging modalities used.]

- 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 things. Adherence to these requirements with your revision will avoid delays during the revision process, as well as avoid re-revisions on your part in order to comply with the formatting. For instance, we don't number the headings.

- instead of "multidisciplinary approach" which is really a throw-away term, consider something like "This case highlights the need to consider all aspects of her proposed oncologic and obstetrical care, as well as neonatal risks". That specifies what the "multidisciplinary" refers to and adds a lot more meaning.

- she is of course female. Please omit. Just A 38 year old, G4 P 1021 whose....

- As noted by one of your reviewers, you have submitted this to an OB journal. As such, much of what is commonly known information in the oncology domain will be unintelligible to the OB community. Rather than shorthand this information (which is fine to include) can you also tell us what this means? Is this TI RADS risk category of TR4 a high risk? Low risk? I recommend you have an Ob resident read your paper at submission and see if they understand all of the oncology information to see if you have it clearly written

- Your paper has a lot of extra words. Please try to condense: Perhaps: "Results of tissue analysis from fine needle aspiration including morphologic, immunophenotypic and molecular cytogentic studies supported the diagnosis of..." and then include the specifics that will important for oncologic readers in the footnote of the images.

- who was on the team? Why was 34 weeks chosen? What considerations were include (for instance, is there are typical rate of progression? Where you worried about her airway? Articulate the factors that caused this recommendation to be made.

- why was staging done after management plan was made? This whole paragraph 102-112 is critical to your case as you modified several things, apparently. (Staging method, chemo timing after diagnosis, etc). Be clear what considerations were being made in this planning---this is where the give and take of the multiple disciplines needs to get described and a comment about what the potential problems of the different modifications in standard care should be
described.

- what does this mean?

- At about 45 days post partum, she was doing well and undergoing cycle 3 of her chemotherapy. Her infant is well. You don't mention her avoidance of breastfeeding here. Please comment.

- please provide the search terms and database used (Pubmed? Embase? Scopus? clinicaltrials.org?) that you used to be able to describe the existing literature as "small"? Also, what does a 'subset of literature' refer to?

- do we know if these were indicated or spontaneous preterm births? Also, wouldn't be known if the cases were spontaneous if they were chemo related or related to her underlying illness or of course, just the occurrence of a spontaneous preterm birth that might have happened if the woman had not been ill. Please rephrase.

- its not care for preterm birth, its care for women at risk of preterm birth

- This paragraph is a superb example of the type of give and take I've mentioned above that needs to be considered in these sorts of cases.

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

3. As of December 17, 2018, Obstetrics & Gynecology has implemented an "electronic Copyright Transfer Agreement" (eCTA) and will no longer be collecting author agreement forms. 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.

4. Our journal requires that all evidence-based research submissions be accompanied by a transparency declaration statement from the manuscript's lead author. The statement is as follows: "The lead author* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained."
   *The manuscript's guarantor.

   If you are the lead author, please include this statement in your cover letter. If the lead author is a different person, please ask him/her to submit the signed transparency declaration to you. This document may be uploaded with your submission in Editorial Manager.

5. 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.

6. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Case Reports should not exceed 8 typed, double-spaced pages (2,000 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.

7. 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).

8. Provide a short title of no more than 40 characters, including spaces, for use as a running foot.

9. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

In addition, the abstract length should follow journal guidelines. The word limits for different article types are as follows: Case Reports, 125 words. Please provide a word count.

10. Only standard abbreviations and acronyms are allowed. A selected list is available online at http://edmgr.ovid.com/ong/accounts/abbreviations.pdf. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

11. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

12. Figure 1: Please upload as a high-res figure file (eps, tiff, jpeg) to Editorial Manager. Please remove the A-D labels on the figure. These will be added back per 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 http://edmgr.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.

14. 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.

