October 5th, 2020
Prof. Sami Akbulut, FACS, MD
Prof. Vassilios Papalois, FEBS, FICS, FRCS, MD, PhD
Prof. Maurizio Salvadori, MD
Editors-in-Chief
*World Journal of Transplantation*

Dear Prof. Akbulut, Papalois, and Salvadori:

We are pleased to re-submit for publication our review article titled: ***"Obstetrical and Gynecologic Challenges in the Liver Transplant Patient"***.

We are grateful to the editors and reviewers for providing insightful feedback on our study. We have carefully reviewed the recommendations and have revised our manuscript accordingly. Addressing each of their comments has certainly improved our manuscript. Detailed responses to the reviewers' comments are provided below.

**Reviewer 1:**

**Comment 1.1:** "*1- the authors mentioned that first post partum ltx was reported in 1990 please add the etiology of ltx in this case*"

**Response:**
We added that information.

**Comment 1.2:** "*2- in pregnancy after ltx section: the method of contraception is a matter of controversy in women after ltx please add the pro and cons of the different methods of contraception. The authors mentioned oral contraceptives and transdermal patches however there are some withdrawals on these methods.*"

**Response:**
We elaborated further on that section.

**Comment 1.3:** "*3- in outcomes of pregnancy after ltx section: The authors mentioned the rate of rejection varies between 0-20% More details on management and outcome of rejection in such cases such as prognosis, adding MMF after labor.....*"

**Response:**
There is insufficient evidence on the management of rejection during pregnancy in LT recipients. However, we further elaborated on the immunosuppressive regimens used during pregnancy in LT recipients. We also added the FDA pregnancy category for each agent in **Table 2**.

**Comment 1.4:** "*4- the authors didn't come to the issue of breast feeding which is important aspect in this context*"

**Response:**
We would like to thank the reviewer for pointing out that we did not elaborate on this important aspect. We now added a whole paragraph on this topic.

## Reviewer 2:

**Comment 2.1:** "*To increase its value, I would recommend a more detailed analysis regarding etiology of liver disease and possible complications during pregnancy. The authors have stated about the effect of alcohol on fertility, but for example autoimmune disease and impact on recrudescence or rejection would be important to tailor the immunosuppression regimen.*"

**Response:**
The evidence on pregnancy outcomes by liver disease etiology is scarce. The authors of a recent meta-analysis performed meta-regression to identify factors associated with the rate of live birth and showed that the indication for LT is generally not associated with adverse pregnancy outcomes, except for Wilson's disease which has been associated with lower live birth rates. We added that information.

We have also further elaborated on the risk of immunosuppression during pregnancy based on the available data in the literature.

**Comment 2.2:** "*Furthermore a comparison with the outcomes of pregnancy in solid organ transplantation in general would help the reader to understand what is peculiar of liver patients and what is common instead to transplantation and immunosuppression.*"

**Response:**
We added that information in an additional table (**Table 3**).

**Comment 2.3:** "*Finally, what is the authors' approach in the case of induced delivery? How would they manage pregnant woman with acute liver failure?*"

**Response:**
Life of the mother takes precedence in order to save the life of the fetus. The acute liver failure would need to be addressed and treated both from the standpoint of supporting the liver function as well as from identifying potential causes. Additionally, there would need to be consideration for an emergency transplantation if the patient meets criteria. Options would include, apart from a deceased donor which is not readily available, a living donor liver transplantation or even a heterotopic transplantation of a partial graft. The thinking behind the latter is that if you believe that the patient's liver will regain function eventually if she is able to survive the acute episode, then you transplant a partial graft heterotopically to provide liver function for the needed period of time, and then once the patient's liver is improved you can stop the immunosuppression so that the heterotopic liver gets rejected and the patient still has function from her own. This way you can also avoid long-term immunosuppression. The timing of the delivery will have to be in coordination with how the mother is responding to the treatment of the acute liver failure and it could even be at the time of the transplant as a C-section, again depending on the overall condition of the mother and the fetus viability.

We hope that with these revisions, our work is felt appropriate to publish in *World Journal of Transplantation* and perceived as educational to the Journal's readership. Thank you again for inviting us to submit the second revision our work to your journal. We would be pleased to answer any additional concerns or questions you may have.

Sincerely,

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