either waning adaptive immune response or antigenic drift or shifts as occurs in the influenza virus.[9]

CoV ARI was not significantly associated with a wheezing episode during 3 years of follow-up in this study. A study from Madison, the United States, also did not find any association of wheezing with CoV infection.[10]

Viral ARI during infancy can lead to impaired pulmonary function, which in turn results in the development of asthma in childhood or beyond.[3,9] There are limited data on the effect of CoV infection on pulmonary function. In this study, we documented that CoV ARI during infancy had significantly decreased $FEV_{0.5}$, $FEF_{25–75}$, and peak expiratory flow at 3 years of age. Besides, 47% of the children with CoV ARI had positive BDR at 3 years of age.

The main strength of this study is that it is a prospective birth cohort study with excellent follow-up data until 3 years of age. We have also attempted to document the impact of CoV infection during infancy on IPFT. The major limitation of this study is that children were enrolled from single center, which may not be representative of the entire country. However, our institute is a tertiary-care center, and patients are being referred from around the country. Although virus with lowest cycle threshold values in samples where more than 1 virus was detected was considered as the primary infecting virus in this study, it may be challenging to differentiate them as primary infecting or coinfecting virus.

In conclusion, CoV infection is common in children and usually manifests with mild symptoms. The most common strain was OC43 in our cohort. Children with CoV ARI during infancy had a significant increase in airway resistance at 3 years of age. However, more studies are warranted to confirm this finding with a longer follow-up period.

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NEWBORN DRIED BLOOD SPOTS FOR SEROLOGIC SURVEYS OF COVID-19

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Abstract: There is an urgent need for inexpensive, population-wide surveillance testing for COVID-19. We tested newborn dried blood spot (DBS) anti-SARS-CoV-2 antibodies for all infants born at Yale from March to May 2020, and found that newborn DBS serologies reflect maternal and population-wide infection rates during the study period. This suggests a role for DBS in COVID-19 surveillance in areas where viral testing is limited.

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Population seroprevalence surveys are important tools for COVID-19 public health decision-making. However, there are significant hurdles to implementing large-scale serologic surveys, especially in resource poor settings. Newborn dried blood spot (DBS) is an easy, inexpensive and widely used method to collect and store newborn blood specimens, and, in cases where newborn antibody results reflect maternal seropositivity, DBS is an appealing tool to measure COVID-19 population seroprevalence trends among pregnant women.[1] Here, we evaluated DBS as a potential COVID-19 surveillance tool.

METHODS

Discarded newborn DBS was obtained for all infants born in the Yale New Haven hospital system from February 19 to May 26, 2020, a time period that began 2 weeks before the first confirmed case in Connecticut (March 8). Routine SARS-CoV-2 PCR testing of all women who presented to labor and delivery began on April 1, 2020. We adapted a standardized ELISA serology assay[2] for detecting anti-SARS-CoV-2 antibody using newborn DBS. Anti-SARS-CoV-2 IgG was measured in all samples, and IgM was measured where the IgG result was positive. The threshold for a positive result was set at the 99% CI, at which 1% of true negatives would be reported as false positives. Banked cord blood from infants born
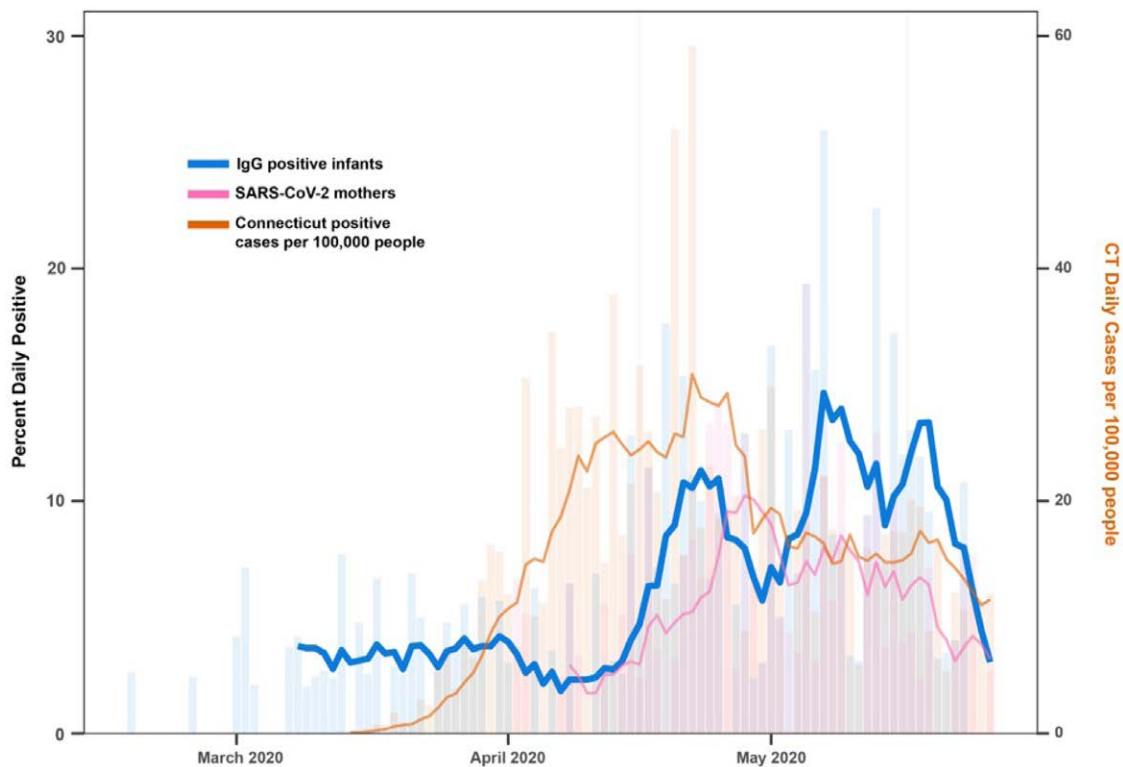
FIGURE 1. Rate of newborn COVID-19 positive antibody and cases in Connecticut from February to May 2020. Daily positive rate (bars) and 7-day moving average (lines) of newborn IgG antibody (blue) in relation to SARS-CoV-2 PCR in mothers (pink), and positive cases per 100,000 people in Connecticut State (orange). Connecticut statewide data were retrieved from Hughes et al (2020) and rate per 100,000 calculated using the US Census estimates.

