SARS-CoV-2 infections among neonates born to women with SARS-CoV-2 infection: maternal, pregnancy and birth characteristics

Emily O'Malley Olsen (eocevent397@cdc.gov)
Centers for Disease Control and Prevention

Nicole M. Roth
Centers for Disease Control and Prevention

Kathryn Aveni
New Jersey Department of Health

Lindsey Sizemore
Tennessee Department of Health

Eirini Nestoridi
Massachusetts Department of Public Health

Samantha Siebman
Minnesota Department of Health

Pauline Santos
New York State Department of Health

Umme-Aiman Halai
Los Angeles County Department of Public Health

Jerusha Barton
Georgia Department of Public Health

Paul H. Patrick
Oklahoma State Health Department

Similoluwa Sowunmi
California Department of Public Health

Sarah Chicchelly
Kansas Department of Health and Environment

Levi Schlosser
North Dakota Department of Health

Jennifer S. Read
Vermont Department of Health

Sascha R. Ellington
Centers for Disease Control and Prevention

Aron Hall

Centers for Disease Control and Prevention
Suzanne M. Gilboa
Centers for Disease Control and Prevention
Van T. Tong
Centers for Disease Control and Prevention
Kate R. Woodworth
Centers for Disease Control and Prevention

Short Report

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Abstract

Among 10,011 neonates of SARS-CoV-2-infected mothers, 1448 (14%) underwent PCR testing (and 1347 (95%) had mothers with third trimester infections). Fifty-nine (4%) were PCR-positive. Neonates testing positive were born to both symptomatic and asymptomatic women, and nearly all were born to women with infection identified near delivery.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection can lead to serious coronavirus disease 2019 (COVID-19) in pregnant women, may be associated with adverse pregnancy outcomes, and poses a potential risk of transmission to the neonate [1-3]. Multiple reports have described perinatal infection, including likely *in utero* transmission and early postnatal infection [3 (systematic review), 4]. Most neonatal infections reported to date have been asymptomatic or mild disease; however, severe cases, including respiratory failure requiring intensive care unit (ICU) admission, have been described [5]. The American Academy of Pediatrics (AAP) and the Centers for Disease Control and Prevention (CDC) recommend all neonates born to women with suspected or confirmed COVID-19 be tested for SARS-CoV-2 by real-time reverse transcription polymerase chain reaction (RT-PCR) [6,7]. However, data describing factors associated with infection among exposed neonates are limited. We sought to describe maternal, pregnancy and infant characteristics among neonates born to women with SARS-CoV-2 infection during pregnancy by SARS-CoV-2 testing results.

Methods

The Surveillance for Emerging Threats to Mothers and Babies Network (SET-NET) is a collaboration between CDC and state, local, and territorial health departments to conduct linked-longitudinal surveillance of pregnant women and their infants to understand the effects of emerging and reemerging threats, including COVID-19 [8]. Pregnant women with laboratory confirmed SARS-CoV-2 infection from January 1 to December 31, 2020, are retrospectively ascertained through reporting of pregnancy in COVID-19 surveillance and cross-matching of COVID-19 surveillance data with local data systems that contained data on births (e.g., vital records, administrative datasets) to assess pregnancy status.The data are then enhanced through a variety of supplemental data sources at the jurisdiction level including, but not limited to, vital statistics, prenatal screening data, administrative datasets, electronic laboratory reporting, and maternal and neonatal medical record review. The aggregated SET-NET data contain variables on maternal demographics and prenatal history (e.g., pregnancy complications), maternal SARS-CoV-2 infection (e.g., timing of infection relative to pregnancy, severity), neonatal outcome (e.g., gestational age, SARS-CoV-2 testing), among others. Using aggregated SET-NET data compiled through February 5, 2021, we identified neonates who were: 1) born to women who were SARS-CoV-2 RT-PCR positive at any time during their pregnancy, and 2) tested for SARS-CoV-2 by RT-PCR during the birth hospitalization. For neonates with extended hospitalization at birth (>14 days) or whose date of

discharge was unknown, only SARS-CoV-2 tests conducted ≤14 days following birth were included in order to focus on infections from perinatal transmission, rather than community transmission.

