


Short-term outcomes of infants born to mothers with SARS-CoV-2 infection

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ABSTRACT

Objective: The rate of transmission of SARS-CoV-2 from mothers to infants in the peri- and post-natal period remains an area of ongoing investigation. This study aims to determine rates of development of clinically significant COVID-19 disease within 1 month among infants born to symptomatic and asymptomatic SARS-CoV-2 positive mothers.

Materials and methods: This was a single-center, retrospective cohort study of all infants born to SARS-CoV-2 positive mothers who were admitted to the Well Baby Nursery (WBN) at New York University Langone Hospital-Brooklyn from 23 March–23 September 2020. Infants born to asymptomatic mothers were allowed to room-in, while infants born to mothers with symptoms of SARS-CoV-2 were isolated and discharged home to an alternate primary caregiver. A phone follow-up program contacted mothers at 2 weeks and 1 month post discharge to inquire about newborn symptoms, maternal symptoms, personal protective equipment (PPE) usage, and any presentations to care. Medical records were also reviewed for clinic and hospital visits to determine if exposed infants developed any symptoms following discharge.

Results: Of 1903 deliveries during the study period, 131 mothers (21 symptomatic, 110 asymptomatic) tested positive for SARS-CoV-2 and had infants admitted to the WBN. 57 infants (21 born to symptomatic mothers, 36 born to asymptomatic mothers) were tested prior to discharge, and none were positive. 121 of 133 infants had at least 1 follow up call in the study period. Of these, 31 had symptoms potentially concerning for SARS-CoV-2 infection or Multisystem Inflammatory Syndrome in Children, and 19 presented to medical care for these symptoms. 4 infants had SARS-CoV-2 testing after discharge, and none were positive. 2 infants were admitted to the hospital for fever but neither had a positive SARS-CoV-2 result. 65% of mothers reported always adhering to PPE recommendations.

Conclusion: Our results suggest that infants born both to symptomatic and asymptomatic mothers are unlikely to develop clinically significant COVID-19 disease in the peri- and post-natal periods.

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Introduction

The novel coronavirus SARS-CoV-2, which causes coronavirus disease 19 (COVID-19), was declared a global pandemic by the World Health Organization in early March 2020. Initial studies suggest children are less affected, but severe disease and even deaths have been reported as well as Multisystem Inflammatory Syndrome in Children (MIS-C), a rare inflammatory condition, which involves multiple organ systems and occurs after acute SARS-CoV-2 infection [1].

The potential harm of this novel disease in neonates is an area of active investigation. The rate of asymptomatic infection among mothers presenting to the Labor and Delivery (L&D) unit between 22 March and 4 April 2020 at one hospital in New York City was

14%, and studies show that the majority of delivering patients with SARS-CoV-2 are asymptomatic [2,3]. Growing evidence suggests low risk of perinatal transmission among infants born to mothers with SARS-CoV-2 [4–6]. Small studies have also suggested low incidence of transmission from mothers to infants in the postnatal period, and recommendations from national and international medical organizations regarding rooming-in and dyad discharge planning are rapidly changing [7–11].

This study aimed to determine rates of development of clinically significant COVID-19 disease in the first month of life among infants born to symptomatic and asymptomatic SARS-CoV-2 positive mothers. We hypothesized that infants would have low rates of

developing clinically significant infection in both the perinatal and postnatal periods following the dyad's discharge.

Materials and methods

This was a single-center, retrospective cohort study at a community, academic-affiliated, hospital in New York City with approximately 4,000 annual deliveries. Eligible patients were mothers with SARS-CoV-2 infection admitted to L&D from 23 March to 23 September 2020 and their newborn infants admitted to the Well Baby Nursery (WBN) for the duration of their hospitalization. Infants greater than or equal to 35 weeks gestational age, well-appearing with normal physical exam findings, birth weight greater than 2 kilograms, and without maternal intrapartum fever were admitted to the WBN. Infants admitted to the Neonatal Intensive Care Unit (NICU) at any point during their hospitalization were excluded.

As New York City became the early epicenter of coronavirus infections in the United States in March 2020, our hospital saw high volumes of COVID-19 cases and had rapidly evolving policies for the care of infected mothers and their newborns. At study onset, testing was sent on mothers presenting to L&D who reported symptoms of SARS-CoV-2, had exam findings of infection, or had close household contacts with these symptoms. On 17 April 2020, due to rising local infection rates, evidence for asymptomatic spread, and increased testing capacity, we began testing all mothers presenting to L&D. Mothers were allowed one support person for the duration of their hospitalization.

Hospital policy recommended that asymptomatic, positive mothers room-in with their infants. They were encouraged to breastfeed but advised to wear a mask and gloves while feeding and caring for the infant. Infants stayed with their mothers in an open crib rather than an isolette. Infants of asymptomatic mothers were discharged with their mothers as primary caregivers. Mothers were advised to wear a mask and practice hand hygiene while caring for the infant until 14 days of life and encouraged to breast-feed with these precautions.