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 Oct 31, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Nancy C. Chescheir, MD
Editor-in-Chief

2018 IMPACT FACTOR: 4.965
2018 IMPACT FACTOR RANKING: 7th out of 83 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.
Dear Editor and Reviewers,

Thank you for your correspondence regarding our case report entitled, “Diffuse large B-cell lymphoma during third-trimester pregnancy and lactation”. We are delighted that the Editorial Board is willing to reconsider our manuscript following revisions and re-submission for possible publication in the Obstetrics & Gynecology.

We would like to thank the Reviewer’s and the Editor for their time and consideration. We appreciate the thoughtful comments and have made every effort to incorporate these into the revised case report. The manuscript now highlights the unique considerations of this case, including the theoretical risk of tumor lysis syndrome with antenatal steroids, preliminary staging in the antepartum period, and lactation during chemotherapy.

As requested, we revised the manuscript and provided a point-by-point account describing how we responded to the Reviewers’ comments starting on page 2 of this cover letter. Each response is below the comment it is meant to address, and additions to the text are indicated in bold font. The manuscript shows revisions with tracked changes.

We hope you find these revisions acceptable as we have sought to be highly responsive to the Reviewers and Editor’s comments. As requested, the authors read the Instructions for Authors closely and have adhered to the formatting guidelines. All authors have considered the comments and have approved the revised manuscript. Thank you again for your consideration.

Sincerely,

Alicia Hersey (Corresponding Author)
Our responses to the comments are below, noting the corresponding changes in the paper with **bold** typeface in this document and tracked changes of the submitted manuscript. All line numbers citing changes by the authors in this document are corresponding to lines when viewing the case report as “Show all markup” in Word.

REVIEWER COMMENTS:

Reviewer #1:

GENERAL

The submitted case report describes clinical management of a patient following diagnosis of diffuse lymphatic B-cell lymphoma (DLBCL) at 27 weeks gestation.

* Focusing on the raison d'être of this report: in the authors' opinion, what distinguishes this manuscript from previous publications describing antepartum management of non-Hodgkin's lymphoma? (perhaps synchronization of lactation during postpartum chemotherapy and/or potential precipitation of tumor lysis syndrome by antenatal corticosteroids?) At present the report reads as a descriptive narrative, and this should be explicit in the text.
  - We thank Reviewer 1 for this comment. We have edited the manuscript for brevity and to further focus on these 2 unique points.

* The case section can be substantially condensed; as an example: for intended publication in an obstetrical journal, the section on immunohistochemical staining may be reduced to notation of positive pan-B cell antigen immunophenotyping confirming the diagnosis of DLBCL.
  - We thank Reviewer 1 for this general comment. We agree that the case section can be condensed and have made the following changes:
    - The section on immunohistochemical staining (lines 88-103) was condensed to the following statement (lines 101-103): **Fine needle aspiration revealed morphologic, immunophenotypic, and molecular cytogenetics supporting the diagnosis of DLBCL.**

* What was this patient's clinical stage? (staging evaluation is mentioned in multiple sections, but the actual stage is not provided).
  - We greatly appreciate Reviewer 1’s comments regarding clinical stage.
    - We have incorporated the accurate clinical staging into this manuscript on lines 159-160: **Single nodal involvement without symptoms was consistent with Ann Arbor Stage IA DLBCL.**

* Lines 172-174: Were teratogenic effects a concern during imaging evaluation at 27 weeks gestation?
  - In accordance with ACOG Guidelines (Committee No 723), MRI is preferred over CT to avoid harms of ionizing radiation during pregnancy. CT may be considered if deemed clinically necessary. In this case, the specialists determined that MRI was adequate for initial staging. We have revised the manuscript to clarify this.
As antepartum chemotherapy was deferred, was any surveillance maternal or fetal imaging performed between diagnosis and delivery?
- The patient was followed with weekly visits without any clinical progression. Her antepartum MRI was also reassuring, and therefore she did not undergo further imaging prior to delivery.
  - This was added to the manuscript on lines (147-149): The patient was followed with weekly Hematology-Oncology and obstetric visits under close surveillance and had no further mass enlargement or new symptoms.

