Reviewer’s report

Title: Adjuvant breast cancer chemotherapy during late-trimester pregnancy - evidence-based standard of care, or irrational fashion?

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Reviewer: Matthew Ellis

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The title—while adjuvant chemotherapy may not be ‘evidence based standard of care’ it does not appear to be ‘irrational fashion’

Therapeutic effect:

The author proposes that chemotherapy may not be as effective during the hormone milieu of pregnancy. This may be true, but it may also be untrue, and it will likely never be studied or known. The majority of breast cancers occurring during pregnancy are likely to be ER negative (same as age matched controls) and the value of hormone therapy only applies to the ER+ cases.

Altering adjuvant chemotherapy regimens during the second trimester will often not necessary. For node negative cancers, four cycles of an anthracycline containing regimen would be considered adequate. For node positive cases, where a taxane would be considered, four to six cycles of an anthracycline containing regimen could be given during pregnancy, with the taxane give after delivery. For her-2-neu positive patients, there is good evidence that delaying trastuzumab until after delivery is likely still effective (HERA). So, there are few patients for whom the design of the adjuvant chemotherapy regimen will need to be compromised.

A major component of the argument is that immediate chemotherapy may have adverse effects on the fetus. I have several problems with this portion of the argument:

At what point does the fetus become a ‘client’ in this healthcare decision? This is a philosophical and ethical issue that is not addressed at all in the paper.

Currently therapeutic abortion is considered a reasonable practice for pregnant women diagnosed with breast cancer. Is not chemotherapy during pregnancy a better option for the unborn child?

While chemotherapy during pregnancy has not been proven absolutely safe, the case series that have been reported have generally supported its safety. This is not definitive evidence of long term safety, but why suppose an adverse effect when none has been seen in the studies reported so far?

The claim is made that prioritization of decisions in favor of the fetus would support delaying all therapy until after delivery. I’m not sure this is true. What are the potential effects of progression of the cancer during pregnancy on the fetus? What are the potential effects of recurrence in the mother after delivery—both physically and psychologically on the child? Could the psychological effects be worse if the child new the mother deferred therapy for his/her sake?

While overall, this paper is more clearly written and argued, I have several reservations and specific points of argument that are problematic. In what world would the fetus be considered the primary ‘client’ in making these decisions? Would not the optimal approach to treating these women offer both the mother and fetus a high probability of healthy survival? The basic premise, that gestational chemotherapy has not been proven safe and effective is true. Even the general conclusion that delaying or deferring chemotherapy in certain women is rational. I am not sure the argument supporting these facts is presented in the clearest fashion.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare no competing interests