Hospital policy recommended that symptomatic, positive mothers be placed in isolation and their infants be isolated in the WBN. Mothers were encouraged to pump to provide expressed breast milk rather than directly breastfeeding. Upon discharge, they were encouraged to make alternative disposition arrangements for their infants, either having the infant reside with another family member until the mother showed

clinical improvement, or, if this wasn't possible, to have a different, asymptomatic person be the primary caregiver of the infant.

Testing of infants changed frequently throughout the study period. Initially, all infants born to symptomatic and asymptomatic mothers had SARS-CoV-2 testing at 24 h of life and again prior to discharge. Starting 5 May 2020, infants had only one test sent prior to discharge. On 1 June 2020, our hospital stopped routinely testing infants of asymptomatic mothers due to institutional data showing no evidence of transmission of infection in these cases. We used the Cepheid Xpert Xpress SARS-CoV-2 RT-PCR assay (Sunnyvale, CA) or the Cobas SARS-CoV-2 real time RT-PCR (Roche Molecular Systems, Branchburg NJ). Most infants were discharged between 24-48 h after vaginal deliveries and 48-72 h after Cesarean deliveries.

A telephone follow-up program was established as part of routine clinical care. As of 11 May 2020, any mother who tested positive and had an infant who stayed in the WBN was contacted by a clinician from the Department of Pediatrics. The purpose of this call was (1) to determine if the infant had developed any symptoms of COVID-19 disease or required any presentation to medical care; (2) to determine if asymptomatic mothers had developed symptoms in the interim; (3) to advise about personal protective equipment (PPE) usage among mothers when handling infants; and (4) to answer questions regarding these issues. Most families were contacted twice: at 10-14 days (based on presumed length of mothers' viral shedding) and again at one month post-discharge (based on expected temporal profile for development of MIS-C) [7,12-15]. All calls were documented in the medical record using a standardized note template.

We reviewed the medical records of mothers and infants who met study criteria. Chart review included data from the two telephone encounters, including infant symptoms and presentations to medical care, maternal symptoms, and PPE use. We also reviewed records from any presentations to care at any of our health system's clinical sites within one month of discharge, including reason for presentation, clinical interventions, laboratory and other diagnostic testing, disposition, and diagnosis.

Our primary outcome was the rate of developing clinically significant COVID-19 infection among infants, defined as development of symptoms that required presentation to medical care during which a SARS-CoV-2 test was positive. Secondary outcomes included the proportion of infants who developed any symptoms, reported adherence to PPE recommendations,

Table 1. Characteristics and clinical care of mothers with SARS-CoV2 infection and their infants.

	Total maternal population (n = 131)	Symptomatic (n = 21)	Asymptomatic (n = 110)
Mother's age in years, mean (SD)	28.5 (± 6.3)	30.2 (± 6.3)	28.1 (± 6.3)
Mother's parity, mean (SD)	2.6 (± 2.0)	3.6 (± 3.0)	2.4 (± 1.7)
Mother's primary language, n (%)			
English	77 (58.8)	11 (52.4)	66 (60)
Spanish	45 (34.4)	8 (38.1)	37 (33.6)
Chinese	2 (1.5)	1 (4.8)	1 (0.9)
Russian	2 (1.5)	0	2 (1.8)
Arabic	4 (3.1)	1 (4.8)	3 (2.7)
Other	1 (0.8)	0	1 (0.9)
	Total infant population (n = 133)	Symptomatic (n = 22)	Asymptomatic (n = 111)
Infant's Gestational Age (wks), mean (SD)	39.1 (± 1.4)	38.9 (± 1.4)	39.1 (± 1.4)
Infant Sex, n (%)			
Male	60 (45.1)	8 (36.4)	52 (46.8)
Female	73 (54.9)	14 (63.6)	59 (53.2)
Infant Co-Morbidities, n (%)			
Small for gestational age	13 (9.8)	2 (9.1)	11 (9.9)
Large for gestational age	4 (3)	0	4 (3.6)
Infant of diabetic mother	12 (9)	2 (9.1)	10 (9)
Coombs positivity	3 (2.3)	0	3 (2.7)
Hyperbilirubinemia	2 (1.5)	0	2 (1.8)
Inadequately treated maternal GBS infection	13 (9.8)	2 (9.1)	11 (9.9)
Maternal prolonged rupture of membranes	11 (8.3)	3 (13.6)	8 (7.2)
Post-partum rooming in with mothers, n (%)			
Yes	108 (81.2)	5 (22.7)	103 (92.8)
No	25 (18.8)	17 (77.3)	8 (7.2)
Discharge care plan, n (%)			
Cohabitate with mother, mother as primary caregiver	114 (85.7)	6 (27.3)	108 (97.3)
Cohabitate with mother, other person as primary caregiver	4 (3)	2 (9.1)	2 (1.8)
Cohabitate with another caregiver	15 (11.3)	14 (63.6)	1 (0.9)
Infant feeding type at discharge, n (%)			
Breast only	56 (42.1)	6 (27.3)	50 (45.0)
Formula only	18 (13.5)	7 (31.8)	11 (10.0)
Mixed breast and formula	59 (44.4)	9 (40.9)	50 (45.0)
Infant SARS-CoV2 result prior to nursery discharge, n (%)			
Positive	0	0	0
Negative	57 (42.9)	21 (95.5)	36 (32.4)
Not tested	76 (57.1)	1 (4.5)	75 (67.6)

reported adherence to discharge care plan among symptomatic mothers, rate of symptom development among previously asymptomatic mothers, and positive infant SARS-CoV-2 tests in the neonatal period.

