CORRESPONDENCE

Response to "Diffuse trophoblast damage is the hallmark of SARS-CoV-2-associated fetal demise."

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TO THE EDITOR:

We read with interest the recent manuscript by Garrido-Pontnou and colleagues entitled "Diffuse trophoblast damage is the hallmark of SARS-CoV-2-associated fetal demise"[1]. In their study, the authors searched for potential placental lesions that were significantly associated with SARS-CoV-2 placental infection by reviewing 198 placentas from SARS-CoV-2-positive pregnant women. Previous studies had found varied associations, including maternal vascular malperfusion, fetal vascular malperfusion, pervillous fibrin deposition, and inflammatory lesions[2–11], but these studies were largely retrospective studies of placentas from all SARS-CoV-2-infected mothers irrespective of placental infection. More recent studies described a lesion characterized by the triad of histiocytic or mixed inflammatory intervillositis, increased perivillous fibrin, and villous trophoblast necrosis[12–20]. This newly described histologic alteration was of particular interest to the authors, who found that all of their 9 placentas that tested positive for SARS-CoV-2 by immunohistochemical and RT-PCR analysis showed trophoblast necrosis to variable degrees. The authors found that a diffuse pattern of trophoblastic damage was significantly associated with fetal loss in the SARS-CoV-2-infected placentas, which they considered the hallmark of SARS-CoV-2-associated fetal demise.

One point that we wish to clarify and highlight is that diffuse trophoblast damage is a hallmark of placental SARS-CoV-2 infection, not a hallmark of SARS-CoV-2-associated intrauterine fetal demise per se, even when found in a diffuse pattern. In a recent publication describing our institution's experience, we found that of seven placentas with SARS-CoV-2 infection, six were from live-born neonates[21]. We found that our cases demonstrated characteristic pathologic alterations, which consisted of a histopathologic triad of histiocytic (and neutrophilic) intervillositis, perivillous fibrin deposition, and trophoblast necrosis, termed officially as "SARS-CoV-2 placentitis." In addition, outside of our published results, we performed a search of our pathology information system for a more recent period (January to September 2021) and discovered that 14 of 26 cases of SARS-CoV-2 placentitis resulted in livebirths. Thus, while the massive placental injury has the potential to cause fetal demise with or without transplacental infection and the diffuse pattern may be more significantly associated with fetal loss, it does not necessarily result in fetal demise. We do feel that this is a characteristic and critical pattern to recognize as it is characteristic of SARS-CoV-2 infection of the placenta and thus warrants confirmation of infection through further testing such as RNA in situ hybridization or immunohistochemistry as available (although the histopathologic triad is not exclusively seen in SARS-CoV-2 infection and may occasionally be seen in other placentas as well).

As the authors note in their manuscript and we agree, few diseases in human history have impacted the way of life the way that the COVID-19 pandemic has. As the pandemic continues, more virulent strains are emerging and pregnant women and their unborn children are increasingly being infected and affected. It is yet to be seen what the impact will be. More studies are needed investigating the impact of the virus and its variants as well as exploring the placental effects as these may provide explanations into the mechanisms of trophoblast destruction. We as well as others have demonstrated evidence of C4d deposition along the trophoblastic surface of villi, suggesting complement fixation along villi borders may lead to its destruction and thus, theoretically, corticosteroids could be administered prenatally in attempt to lessen the placental response to infection[21–23]. However, additional studies are needed at this time, particularly to determine if other mechanisms are also at play.

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AUTHOR CONTRIBUTIONS

All authors have contributed to this work and have read and approve this work.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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