For the current analysis, we describe neonates by SARS-CoV-2 testing. We focused on SARS-CoV-2 positive neonates and described maternal and birth characteristics, including maternal demographics, maternal COVID-19 disease severity[9], timing of maternal infection relative to delivery (determined by date of first positive SARS-CoV-2 or symptom onset, if testing date was missing) and pregnancy complications (e.g., preeclampsia). We assessed neonatal characteristics including gestational age and birthweight. We also described these characteristics among neonates who were tested by SARS-CoV-2 RT-PCR following birth but who tested negative. Because negative results are not reported consistently to all jurisdictions in our sample and because medical record abstraction is still ongoing for the cohort, the group of test-negative neonates are not representative of all neonates testing negative. Therefore, we did not perform statistical comparisons between neonates testing positive and negative for SARS-CoV-2. Nevertheless, the SET-NET data offer a glimpse of the current state of perinatal testing of neonates, and neonates with negative results are included here for context. This activity was reviewed by CDC and conducted consistent with applicable federal law and policy[a].

Results

Maternal demographics and underlying conditions are summarized in the Table. The most frequent maternal race/ethnicity was Hispanic or Latina. Of SARS-CoV-2 positive neonates with date of maternal infection reported (n=52), 98.1% were born to women with either initial positive testing or symptom onset occurring <14 days before delivery. One infected neonate was born to a woman with initial positive SARS-CoV-2 testing more than 14 days before delivery but who remained SARS-CoV-2 positive one day prior to delivery. The percent positivity among neonates tested for SARS-CoV-2 was 0.4% (1/254), 3.4% (5/148), 5.9% (10/169), and 4.4% (36/817) for those born to women with infection diagnosed >14 days, 7-14 days, 3-6 days and 0-2 days before delivery. Of positive neonates whose maternal symptom status was known (n=42), 26 (61.9%) were born to mothers reported to be asymptomatic at time of COVID-19 diagnosis.

The 59 SARS-CoV-2-positive neonates were 51.7% female, and 12.5% were small for gestational age (<10th percentile). Sixteen (28.6% of 56 with known gestational age) of the SARS-CoV-2 infected neonates were born prematurely (<37 weeks gestation), including 10.7% (6/56) born moderate to extremely preterm (<34 weeks). Among neonates born at ≥37 weeks, percent SARS-CoV-2 positivity was 3.7% (40/1,092), compared to 6.9% (16/232) positivity among neonates born preterm. Timing of RT-PCR testing was available for 57 of the positive neonates: six (10.5%) neonates were first tested on the day of birth, 39 (68.4%) on the second day of life (DOL), and 9 (15.8%) on the third DOL. The timing of RT-PCR testing was similar for negative neonates.

Discussion

SARS-CoV-2 infection among neonates born to women with COVID-19 was uncommon, occurring in 4.1% of neonates known to be tested for the virus. However, this is likely an overestimate because negative test results are less frequently reported to health departments; the true percentage lies between 4.1% and 0.6% (the total positive neonates among all livebirths). While uncommon, neonatal infection was more frequent among neonates born to mothers diagnosed with COVID-19 close to delivery (<7 days) and among neonates born preterm (<37 weeks). Previous studies of SARS-Cov-2-RT-PCR-positive pregnant women have shown higher prevalence of preterm birth compared with non-infected pregnant women or national baseline estimates [3, 10]. Infected neonates were born to both symptomatic and asymptomatic mothers. These findings underline the need for infection prevention and control (IPC) measures in delivery and outpatient pediatric settings, as well as counselling for persons who acquire COVID-19 during pregnancy about potential risk to their neonates.

Identification of neonates with SARS-CoV-2 infection will be influenced by testing practices. Although these data are not representative of all perinatal testing practices, they indicate that RT-PCR SARS-CoV-2 testing of neonates born to women with SARS-CoV-2 infection during pregnancy primarily occurred for women with third trimester infection, especially for women with infection identified within 14 days of delivery. These testing patterns are consistent with the idea that transmission from mother to neonate through respiratory droplets is most likely to occur during the mother's infectious period. Nearly all neonates born to women with infection occurring more than 14 days prior to delivery tested negative; one possible additional explanation is protection against SARS-CoV-2 infection by transplacental transfer of maternal antibodies, but further studies are needed.