ABSTRACT
* Line 40: Syntax of "...is rare with limited research" is awkward. Consider omitting the first two sentences and beginning the manuscript with the third sentence.
- We agree with Reviewer 1 that the syntax of the first sentence is awkward. After consideration, the authors have removed the first 2 sentences.
  - The first sentence of the manuscript now reads (Lines 64-66): The fourth most common malignancy affecting pregnancy is lymphoma, affecting 1 in 1,000-6,000 pregnancies with potential to metastasize to the placenta and fetus.

* Line 42: I infer the authors intend "intervention" in reference to Oncologic therapy, but this should be clarified.
- We thank Reviewer 1 for these remarks, as we understand our language was vague and needed clarification. The authors changed the word “intervention” to “management” to clarify that the management of DLBCL in pregnancy is based on the balance between oncologic therapy and obstetrical management.
  - The sentence now reads (Lines 40-41): Management of lymphoma during pregnancy highlights the need to consider all aspects of proposed oncologic and obstetrical care, as well as neonatal risks.

* Line 48: Consider revising this sentence to reflect the chronologic order of occurrence: i.e. staging - timing of delivery - lactation.
- We thank Reviewer 1 for this suggestion. Due to additional comments from other reviewers, we have revised this sentence.
  - Lines 40-45: Management of lymphoma during pregnancy highlights the need to consider all aspects of proposed oncologic and obstetrical care, as well as neonatal risks. Considerations highlighted in this case include of staging methods, antenatal steroids, timing of delivery, and lactation.

* Line 52: "Teaching point #1" is not a teaching point; consider revision to state "antenatal corticosteroids may have the potential consequence of precipitating tumor lysis syndrome".
- Reviewer 1 noted that Teaching point #1 is a statement, not a teaching point. We agree with the suggested wording Reviewer 1 provided and have made the appropriate changes.
  - Line 51-52: Antenatal corticosteroid administration for fetal lung development may have the potential consequence of precipitating tumor lysis syndrome.

* Line 55: Consider "MRI can substitute for other imaging modalities during pregnancy"
- We thank Reviewer 1 for this suggestion. Teaching point 2 now states (lines 53-55):
Although suboptimal, MRI can substitute for standard imaging modalities, such as CT or PET scan, for initial cancer staging during pregnancy.

* Line 57: Consider "Pharmacokinetics can be utilized to determine a lactation schedule to minimize neonatal chemotherapy exposure".
- We agree this phrasing is preferred and have changed teaching point 3 to the following sentence (Lines 56-59): Although there is limited data explicitly quantifying the amount of some chemotherapy drugs in breastmilk, pharmacokinetics can be utilized to determine a lactation schedule to minimize neonatal chemotherapy exposure.

INTRODUCTION:
* The first sentence may be omitted.
- We thank Reviewer 1 for this suggestion and agree this sentence does not substantially contribute to the case report. This sentence was removed.

* Line 66: "usually occurs later in life".
- This edit was made on line 67.

* The last sentence may be relocated to the conclusion of the discussion section.
- We agree with Reviewer 1 that this is a summary statement and would better serve this case report if it were moved to the conclusion of the discussion section.
- The following sentence is found on Lines 269-275: This case of DLBCL in pregnancy discusses the following unique considerations; the theoretical risk of preterm birth with antepartum chemotherapy versus induction at 34 weeks, the potential risk of tumor lysis syndrome with antenatal steroids, the use of MRI for preliminary antepartum staging, and lactation during chemotherapy.

CASE:
* As noted above, this section should be edited for brevity.
- The authors have edited for brevity. See tracked changes in the manuscript.

* Line 102: What specialties were represented in the multidisciplinary team? This would be instructional to readers in constructing a team during a similar clinical scenario.
- We appreciate Reviewer 1 for noting that adding the specialties involved in the patient’s care team would be instructional to future providers.
- The following revisions were made on (104-106): A team of specialists from General Obstetrics, Maternal-Fetal Medicine (MFM), Hematology-Oncology, Neonatology, and Obstetric & Consultative Medicine was assembled to discuss the patient’s care plan.

