No SARS-CoV-2 detected in amniotic fluid in mid-pregnancy

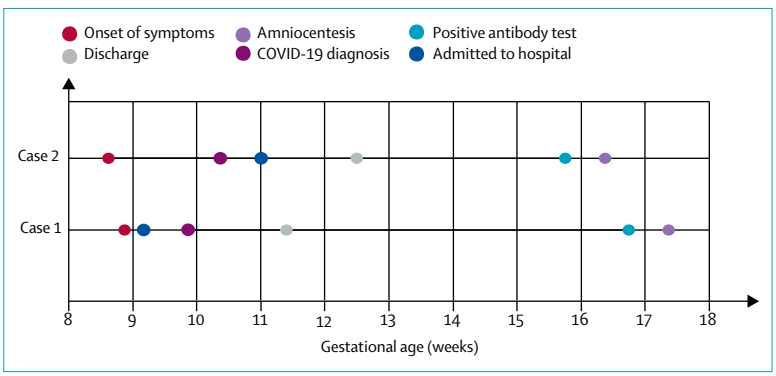

Figure: **Timeline of exposure to SARS-CoV-2 and amniocentesis**
COVID-19=coronavirus disease 2019. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

Controversy exists regarding whether severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can be transmitted in utero from an infected mother to her infant.[1] To date, studies have mainly focused on women in late pregnancy.[2–4] We report SARS-CoV-2 negativity in amniotic fluid from two pregnant women who were diagnosed with coronavirus disease 2019 (COVID-19) in the early stage of pregnancy. The ethics committee of Tongji Hospital approved the study, and written informed consent was obtained from both patients.

Clinical records and laboratory results were retrospectively reviewed for two pregnant women with COVID-19 admitted to Wuhan Tongji Hospital (Wuhan, China) in the first trimester of pregnancy. The first patient (case 1; figure; appendix) was a 34-year-old primiparous woman who was admitted to hospital on Jan 30 after developing a cough on Jan 26 (8 weeks plus 5 days of gestation); her husband had previously had a fever and been diagnosed with COVID-19. On Feb 3, chest CT showed typical signs of viral infection of both lungs, and so a clinical diagnosis of COVID-19 was made. On Feb 13, the patient was observed as being in the recovery phase on CT, discharged from hospital, and isolated at home.

The second patient (case 2; figure; appendix) was a 27-year-old multiparous woman who attended an outpatient clinic on Feb 12 (10 weeks plus 1 day of gestation) after developing a fever, weakness, diarrhoea, and dyspnoea on Feb 1 (8 weeks plus 4 days of gestation). On Feb 12, she tested positive for SARS-CoV-2 in a nasopharyngeal swab, and her chest CT scan showed typical signs of viral infection of both lungs on Feb 14. After isolating at home, the patient was admitted to hospital on Feb 18 due to persistent fever. On Feb 28, the patient was discharged from the hospital following two consecutive negative nucleic acid tests and observation that she was in the recovery phase on CT; she went into isolation at home.

On March 23, the patients—both of whom were in the second trimester of pregnancy—tested positive for SARS-CoV-2 total antibodies in serum and were negative for SARS-CoV-2 RNA in throat swabs (appendix). On March 26, amniotic fluid samples were collected from the patients via percutaneous, ultrasound-monitored amniocentesis. The results of RT-PCR tests of the patients' amniotic fluid on March 26 were negative, and tests for SARS-CoV-2 IgM and IgG in amniotic fluid were also negative (normal IgM and IgG <10 AU/mL; figure; appendix). The patients' IgM and IgG concentrations in serum were also tested on March 26, with positive results for IgG in both cases; by contrast, only case 1 tested positive for IgM (appendix).

Although SARS-CoV-2 was not detected in the amniotic fluid of these two patients, the possibility of vertical transmission in early and middle pregnancy could not be ruled out for several reasons. First, RNA is much less stable in amniotic fluid than is DNA.[5] Second, the number of patients was insufficient to make a definite conclusion. Third, only transient positive results in amniocentesis have been reported for pregnant women infected with Zika virus, another RNA virus.[5] Finally, the virus might have been undetectable in amniotic fluid because of insufficient gestational age—the best time for amniocentesis is after 18–21 weeks' gestation.[6]

The study was limited by a small sample size and a lack of cord blood. However, we hope these findings will contribute to understanding of the potential for intrauterine vertical transmission of SARS-CoV-2 in early pregnancy. Larger, prospective studies and more data are needed.

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See Online for appendix

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Supplementary webappendix

This webappendix formed part of the original submission. We post it as supplied by the authors.

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Table: **Clinical characteristics and laboratory results for mothers and infants**

Clinical value	Case 1	Case 2
Onset of symptoms (weeks+days)	8+5	8+4
Drug therapy	Abidol, Interferon, Moxifloxacin, LTT, TCM	Abidol, Interferon, Moxifloxacin, TCM
Gestational age at cure (weeks+days)	11+2	12+3
Time from onset of symptoms to cure (days)	18	27
Maternal total antibody on March 23 (S/CO)*	886.56	11.51
Gestational age at amniocentesis (weeks+days)	17+2	16+2
Time from onset of symptoms to amniocentesis (days)	60	54
Amniotic fluid RT-PCR test	negative	negative
Amniotic fluid IgM (AU/mL)	0.08	0.13
Amniotic fluid IgG (AU/mL)	1.23	3.38
Maternal IgM on March 26 (AU/mL)	17.1	4.38
Maternal IgG on March 26 (AU/mL)	37.87	67.73

LTT=lopinavir and ritonavir tablets. TCM=traditional Chinese medicine. S/CO=signal to cutoff. *Normal is ≤1·2 S/CO.

Test information

Quantitative RT-PCR (BioGerm Biotech, Shanghai, China) was used to test for SARS-CoV-2 RNA in throat swabs and amniotic fluid, and maternal sera samples and amniotic fluid were tested for IgG and IgM antibodies with a chemiluminescent immunoassay (YHLO Biotech, Shenzhen, China). The sensitivity and specificity reported by the manufacturer for IgM are 88·2% and 99·0%, respectively, and for IgG are 97·8% and 97·9%, respectively. Results of 10 AU/mL or higher were reactive (positive) and results of less than 10 AU/mL were nonreactive (negative). Maternal sera samples were tested for total antibodies with a Chemiluminescence Microparticle Immuno Assay (Innodx Biotech, Xiamen, China) on March 23. The sensitivity and specificity reported by the manufacturer are 80·29% and 98·06%, respectively. Results of 1·2 S/CO or higher were reactive (positive) and results of less than 1·2 S/CO were nonreactive (negative). All tests were performed by two researchers, with antibody tests done twice. Sample collection, processing, and laboratory testing followed guidance from WHO.