

A Case Report to Assess Passive Immunity in a COVID Positive Pregnant Patient

Lorraine E. Toner, MD, MS^{1,2} Shari E. Gelber, MD, PhD^{1,3} Juan A. Pena, MD, MPH^{1,2}
Nathan S. Fox, MD^{1,3} Andrei Rebarber, MD^{1,3}

¹Department of Obstetrics, Gynecology, and Reproductive Science, Icahn School of Medicine at Mount Sinai, New York, New York

²Division of Maternal Fetal Medicine, Icahn School of Medicine at Mount Sinai, New York, New York

³Maternal Fetal Medicine Associates, PLLC, Gynecology, and Reproductive Science, Icahn School of Medicine at Mount Sinai, New York, New York

Address for correspondence Lorraine E. Toner, MD, MS, Division of Maternal Fetal Medicine, Department of Obstetrics, Gynecology, and Reproductive Science, Icahn School of Medicine at Mount Sinai, 5 East 98th Street, Room 249, New York, NY 10029 (e-mail: Lorraine.toner@mssm.edu).

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Abstract

Introduction Data regarding transplacental passage of maternal coronavirus disease 2019 (COVID-19) antibodies and potential immunity in the newborn is limited.

Case Report We present a 25-year-old multigravida with known red blood cell isoimmunization, who was found to be COVID-19 positive at 27 weeks of gestation while undergoing serial periumbilical blood sampling and intrauterine transfusions. Maternal COVID-19 antibody was detected 2 weeks after positive molecular testing. Antibodies were never detected on cord blood samples from two intrauterine fetal cord blood samples as well as neonatal cord blood at the time of delivery.

Conclusion This case demonstrates a lack of passive immunity of COVID-19 antibodies from a positive pregnant woman to her fetus, neither in utero nor at the time of birth. Further studies are needed to understand if passage of antibodies can occur and if that can confer passive immunity in the newborn.

Keywords

- ▶ SARS-CoV-2
- ▶ pregnancy
- ▶ COVID-19
- ▶ passive immunity

In January 2020, a novel coronavirus similar to the one that causes severe acute respiratory syndrome (SARS) was identified after an increase in the rate of aggressive respiratory illnesses was identified in Wuhan, China. Evidence for human-to-human transmission occurred in mid-January. By March 2020, the virus had spread globally and was declared a worldwide pandemic. By June 1, 2020, there were nearly 6 million confirmed cases and over 375,000 deaths reported worldwide.

The impact of COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in pregnancy and in children is limited. The majority of severe disease and fatalities have been in the elderly and those with comorbid conditions. In contrast, fewer severe cases have been identified in pregnant women and children. While case reports have identified severe illness in some pregnancies, current

data do not support a large increase morbidity and mortality in pregnant women or in children.^{1,2} There is mixed data on vertical transmission,^{3–5} and no congenital syndrome has been identified to date. A recent research letter described a woman with SARS-CoV-2 pneumonia who experienced a miscarriage at 19 weeks with evidence of the virus in the placenta. Amniotic fluid was negative by polymerase chain reaction (PCR).⁴ Similarly, an early report described both IgM and IgG in newborns born to women with COVID pneumonia indicating that the fetal infection may occur and that IgG may be passed from mother to fetus.⁵

Transplacental passage of maternal IgG is crucial for protection from disease in early life.

Immunoglobulin (Ig) synthesis is low to negligible in the developing fetus; thus, most fetal and newborn IgGs are derived from the mother. This is an efficient process leading

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Key Points

- Passive immunity should not be assumed in COVID-19 infection in pregnancy.
- Isoimmunization may impair passive immunity of certain antibodies.
- Vaccination to or maternal infection of COVID-19 may not be protective for the fetus.

to newborn antibody concentrations that exceed those of the mother in many cases.⁶ Nonetheless, placental transfer is modulated by numerous factors, and the fetus may receive protective antibodies for some but not all pathogens. Understanding passive immunity to SARS-CoV-2 is necessary to understand risk in the newborn. The presence of disease specific antibodies in the mother is not a guarantee of immunity in the newborn.

Case Report

We present the case of a 25-year-old multigravida (G4P1111), with known isoimmunization to red blood cell D, C, and Le (^a) antigens. Her initial anti-D titer was noted to be 512 and that of anti-C was 8. Paternal zygosity testing was homozygous for the D locus and heterozygous for the C locus. At 18 weeks 2 days, the fetal middle cerebral artery (MCA) Dopplers indicated high-peak systolic velocity (PSV) indicative of fetal anemia, and percutaneous umbilical blood sampling (PUBS) and intrauterine transfusion (IUT) were performed. She then received a second and third PUBS and IUT at 20 and 23 weeks of gestation, respectively. At 26 weeks of gestation in March 2020, she had a screening nasopharyngeal swab that tested positive for SARS-CoV-2 by PCR. The patient reported mild symptoms including anosmia, but did not report fever or shortness of breath. Subsequent SARS-CoV-2 IgG testing performed on April 6 at 27 weeks of gestation, at the time of her fourth PUBS procedure, was positive at a dilution of 1:160 (→Table 1). Fetal blood obtained that day was SARS-CoV-2 IgG negative. After 1 month at the time of her fifth PUBS procedure, the patient's nasopharyngeal swab was negative for SARS-CoV-2 by PCR.

Antibodies were again not detected in the fetus blood sample that day.