* Line 113: "Under close surveillance" is a colloquial expression; in a formal submission specifics should be stated (i.e. "weekly prenatal visits, etc.").
- We thank Reviewer 1 for this comment and have added the specifics of her antepartum monitoring.
* The description of the postpartum lactation protocol (Lines 188-192) should be included in this section.
- We agree with Reviewer 1 that a statement of the lactation protocol should be included here. A sentence was added in the case section (Lines 142-146) and expanded upon in the discussion.
  - **Based on her strong desires to breastfeed, a lactation protocol was also developed for the postpartum period using the pharmacokinetics of the chemotherapy agents. The patient would be on a 21-day chemotherapy schedule, which would allow her to pump and discard breast milk for the first 10 days following treatment, and then breastfeed for the remaining 10 days before her next treatment.**

* Lines 167-177: Consider briefly describing standard evaluation, with modifications for pregnancy.
- We thank Reviewer 1 for this suggestion. In the discussion, we described the standard evaluation for DLBCL staging and the modifications for pregnancy in adherence with ACOG practice guidelines (Committee No 723).

**DISCUSSION:**
* Line 143: Caution should be exercised in concluding chemotherapy is associated with spontaneous preterm delivery: in the citation listed (Lee, 2014), only 2 of the 4 preterm deliveries (50%) resulted from spontaneous preterm labor (Table 1); in further reviewing the source citations, 1 of the patients underwent indicated induction of labor and the other is unspecified.
- We appreciate Reviewer 1 for noting that the current wording may overstate the relationship between spontaneous preterm delivery and chemotherapy.
  - We have reworded the sentence as follows (Lines 184-186): **In a case report and literature review, Lee et al. discusses a possible risk of chemotherapy-related preterm labor.**

* (as above) Antenatal corticosteroids precipitating tumor lysis syndrome is an interesting concept (I was unable to locate any case reports), and together with coordination of chemotherapy and lactation constitute the unique aspects of the current manuscript.
- We thank Reviewer 1 for highlighting this. We have edited the manuscript to help highlight these unique considerations in this case.

**TABLE/Figure:**
* Figure 1 (histopathologic images) may be omitted for publication in an obstetrical journal.
- We thank Reviewer 1 for this comment. We have reduced technical description in text and have removed the figure.

Reviewer #2: The authors submit a case report of diffuse large B cell lymphoma in pregnancy. I have the following comments regarding the manuscript:

Teaching Points
1. Point 1: The consideration in this case seemed more related to tumor lysis syndrome in the setting of antenatal corticosteroid administration for fetal lung development. This seems like a better teaching point than what is currently written.
   - We appreciate Reviewer 2’s feedback regarding teaching point 1. This teaching point was rephrased to reflect this suggestion and now states:
     - (Lines 51-52): Antenatal corticosteroid administration for fetal lung development may have the potential consequence of precipitating tumor lysis syndrome.

2. Point 2: To say that MRI is the preferred staging method in pregnancy seems to go beyond what can be demonstrated in this case report. Perhaps something more like: Although suboptimal, MRI can be used for initial staging during pregnancy. The patient still needed a postpartum PET scan for staging to be completed.
   We thank Reviewer 2 and agree that teaching point 2 should be re-worded to avoid overstating the use of MRI for cancer staging in pregnancy.
   - Teaching point 2 was rephrased (Lines 53-55): Although suboptimal, MRI can substitute for standard imaging modalities, such as CT or PET scan, for initial cancer staging during pregnancy.

3. Point 3: Change "there is data" to "there are data" since the word data is plural.
   - Thank you for noting this error, the above change was made.

Case
1. Line 164. I am not sure that one can argue that the benefit of one dose of late preterm steroids "greatly outweighed" the risk of tumor lysis syndrome. In the ALPS trial, there was a small benefit related to short term respiratory morbidity. Would be cautious in making a statement like this and favor just taking it out or significantly revising it.
   - We thank Reviewer 2 for this comment and agree that this statement should be removed from the case report.
     - The following changes were made to lines 207-216: After preliminary staging MRI confirmed stage 1A localized disease, with low likelihood of placental or fetal involvement, the team concluded that there was a low risk of tumor lysis syndrome. The patient ultimately received intramuscular betamethasone prior to induction of labor. The benefit of steroid use for fetal lung maturity prior to induction therefore greatly outweighed the risk.