Limitations of our analysis include the inability to assess route of SARS-CoV-2 transmission (e.g., *in utero*, peripartum, postnatal), given lack of immunoglobulin-M serology and RT-PCR testing data on sterile specimens (e.g., blood). We were also not able to assess IPC measures implemented during delivery hospitalization, which may vary [11]. Maternal characteristics were more often missing among mothers of positive neonates, potentially because of reporting bias towards positive RT-PCR results (e.g., from electronic laboratory reports) even in the absence of additional information, whereas neonates with negative testing are less likely to be reported to health departments. Jurisdictional medical record abstraction in SET-NET is ongoing, which may help identify additional infants who tested negative, as well as allow for description of clinical disease (e.g., NICU admission, respiratory support).

Previous studies have demonstrated that risk of postnatal transmission from SARS-CoV-2- infected mother to neonate is low when appropriate IPC is followed [3]. The AAP and CDC recommend that mothers with COVID-19 utilize appropriate IPC measures (e.g., masks, hand hygiene) when rooming in with their infants [6,7], even if the mother is asymptomatic. Neonates born to women with COVID-19 should be tested for SARS-CoV-2 [6,7], particularly those born to women with infection identified close to delivery or who are born preterm. Future studies-- that compare infected neonates to a representative sample of non-infected neonates-- are needed to identify risk factors for neonatal SARS-CoV-2 infection and other neonatal adverse outcomes.

[a]45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

Abbreviations

SARS-CoV-2 — Severe acute respiratory syndrome coronavirus 2

COVID-19 — coronavirus disease 2019

AAP — American Academy of Pediatrics

CDC — Centers for Disease Control and Prevention

RT-PCR — real-time reverse transcription polymerase chain reaction

SET-NET — Surveillance for Emerging Threats to Mothers and Babies Network

IPC — Infection Prevention and Control

SGA — small for gestational age

DOL — day of life

IQR — inter-quartile range

Declarations

This activity (the Surveillance for Emerging Threats to Mothers and Babies SET-NET COVID-19 module) was deemed as non-research and IRB review was not required. Our statement in the paper related to IRB and Human Subjects review is "This activity was reviewed by CDC and conducted consistent with applicable federal law and policy." This language verbatim is required per CDC COVID-19 Emergency Response regulations.

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CDC Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

Contributors statement

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Table

Table. Maternal demographics, maternal disease characteristics, and neonate characteristics by neonate SARS-CoV-2 real-time polymerase chain reaction (RT-PCR) test results – SET-NET, 12 jurisdictions[a], March 29, 2020 – February 5, 2021

	Neonate RT-PCR test results (N=1448)	
	Positive	**Negative**
n (%)	**59 (4.1%)**	**1389 (95.9%)**
Maternal characteristics		
Age in years	**N=49**	**N=1300**
Median (IQR)	31.1 (24.5-35.4)	28.8 (24.3-33.3)
<25	14 (28.6%)	370 (28.5%)
25-34	21 (42.9%)	701 (53.9%)
≥35	14 (28.6%)	229 (17.6%)
Not reported, n (%)	*10 (16.9%)*	*89 (6.4%)*
Race/ethnicity	**N=52**	**N=1313**
Hispanic or Latina	28 (47.5%)	647 (49.3%)
Black, non-Hispanic	8 (13.6%)	259 (19.7%)
White, non-Hispanic	13 (22.0%)	329 (25.1%)
Multiple or other race, non-Hispanic	3 (5.1%)	78 (5.9%)
Not reported, n (%)	*7 (11.9%)*	*76 (5.5%)*
Underlying conditions		
	N=58	**N=1356**
Any underlying condition[b]	22 (37.9%)	623 (45.9%)
	N=54	**N=1290**
Hypertensive disorders of pregnancy[c]	4 (7.4%)	139 (11.3%)
Trimester of maternal infection	**N=58**	**N=1366**
First	0 (0%)	9 (0.7%)
Second	1 (1.7%)	67 (4.9%)
Third	57 (98.3%)	1290 (94.4%)
Not reported, n (%)	*1 (1.7%)*	*23 (1.7%)*