The patient went into preterm labor and delivered at 33 weeks on May 16, 2020, with umbilical cord blood sent for antibody testing, which remained negative. Maternal antibody testing was still positive at a dilution of 1:320 at the time of delivery. Despite lack of detectable antibodies to SARS-CoV-2, cord blood demonstrated protective levels of antibodies to rubeola and varicella.

All testing was performed in the clinical laboratory at Mount Sinai Hospital, one of the first to receive emergency use authorization for antibody testing from the Food and Drug Administration. The test sensitivity is 94% with a specificity of >99%. A negative antibody screen result indicates that a serum dilution of 1:50 showed no specific antibodies to COVID-19 virus.

Comment

Healthy pregnant women should be able to mount similar immune responses to pathogens and vaccines as healthy nonpregnant women.³ Low molecular weight substances generally passively diffuse across the placenta, whereas higher molecular weight substances such as immunoglobulins undergo active transport across the syncytiotrophoblast, villous stroma, and endothelium from mother to fetus. The successful transfer of immunoglobulin across the placenta is modulated by numerous factors including gestational age, overall maternal IgG quantity, the maternal IgG concentration of the particular antibody, antibody type, and antibody subtype as well as antibody glycosylation.⁶ IgG transfer across the placenta begins at the end of the first trimester

Date	Test	Maternal result	Fetal result
March 30, 2020	Nasopharyngeal (PCR)	Positive	
April 6, 2020	Serum COVID-19 antibody	Positive (titer 160)	
April 6, 2020	In utero umbilical cord blood COVID-19 antibody		Negative
May 4, 2020	Nasopharyngeal (PCR)	Negative	
May 4, 2020	In utero umbilical cord blood COVID-19 antibody		Negative
May 16, 2020	Neonatal umbilical cord blood COVID-19 antibody		Negative
May 16, 2020	Neonatal umbilical cord blood rubeola antibody		Positive
May 16, 2020	Neonatal umbilical cord blood varicella antibody		Positive
May 18, 2020	Serum COVID-19 antibody	Positive (titer 320)	
January 1, 2020	Prenatal labs: maternal rubeola maternal varicella	IgG 125 AU/mL (Pos > 16.4) IgG 1889 (index) (Pos > 165)	

Abbreviations: COVID-19, coronavirus disease 2019; PCR, polymerase chain reaction.

of pregnancy and increases throughout gestation reaching 10% of maternal concentration at 17 to 22 weeks to 50% at 28 to 32 weeks. Concentration continues to rise in the third trimester allowing fetal antibody concentrations to exceed maternal levels by 20 to 30%.⁶ The factors controlling placental IgG transfer are complex, and differences in transplacental IgG transport have been reported based on both individual characteristics and antibody characteristics.⁷ It is well described that despite adequate antibody levels in the mother, antibodies to some pathogens are transferred more efficiently than others.⁷ In addition, maternal illness may impair antibody transport. It should be noted that swallowing of amniotic fluid likely represents an additional, non-placental pathway of IgG transfer to the fetus.

In our case, it is unclear why ineffective fetal transfer of SARS-CoV-2 IgG occurred. This is a unique case where umbilical cord blood was sampled multiple times over a series of weeks and demonstrated no significant transfer of antibodies despite detectable maternal antibodies and a test sensitivity of 94%. The early gestational age and initial low titer of 160 may have contributed to the initial inability of specific antibodies to cross the placenta at a detectable level; however, it is unclear why at 33 weeks transfer of antibodies for SARS-CoV-2 did not occur. We can hypothesize that given the Rh isoimmunization in this case, possible competition for IgG transfer within the neonatal Fc receptor (FcRN) in the syncytiotrophoblast may have led to a decreased efficiency of expected immunoglobulin transfer. Nonetheless, despite high titers of anti-D antibodies, protective antibodies to other pathogens (i.e., rubeola and varicella) successfully crossed the placenta. Therefore, there may be specific characteristics of SARS-CoV-2 IgG that impeded transplacental transport.

A prior report documented IgG antibodies to SARS-CoV-2 in five of six newborns born to mothers who had been diagnosed with COVID-19 pneumonia.⁵ Notably, antibody levels in the newborns were less than those seen in the mothers. While the test used in that report also has a high sensitivity and specificity, the testing was done in a research laboratory setting. Notably, inclusion in that cohort required diagnosis of COVID-19 pneumonia. Those patients may mount greater antibody responses than patients with mild disease as in our case. Gestational age was not reported in that cohort.

Being a single case complicated by red blood cell isoimmunization, the generalizability of our results to the preg-

nant population may be limited. However, the lack of passive immunity in this case has significant clinical implications.

Vaccination in pregnancy is a strategy to improve the health of the mother, fetus, and newborn. However, an effective vaccine strategy requires transfer of protective IgG to the fetus. Understanding the characteristics of antibody transfer is crucial to development of a vaccine that will protect the newborn.

In general, maternal disease, history of disease predating pregnancy, or immunization in pregnancy are thought to provide some protection in the newborn. The lack of detectable antibody to SARS-CoV-2 in this newborn, despite passive immunity to other viral illnesses, raises concern that specific immunoglobulin characteristics may leave newborns uniquely susceptible to COVID-19. Further studies looking at immunoglobulin transfer in patients with COVID-19 is warranted and passive immunity should not be assumed. Finally, the effect of isoimmunization on placental transfer of protective antibodies should be further studied.

Conflict of Interest

None declared.

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