2. Line 116. Change APGARS to Apgar scores. It is not an acronym (named after Virginia Apgar).
   - We thank Reviewer 2 for noting this error and have made the appropriate correction.

3. Line 184. Can the authors provide a reference for the idea that the half-life of drug in the breastmilk is the same as the half-life of the drug? This is often not the case.
   - We appreciate Reviewer 2 for bringing this to the authors’ attention. It is true that the half-lives are usually not the same. However, the half-life of this drug was used because there is limited data on the concentration of chemotherapy drugs in breastmilk, and there is no published data on
the maternal or infant levels of vincristine. Therefore authors utilized the half-life as described in Anderson’s 2016 commentary and briefly in Pistilli’s 2013 review.

- The following changes were made on lines 253-258: One method of determining the timing of breastfeeding if there are no pharmacologic data available is the use of the drug’s half-life as a “proxy” for its half-life in breastmilk. The waiting period between chemotherapy and breastfeeding can be determined by using the longest half-life in the drug regimen. A waiting period between 3 and 5 times the half-life is considered safe.(8) There are currently no published data on breastmilk or infant concentrations of vincristine.

Discussion

1. In my opinion, the discussion needs to clarify that in the vast majority of cases, chemotherapy should not be withheld during pregnancy. I realize that this patient had a favorable risk profile, but I do not want the course in this case to be extrapolated inappropriately to women in early pregnancy or with more advanced or aggressive cancer.

- We appreciate Review 2 highlighting this. We have reworded this section to make clear this patient had a favorable risk profile and presented late in pregnancy, and this is not the standard of care for other cases of DLBCL in pregnancy. Please see the modifications below (Lines 179-197):

This case joins a small number of case reports that discuss the diagnosis and management of DLBCL during pregnancy. Other case reports discuss patients diagnosed in the first or second trimester, who received at least 3 cycles of chemotherapy prior to delivery.(3)

Antepartum chemotherapy treatment is often deemed necessary in cases of DLBCL diagnosed early, at an advanced stage, or as an aggressive subtype. In a case report and literature review, Lee et al. discusses a possible risk of chemotherapy-related preterm labor. Other risks of antepartum chemotherapy have also been elucidated, including transient myelosuppression of the neonate, fetal growth restriction, and neonatal dilated cardiomyopathy.(2) This case describes a patient who presented in the third trimester with a favorable risk profile based on clinical presentation, preliminary staging, and histopathology. A team of specialists convened to determine a management plan after considering the various risks: antepartum chemotherapy with possible adverse neonatal outcomes, delayed postpartum chemotherapy with disease progression, and a planned preterm delivery. The ultimate management was influenced by the patient’s presentation in the third trimester, early stage, and low-grade disease without clinical evidence of rapid progression.

EDITOR COMMENTS:

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

***The notated PDF is uploaded to this submission's record in Editorial Manager. If you cannot locate the file, contact Randi Zung and she will send it by email - rzung@greenjournal.org.***
- please amend the "multidisciplinary approach" aspect here. It goes without saying that such care of such a patient requires many disciplines.
We thank the Editor for suggesting we amend the “multidisciplinary approach” aspect. We have removed this from the manuscript.

- what is the denominator here? Live births? Or is that 1/1000 people with lymphoma are pregnant?
We thank the Editor for noting this is unclear and removed for brevity of abstract.

- underwent labor induction
This was clarified, thank you.

- this is an OB journal and none of us will know what the standard R-CHOP protocol is. Perhaps just say "a standard chemotherapeutic protocol" in the abstract.
We thank the Editor for this comment. The suggested revision was made, and the abstract now states on Lines 37-39:
  - The patient underwent labor induction at 34 weeks, started a standard chemotherapeutic protocol postpartum, and breastfed with periods of abstinence between chemotherapy treatments.