Timing of mother's first positive RT-PCR test (days prior to delivery)	**N=52**	**N=1336**
Median (IQR)	1 day (0-4)	1 day (0-9)
>14	1 (1.9%)	253 (18.9%)
7-14	5 (9.6%)	143 (10.7%)
3-6	10 (19.2%)	159 (11.9%)
0-2	36 (69.2%)	781 (58.5%)
Not reported, n (%)	*7 (11.9%)*	*53 (3.8%)*
Maternal disease severity[d]	**N=42**	**N=681**
Asymptomatic	26 (61.9%)	269 (39.5%)
Mild	12 (28.6%)	260 (38.2%)
Moderate/severe	2 (4.8%)	117 (17.2%)
Critical	2 (4.8%)	35 (5.1%)
Not reported, n (%)	*17 (28.8%)*	*708 (51.0%)*
Delivery type	**N=59**	**N=1376**
Vaginal	35 (59.3%)	891 (64.8%)
Cesarean	24 (40.7%)	485 (35.2%)
Not reported, n (%)	*0 (0%)*	*13 (0.9%)*
Infant characteristics		
Gestational age at birth	**N=56**	**N=1268**
Median weeks (IQR)	38.3 (36.0-39.1)	39.0 (37.0-39.6)
Term (≥37 wks)	40 (71.4%)	1052 (83.0%)
Preterm (<37 wks)	16 (28.6%)	216 (17.0%)
Late preterm (34-36 wks)	10 (17.9%)	147 (11.6%)
Moderate to extremely preterm (<34 wks)	6 (10.7%)	69 (5.4%)
Not reported, n (%)	*3 (5.0%)*	*121 (8.7%)*
Neonate Sex	**N=58**	**N=1385**
Female	30 (51.7%)	668 (48.2%)
Male	28 (48.3%)	717 (51.8%)

Not reported, n (%)	*1 (1.7%)*	*5 (0.4%)*
Birth weight		
	N=59	**N=1372**
Low birth weight (<2500 g)	14 (23.7%)	179 (13.0%)
	N=56	**N=1224**
Small for gestational age[e]	7 (12.5%)	91 (7.4%)
Not reported, n (%)	*(3 5.1%)*	*165 (11.9%)*
Neonatal intensive care unit admission	**N=47**	**N=1167**
Admitted during birth hospitalization	13 (27.7%)	297 (25.4%)
Not reported, n (%)	*12 (20.3%)*	*223 (16.0%)*
Day of first RT-PCR test following birth, in days of life	**N=56**	**N=1350**
1	6 (10.7%)	85 (6.3%)
2	38 (67.9%)	973 (72.1%)
3	9 (16.1%)	208 (15.4%)
≥4	3 (5.4%)	84 (6.2%)

[a] Including California [excluding Los Angeles County], Georgia, Kansas, Los Angeles County, Massachusetts, Minnesota, New Jersey, New York [excluding New York City], North Dakota, Oklahoma, Tennessee, and Vermont.

[b]Includes cardiovascular disease, chronic hypertension, chronic lung disease, diabetes mellitus (type 1 or type 2), immunosuppression, obesity (body mass index ≥30 kg/m^2).

[c]Inclusive of preeclampsia, eclampsia, or HELLP (hemolysis, elevated liver enzymes and low platelet) syndrome. Does not include chronic hypertension. Hypertensive disorders of pregnancy were only considered underlying conditions for women with third trimester infection.

[d]Categories of disease severity were based on modified National Institute of Health and World Health Organization criteria as described in Galang et al[9] . Women were considered asymptomatic if reported as having an absence of symptoms using a symptom status variable rather than solely absence of individual symptoms reported. Criteria were applied to classify severity using submitted data including symptoms, intensive care unit admission, invasive ventilation, use of COVID-19 therapies, complications associated with COVID-19, and death.

[e]Defined as weight <10th percentile for sex (presumed female if missing) and gestational age using the INTERGROWTH-21st online percentile calculator http://intergrowth21.ndog.ox.ac.uk. Some gestational ages were reported in completed weeks only (rather than in weeks and days).

