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Placental pathology, neonatal birthweight and Apgar score in acute and distant SARS-CoV-2 infection

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Placental Pathology, Neonatal Birthweight and Apgar Score in Acute and Distant SARS-CoV-2 Infection
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Dear authors,

As per my appraisal below, I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Comments from the editors and reviewers:

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Dear authors,

Thank you for submitting your work to JCTR.

As indicated in your cover letter, your manuscript was submitted to AJOG and subsequently to AJSP, where the editors deemed the research valid and worthy of publication based on the reviewers' comments but ultimately better suited for a more specialized journal, basically referring you to back to the other journal and consequently putting the manuscript in a catch 22 position.

You have subsequently addressed all the reviewers' minor concerns and submitted your work to JCTR.

I have decided that I will do something that I have never done since co-founding the journal in 2014, which is to accept a paper 'as is.'

The reasons I am going to directly accept the paper are that (1) it was frankly delightful to receive a manuscript that was submitted in already pristine state; (2) the content has already been properly vetted by reviewers who had been assigned by two very reputable journals; and (3) the topic is of great importance to JCTR and very much aligned with our core mission.

This leaves me with extending my congratulations to you.

Kindest regards,

Michal Heger
Editor

Authors' cover letter

Dear Dr. Heger and the Editorial Board,

We are pleased to submit our manuscript entitled **"Placental Pathology, Neonatal Birthweight and Apgar Score in Acute and Distant SARS-CoV-2 Infection"** for consideration for publication in the *Journal of Clinical and Translational Research*.

Our research truly bridges the obstetric and pathology fields and has therefore not fit into the scope of other journals. Previously we submitted this manuscript to the *American Journal of Obstetrics & Gynecology* and received comments that it would be best suited for a pathology journal. We then proceeded to submit our manuscript to the *American Journal of Surgical Pathology* where we received feedback that given its clinical perspective would be more appropriate in the obstetrics literature. We have incorporated the feedback of these reviews to strength our manuscript and believe that the translational aspect of this research fits well with the *Journal of Clinical and Translational Research*.

Thank you for your time and consideration.

American Journal of Obstetrics & Gynecology

Editor and Reviewer(s) comments:
Editors' Comments:

This paper was extensively discussed among the editors; regrettably, during this assessment it was decided to decline the opportunity to publish this manuscript.

The key finding of the paper is that recent cases of SARS-CoV-2 infection during pregnancy are associated with a placental lesion called eosinophilic T-cell vasculitis. This is based on four cases in the exposed group and zero in the control group (Table 2). The manuscript is well written and comes from a distinguished group. The figures and tables are informative. However, the paper focuses on placental pathology with a rare lesion, and the other findings have been previously reported.

We want to thank the authors for allowing us to assess the manuscript but recommend that the work is best suited for a pathology journal.

American Journal of Surgical Pathology
Reviewer Comments:

Reviewer #1:
The authors examined the placental pathology and neonatal outcomes in distant SARS-CoV-2 infection earlier in pregnancy compared to acute infections late in pregnancy/at birth and non-SARS-CoV-2 infected women with other placental pathologies/clinical presentations.

This study included 514 singleton placentas (77 acute SARS-CoV-2 infection; 222 distant SARS-CoV-2 infection; and 215 from both RT-PCR negative and serology negative women were used to represent other placental pathologies).

Placentas from the acute group had significantly more villous agglutination and eosinophilic T-cell vasculitis compared to placentas from the distant group and non-SARSCoV-2 placentas. Both the preeclampsia/hypertension and the IUGR groups showed significantly more maternal vascular malperfusion findings compared to the acute and distant groups. Fetal vascular malperfusion findings were significantly higher in the IUGR group compared to acute and distant infection.

COMMENTS:
1. This is a good study with large numbers of cases on a timely topic.

2. This paper will add significant knowledge to the existing literature on this topic.

Reviewer #2:
This manuscript describes placental examination and clinical associations of women infected with SARS-CoV-2 in pregnancy. The inclusion of the control group of serologically negative women is a strength of this study. Another strength is using RT-PCR and serology together to distinguish acute and remote infection. While other studies have included control groups with negative serology, the PCR plus serology is a very effective way to capture the truly acute infections.

The manuscript as a whole is well written and easy to read. Information about remote vs. acute infection and its effect on pregnancy is very important from the perspective of general

medical knowledge.

This manuscript fails to reference the most comprehensive paper on the subject to date (PMID: 35645148, IJSP May 2022) which reports on 870 placentas from women infected during various trimesters of pregnancy. The focus of that study was on variants of concern rather than gestational age of infection, distinguishing the two studies, but the omission of this paper should be rectified.

The case described as chronic histiocytic intervillositis in the preterm infant is clearly SARS-CoV-2 placentitis, not CHI. The additional stillbirth described would also have been SARS-CoV-2 placentitis. This is an important diagnostic distinction. This is clarified later in the discussion, so it's unclear why it's called CHI earlier in the manuscript.

The finding of increased incidence of villous agglutination is interesting, but villous agglutination is poorly reproducible. The finding of increased incidence of eosinophilic T cell vasculitis is interesting and hasn't been reported elsewhere aside from the case report referenced.

The data on placental weight and birth weight are interesting. In general, it is not clear that this manuscript is of general interest to the population served by AJSP. It may be more appropriate in the OB/MFM literature, given the clinical aspects, or in the perinatal/pediatric or gynecologic pathology literature.