- again, please modify the "multidisciplinary approach" comment,
Addressed, as noted above.

- If other staging is the standard method, you may wish to say something like "MRI may be substituted for standard staging using CT scans with contrast if adequate imaging is obtained" [I made that up--I don't know the standard imaging modalities used.]
We appreciate this suggestion and have reworded the sentence to clarify the standard staging method.

- 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 things. Adherence to these requirements with your revision will avoid delays during the revision process, as well as avoid re-revisions on your part in order to comply with the formatting. For instance, we don't number the headings.
We apologize for this oversight. We have re-read the instructions for authors and have fixed these formatting issues within the case report.

- instead of "multidisciplinary approach" which is really a throw-away term, consider something like "This case highlights the need to consider all aspects of her proposed oncologic and obstetrical care, as well as neonatal risks". That specifies what the "multidisciplinary" refers to and adds a lot more meaning.
We thank the Editor for this comment. We have removed this sentence in response to Reviewer 1’s comments. A similar statement is now found at the end of the conclusion section.

- she is of course female. Please omit. Just A 38 year old, G4 P 1021 whose.... Thank you, the word “female” was omitted as suggested.

- As noted by one of your reviewers, you have submitted this to an OB journal. As such, much of what is commonly known information in the oncology domain will be unintelligible to the OB community. Rather than shorthand this information (which is fine to include) can you also tell us what this means? Is this TI RADS risk category of TR4 a high risk? Low risk? I recommend you have an Ob resident read your paper at submission and see if they understand all of the oncology information to see if you have it clearly written
We thank the Editor for this great recommendation. The short-hand was eliminated and we more concretely defined what the imaging results meant and led to.

- The section now reads (lines 84-86): Thyroid ultrasound demonstrated a 4.4 cm solid, hypoechoic, irregular thyroid nodule in the left lobe suspicious for malignancy based on American College of Radiology criteria and prompting fine-needle aspiration.

Your paper has a lot of extra words. Please try to condense: Perhaps: "Results of tissue analysis from fine needle aspiration including morphologic, immunophenotypic and molecular cytogenetic studies supported the diagnosis of..." and then include the specifics that will important for oncologic readers in the footnote of the images.
We thank the Editor for this comment and have condensed the tissue analysis description.

- The section on immunohistochemical staining (lines 88-103) was condensed to the following statement (lines 101-103): Fine needle aspiration revealed morphologic, immunophenotypic, and molecular cytogenetics supporting the diagnosis of DLBCL.

- who was on the team? Why was 34 weeks chosen? What considerations were include (for instance, is there are typical rate of progression? Where you worried about her airway? Articulate the factors that caused this recommendation to be made.
We thank the Editor for this comment and have made edits to be clearer in the thought process amongst the team (lines 104-142). Her management plan was developed over time, with initial MRI that was subsequently reassuring, as well as weekly follow-up visits in which her clinical picture was stable. This solidified a plan to defer delivery to 34 weeks. Because she was stable with a favorable risk profile, we believed deferring chemotherapy for ~3-4 weeks until after delivery would not significantly alter her outcome or survival. 34 weeks also struck a balance between allowing time for fetal lung maturity and still getting prompt postpartum chemotherapy. It is possible for DLBCL to progressively grow or spread. This prompted the weekly visits and a contingency plan to deliver early if there was maternal or fetal compromise. We have edited this section for clarity (see edited paragraphs on lines 104-142):

