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CORRESPONDENCE

Detection of SARS-CoV-2 in placental but not fetal tissues in the second trimester

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To the Editor:

The data on placental and fetal involvement in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy are limited. We analyzed placental and fetal tissues for the presence of SARS-CoV-2 in two infected women who presented with a miscarriage and a preterm labor in the second trimester.

The study was approved by the Institutional Review Board. The tissues were studied by immunohistochemistry (IHC) using antibodies against SARS-CoV-2 spike (clone 1A9; GeneTex, Irvine, CA) and nucleocapsid (clone 0001; Sino Biological, Wayne, PA) proteins and in-situ hybridization (ISH) using the RNAscope-ProbeV-nCoV2019-S (Advanced-Cell-Diagnostics, Hayward, CA). Quantitative reverse transcription polymerase chain reaction (qRT-PCR) was carried out using RNA extracted from formalin-fixed paraffin embedded tissues and SARS-CoV-2 primer/probe sets (Integrated DNA Technology, Coralville, Iowa). Each assay included a standard curve, using the 2019-nCoV_N_Positive Control (Integrated DNA Technology, Coralville, Iowa).

Both women tested positive for SARS-CoV-2 by the nasopharyngeal swab test, but were asymptomatic for COVID-19 before, during or within 14 days after delivery. A 17 year-old gravida 1 para 0 presented with preterm premature rupture of membranes at 18+ weeks and delivered a non-viable female fetus. A 29 year-old gravida 1 para 0 presented in labor at 23+ weeks and delivered a male neonate with Apgar scores 2, 2, and 2. A cardiac arrest was registered on 8 min of life and resuscitation was unsuccessful. The neonatal nasal swab test for SARS-CoV-2 was negative.

Placental and fetal pathologies as well as results of the tissue viral studies are presented in Table 1. SARS-CoV-2 qRT-PCR was positive in placentas and negative in fetal organs in both cases. Neither placentas, nor fetal organs stained for the virus by IHC and ISH. This discrepancy can be explained by a much lower sensitivity of IHC and ISH, comparing to RT-PCR. To date, we found at least ten reported cases of SARS-CoV-2 detected in the placental tissue by RT-PCR [1–5] and only in five cases was the virus demonstrated by IHC and/or ISH [2, 3].

Lack of viral sequences in umbilical cords and fetal organs argues against a vertical transmission of SARS-CoV-2, while the presence of placental and fetal pathologies previously established to be associated with fetal demise can explain the abortion and the preterm labor. In the 1st case, the placenta showed chronic deciduitis (Supplementary Fig. 1), which is known to be associated with an abnormal immune response to pregnancy and spontaneous abortions with normal karyotype. In the 2nd case, placental and neonatal pulmonary pathologies provided a convincing evidence of involvement by Group B *Streptococcus agalactiae* (Supplementaty Fig. 2), a known cause of premature labor and neonatal death.

We demonstrated SARS-CoV-2 involvement of placentas detectable by qRT-PCR in asymptomatic COVID-19-infected pregnant women in the second trimester. Our data are in accord with published reports on the low incidence of vertical transmission of the virus. However, more data are needed to determine the overall feto-maternal risks of SARS-CoV-2 infection at different terms of gestation.

Supplementary information The online version of this article (https://doi.org/10.1038/s41372-020-00877-8) contains supplementary material, which is available to authorized users.

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Table 1 Clinical data and results of SARS-CoV-2 identification in placental and fetal/neonatal tissues.

Case #	Clinical data	Placental pathology	Fetal/Neonatal pathology	Tissue Tested	qRT-PCR	IHC clone 1A9	IHC clone 001	ISH
1	17 yo G1P0 GA 18 4/7 wk	Chronic deciduitis with plasma cells	Intrauterine growth restriction	Placenta	Positive Ct 33.06 VL 12,944		Negative	Negative
	Chlamydia infection, 1st trimester	Decidual hemosiderosis	Negative for congenital anomalies	Umbilical cord	Negative			Negative
				Fetal lungs	Negative		Negative	Negative
	SARS-CoV-2-		Normal karyotype	Fetal heart	Negative		Negative	Negative
	positive			Fetal liver	Negative			Negative
				Fetal kidney	Negative		Negative	Negative
	COVID-19			Fetal small intestine				Negative
	asymptomatic			Fetal ovary and Fallopian tube			Negative	
2	29 yo G1P0 GA 23 2/7 wk	Acute chorioamnionitis	Acute pulmonary inflammatory infiltrate	Placenta	Positive Ct 39.20 VL 224	Negative	Negative	
	SARS-CoV-2 positive	Acute chorionic and umbilical vasculitis	Gram-positive cocci within neutrophils	Umbilical cord	Negative		Negative	
				Neonatal lungs	Negative	Negative	Negative	
	COVID-19 asymptomatic		Post-mortem lung cultures positive for GBS	Neonatal spleen and adrenal	Negative	Negative		
				Neonatal heart	Negative		Negative	
				Neonatal liver	Negative		Negative	
				Neonatal kidney and intestine	Negative		Negative	

GA gestational age, *wk* weeks, *GBS* Group B *Streptococcus agalactiae*, *qRT-PCR* quantitative reverse transcription polymerase chain reaction, C_t threshold cycle, *VR* viral load, *IHC* immunohistochemistry, clone 1A9 anti SARS-CoV-2 spike protein antibody, clone 001 anti SARS-CoV-2 nucleocapsid protein antibody, *ISH* in situ hybridization.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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References

1. Kirtsman M, Diambomba Y, Poutanen SM, Malinowski AK, Vlachodimitropoulou E, Parks WT, et al. Probable congenital SARS-CoV-2 infection in a neonate born to a woman with active SARS-CoV-2 infection. CMAJ. 2020;192:E647–50.
2. Vivanti AJ, Vauloup-Fellous C, Prevot S, Zupan V, Suffee S, Do Cao J, et al. Transplacental transmission of SARS-CoV-2 infection. Nat Commun. 2020;11:3572.
3. Hosier H, Farhadian SF, Morotti RA, Deshmukh U, Lu-Culligan A, Campbell KH, et al. SARS-CoV-2 infection of the placenta. J Clin Invest. 2020;130:4947–53.
4. Baud D, Greub G, Favre G, Gengler C, Jaton K, Dubruc E, et al. Second-trimester miscarriage in a pregnant woman with SARS-CoV-2 infection. JAMA. 2020;323:2198–200.
5. Penfield CA, Brubaker SG, Limaye MA, Lighter J, Ratner AJ, Thomas KM, et al. Detection of SARS-COV-2 in Placental and Fetal Membrane Samples. Am J Obstet Gynecol MFM. 2020;2:100133.