before 2019 was run as negative controls. Maternal demographic and clinical features were examined in association with the likelihood of an antibody positive newborn using multivariable logistic regression performed in STATA 16.1.

This study was deemed exempt from human subjects regulations by the Yale institutional review board.

RESULTS

The first positive DBS in the study was observed from an infant born in Connecticut on February 18, 2020 (Fig. 1). Overall, 182/3048 (5.9%) DBS tested were positive for anti-SARS-CoV-2 IgG. None were positive for anti-SARS-CoV-2 IgM. Of the 182 infants with positive antibody results, 134 had mothers who underwent testing for COVID-19 by viral PCR before delivery, of which 65 (49%) had a positive test and 69 (51%) had a negative PCR test. All pre-2019 cord blood samples were negative for SARS-CoV-2 IgG by this assay.

We examined the inter-relationship between daily newborn IgG antibody positive rates to maternal and statewide SARS-CoV-2 infection rates. The daily positive proportion of DBS specimens were predicted strongly by both maternal SARS-CoV-2 infection rate ($P < 0.001$) and statewide COVID-19 daily positive test counts per 100,000 people ($P = 0.010$). Further investigations using cross-correlation analysis demonstrated that the daily newborn IgG antibody positive rate strongly correlated with the maternal SARS-CoV-2 infection rate at zero lag time (r = 0.47), and the statewide COVID-19 positive test counts at a lag time of 15 days (r = 0.45).

We examined maternal demographics and clinical factors that may be associated with the likelihood of an IgG+ newborn. Of the 92 mothers who tested positive for SARS-CoV-2 during the universal screening period, 90 had complete demographic and clinical data. When controlled for body mass index (BMI), hypertension, diabetes, COVID-19 symptoms, gestational age and time between maternal COVID-19 diagnosis and delivery (lag time), infants that were antibody positive for COVID-19 were more likely to be born later during the study period (adjusted OR, 1.05; 95% CI, 1.01–1.10, $P = 0.01$), and to mothers with older maternal age (adjusted OR, 1.13; 95% CI, 1.02–1.25, $P = 0.01$). No significant associations were found for the other factors.

DISCUSSION

Our findings demonstrate utility of the newborn DBS SARS-CoV-2 antibody assay to detect past maternal infection and suggest a use for DBS to measure population-level trends of COVID-19, as well as a way to monitor for resurgence of this disease. The detection of seropositive newborns before the availability of viral testing in CT indicates that DBS surveillance may be a useful tool for COVID-19 surveillance where viral testing is limited. Most, but not all, mothers who screened positive for SARS-CoV-2 during the study period delivered a newborn with detectable anti-SAR-CoV-2 IgG antibody, a finding that may reflect the lag time in development of detectable antibodies after infection.[3]

This study has limitations. Most mothers were screened for SARS-CoV-2 at the time of hospitalization for delivery, but we were unable to determine the true date of maternal infection. Because we did not have access to the date of infection or serum antibody testing results for all mothers, we could not determine whether mothers

who screened positive for SARS-CoV-2 by PCR but delivered a seronegative newborn had poor antibody responses themselves, had a remote infection with antibody responses that waned before delivery, or whether there was an inefficient transplacental transfer of antibody in these cases. However, given that the majority of PCR positive mothers delivered seropositive newborns, this does not appear to diminish the utility of DBS as a surveillance tool.