- A team of specialists from General Obstetrics, Maternal-Fetal Medicine (MFM), Hematology-Oncology, Neonatology, and Obstetric & Consultative Medicine was assembled to discuss the patient’s care plan. A preliminary plan was made for initial staging with MRI and weekly follow-up with Hematology-Oncology and her general obstetrician. Three weeks after initial presentation, the patient had a stable physical
exam without signs of tumor growth or clinical progression. MRI of the chest, abdomen, and pelvis confirmed a 4.8 cm x 4.6 cm x 3.1 cm left thyroid nodule with no mediastinal, suprACLavicular, axillary, or abdominal lymphadenopathy. Based on her stable clinical picture and reassuring MRI findings, her team subsequently recommended delivery at 34 weeks with continued close monitoring. The timing of delivery was determined based on input from Hematology-Oncology, MFM, and Neonatology. Specialists agreed delivery at 34 weeks balanced the risk of adverse outcomes associated with preterm birth, such as fetal lung maturity, with the risk of disease progression in the setting of delayed chemotherapy. This decision was also influenced by the patient’s close follow-up and proximity to a level III NICU. A plan for earlier delivery was developed if the patient had rapidly progressive tumor growth or fetal compromise.

The team also discussed initiation of chemotherapy. The standard of care for treatment of DLBCL is a combination chemotherapy regimen containing Rituximab, Cyclophosphamide, Doxorubicin Hydrochloride, Vincristine Sulfate, and Prednisone (R-CHOP). In discussion with Hematology-Oncology, the risk of waiting to initiate chemotherapy until after delivery was tumor growth and spread. However, this risk was thought to be low based on the patient’s stable clinical and localized radiologic findings. In discussion with MFM, the risk of antepartum chemotherapy to the fetus was thought to be greater than risk of disease progression, and the patient agreed to defer treatment until the postpartum period.

- why was staging done after management plan was made? This whole paragraph 102-112 is critical to your case as you modified several things, apparently. (Staging method, chemo timing after diagnosis, etc). Be clear what considerations were being made in this planning---this is where the give and take of the multiple disciplines needs to get described and a comment about what the potential problems of the different modifications in standard care should be described.
  - We thank the Editor for this comment and have edited appropriately. We wanted to make it clear that during the initial meeting with the team, a very preliminary plan was made that included obtaining MRI for initial staging. At the time of that meeting, there was discussion about possible timing of delivery. It was not until after her MRI results and subsequent follow-up visits with a stable clinical picture that the team deemed it appropriate to defer delivery to 34 weeks, based on improved outcomes in late preterm infants. We hope we have addressed the multiple considerations in our edits.

- what does this mean?
The patient also had enhanced activity in the right lobe of the thyroid on PET scan. It does not add or change the case, and therefore was removed for brevity.

- At about 45 days postpartum, she was doing well and undergoing cycle 3 of her chemotherapy. Her infant is well. You don't mention her avoidance of breastfeeding here. Please comment. We have added a statement to highlight that the breastfeeding protocol was continued at home
  - (Line 169): She continued the aforementioned breastfeeding protocol at home.

- please provide the search terms and database used (Pubmed? Embase?)
Scopus? [clinicaltrials.org](https://clinicaltrials.org/)?) that you used to be able to describe the existing literature as "small"? Also, what does a "subset of literature' refer to?

- We utilized PubMed and searched for “diffuse large B-cell lymphoma” and “pregnancy” as well as “diffuse large B-cell lymphoma” and “lactation” or “breastfeeding”. We updated this opening of the discussion to highlight the literature is limited to a few case reports.

- do we know if these were indicated or spontaneous preterm births? Also, wouldn't be known if the cases were spontaneous if they were chemo related or related to her underlying illness or of course, just the occurrence of a spontaneous preterm birth that might have happened if the woman had not been ill. Please rephrase.

- We thank the Editor for this comment, it is correct that it is impossible to determine the cause of a spontaneous preterm birth. In the case and review by Lee et al., 1 case was an induction at 34’4 and 3 were spontaneous preterm births. We rephrased the discussion regarding this review as it may suggest a risk of spontaneous preterm birth but is not definitive.

- We have reworded the sentence as follows (Lines 184-186): **In a case report and literature review, Lee et al. discusses a possible risk of chemotherapy-related preterm labor.**

- its not care for preterm birth, its care for women at risk of preterm birth. Thank you, this was clarified.

- This paragraph is a superb example of the type of give and take I've mentioned above that needs to be considered in these sorts of cases.