Figures

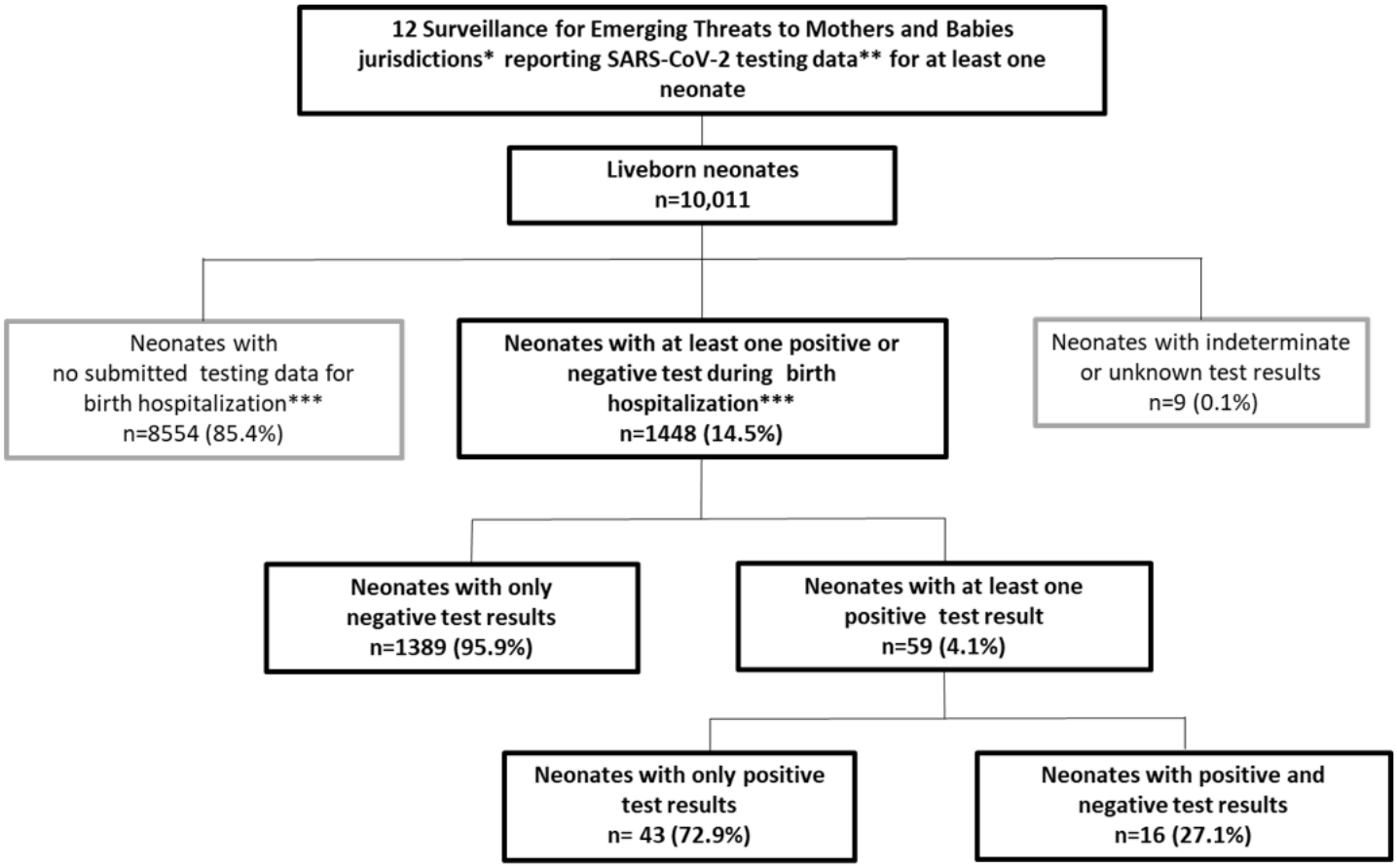

Figure 1

Liveborn neonates born to pregnant women with SARS-CoV-2 infection – SET-NET, March 29, 2020 through February 5, 2021 * 12 jurisdictions reporting SARS-CoV-2 lab data for at least one neonate: California [excluding Los Angeles County], Georgia, Kansas, Los Angeles County, Massachusetts, Minnesota, New Jersey, New York [excluding New York City], North Dakota, Oklahoma, Tennessee, and Vermont. ** All testing data herein was SARS-CoV-2 by real-time reverse transcription polymerase chain reaction (RT-PCR) *** The birth hospitalization period included only SARS-CoV-2 tests conducted ≤14 days following birth for neonates with extended birth hospitalization or whose date of discharge was unknown.