In this study, we demonstrate that levels of IgG in DBS reflect overall population-level trends in case incidence, with a lag that is consistent with the time to the development of detectable antibodies after infection, making DBS antibody testing an attractive option for large-scale population surveillance during the COVID-19 pandemic. As DBSs are routinely collected from newborns, no additional sample collection is required, and specimens can be stored for later assessment. Using DBS as a surveillance tool may therefore be particularly advantageous in resource poor settings, where innovative tools of field epidemiology will be required to control the spread of the virus.

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IS VERTICAL TRANSMISSION OF SARS-CoV-2 INFECTION POSSIBLE IN PRETERM TRIPLET PREGNANCY? A CASE SERIES

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Abstract: There is limited data regarding the vertical transmission (VT) of severe acute respiratory syndrome-coronavirus-2 infection. We report the first case of VT in preterm triplet pregnancy, with all triplets positive for severe acute respiratory syndrome-coronavirus-2 at 20 hours and day 5 of life. This report reiterates the need for an expedited formulation of a simple, standardized, and reproducible international case definition and classification for VT.

Key Words: COVID-19 pregnancy, intrauterine infection, neonates, SARS-CoV-2, vertical transmission

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The novel coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), is one of the worst pandemics the human race has ever experienced. COVID-19 infection affects all age groups, including newborn infants and pregnant women. Most of the SARS-CoV-2 infections in pregnancy are mild, occur in the third trimester, and 1% develop severe disease.[1] COVID-19 infection in the third trimester of pregnancy may be associated with premature rupture of membranes and preterm delivery.[2] The precise incidence of vertical transmission (VT) of SARS-CoV-2 infection is unknown. A systemic review of 18 studies comprising 114 pregnant women with COVID-19 infection demonstrated a lack of VT.[3] A recent study, contrary to the previous one, revealed that the human placenta minimally expresses the angiotensin-converting enzyme 2 receptors (aid in viral cell attachment), and also for an enzyme transmembrane serine protease known as type II (TMPRSS2) (essential for viral replication); this may explain the low occurrence of VT.[4] There is limited convincing data regarding the VT of SARS-CoV-2 and systematic analysis of published studies reported only 28 cases of possible VT from 665 COVID-19 positive mothers.[5] We report the first case of VT in preterm trichorionic triamniotic triplet pregnancy, with all triplets, tested positive for SARS-CoV-2 by reverse transcriptase-polymerase chain reaction (RT-PCR) from nasopharyngeal and throat swabs, taken at 20 hours and day 5 of life. The mother's timeline of infection indicates that COVID-19 possibly triggered preterm labor.

CASE SERIES

Thirty-year-old Omani primigravida woman conceived by in vitro fertilization with trichorionic triamniotic triplets. During this pregnancy, she developed gestational thrombocytopenia and was treated for hypothyroidism, with thyroxin 50 mcg once daily. Her serology screening was negative for HIV, Hepatitis B, and syphilis. Her high vaginal swab was positive for group B Streptococcus infection and received 3 doses of intravenous cefazolin. She was on regular antenatal follow-up, and her last antenatal scan done at 31 weeks gestation was reported as normal.

In July 2020, at 32 weeks and 5 days gestational age, she presented to the local health center with high-grade fever and flu-like symptoms. She had a history of direct contact with her husband and her brother, both of whom were diagnosed with COVID-19 4 days ago. RT-PCR of her nasopharyngeal swab was positive for SARS-CoV-2 infection. She received 2 doses of dexamethasone for early preterm labor. She presented the following day to the delivery ward at Khoula Hospital, Muscat, in active labor. She underwent emergency cesarean section for malpresentation of the triplets: triplet 1 transverse, triplet 2 breech, and triplet 3 breech. The cesarean section was performed under spinal anesthesia in a negative pressure operation theater, with all airborne, droplet, and contact precautions. The membranes were ruptured for all the triplets at operation. The neonatal team attended the delivery, and resuscitation was carried out as per the institutional and international infection prevention and control guidelines. The triplets were separated from the mother immediately after cutting the cord and were taken into a separate isolation room.

Triplet 1 was a baby boy, born vigorous, with birth weight (BW) of 1910 g (64th centile) and did not require any resuscitation at birth. Triplet 2 was a baby girl, born vigorous, with BW 1390 g (13th centile), and required nasal continuous positive airway pressure at birth. Triplet 3 was a baby boy, born vigorous, with BW of 1630 g (31st centile). The Apgar scores for all triplets were 8 and 9 at 1 and 5 minutes. The umbilical cord was clamped immediately, and no skin to skin contact given for all triplets. The babies were transported in closed incubators and admitted to the neonatal intensive care unit (NICU) in a negative pressure isolation room, after