Study data were collected and managed using REDCap electronic data capture tools [16,17]. This study was approved by our Institutional Review Board with a waiver of informed consent. We performed descriptive analyses with results displayed as proportions for categorical variables and medians, means, and simple ranges for continuous variables. SPSS (Belmont, CA) was used for all analyses.

Results

During the six month study period, 1,903 mothers delivered at our hospital. 142 mothers (7.5%) tested positive for SARS-CoV-2 on admission. Of their 144 infants, 11 were excluded because of transfer to the NICU (of note, none were admitted for COVID-19 disease), leaving 133 newborns for analysis. Twelve newborns were lost to phone follow-up entirely, resulting in a follow-up

population of 121 infants. 108 had both follow-up calls completed, while 13 were reached only once but were included in the analysis. Of these, nine newborns who were born prior to the initiation of this follow-up program had only one call, which was made at a mean age of seven weeks. Three newborns were lost to follow up after the first call at 10–14 days, and one newborn was only reached with the second call at one month.

Table 1 describes the demographics and clinical characteristics of our study population. Of 133 newborns, 111 (83.5%) were born to asymptomatic mothers and 22 (16.5%) to symptomatic mothers. Sixty (45%) were male, and the mean gestational age was 39.1 weeks. The majority of infants had no comorbidities. Table 1 also describes the patients' in-hospital clinical care and discharge plans. Based on our hospital recommendations, only 23% of infants of symptomatic mothers roomed-in with their mothers. Nearly all infants of asymptomatic mothers roomed-in. While most mothers were using some amount of breastmilk, more mothers in the symptomatic cohort chose to exclusively formula feed their infants (31.8% vs 10.0%).

Table 2. Follow-up outcomes for infants born to mothers with SARS-CoV-2 infection.

	Total infant population (n = 121)*	Born to symptomatic mothers (n = 20)	Born to asymptomatic mothers (n = 101)
Symptoms at any point during follow-up period, n (%)**	31 (25.6)	8 (40)	23 (22.8)
None	90 (74.4)	12 (60)	78 (77.2)
Fever	4 (3.3)	1 (5)	3 (3.0)
Congestion	8 (6.6)	2 (10)	6 (5.9)
Cough	5 (4.1)	0	5 (5.0)
Vomiting	4 (3.3)	0	4 (4.0)
Diarrhea	6 (5)	3 (15)	3 (3.0)
Rash	15 (12.4)	6 (30)	9 (8.9)
Lethargy	1 (0.8)	0	1 (1)
Other	1 (0.8)	0	1 (1)
Presentation to medical care for evaluation of symptoms, n (%)			
Total	19 (15.7)	5 (25)	14 (13.9)
Clinic	14 (11.6)	4 (20)	10 (9.9)
Emergency department	5 (4.1)	1 (5)	4 (4)
Reported mask use, n (%)***			
Always	—	—	66 (66)
Sometimes	—	—	25 (25)
Infrequently	—	—	9 (9)
SARS-CoV-2 test after nursery discharge, n (%)	4 (3.3)	1 (5)	3 (3)
Detected	0	0	0
Not Detected	4 (3.3)	1 (5)	3 (3)

*Excludes 12 infants lost to follow-up (2 to symptomatic mothers, 10 to asymptomatic mothers). **Some infants had more than 1 symptom reported.

***Only asymptomatic mothers who cohabitated with their infants were asked this question.

96% of infants of symptomatic mothers and 32% of infants of asymptomatic mothers were tested for SARS-CoV-2 by nasopharyngeal PCR prior to hospital discharge. All of these were negative. One infant born to a symptomatic mother was monitored in the WBN for an additional day due to congestion. She had two SARS-CoV-2 tests, both negative. She had no other testing and no other abnormalities on examination. Within 24 h, her symptoms improved, and she was discharged. 64% of infants born to symptomatic mothers were discharged to cohabitate with another family member, 27% were discharged with their mother as primary caregiver, and 9% cohabitated in the same household as their mother but with another primary caregiver. 97% of infants born to asymptomatic mothers were discharged with their mother as primary caregiver.

Patient outcomes from telephone follow-up encounters are summarized in Table 2. Of infants born to symptomatic mothers, 8 (40%) reported symptoms at either or both follow-up calls. The most common symptom was rash, followed by diarrhea. Of these 8 infants, 5 (63%) presented to medical care, but only one had a SARS-CoV-2 PCR test, which was negative. This infant presented to the Emergency Department (ED) at 31 days old with fever and diarrhea. She received a full sepsis evaluation and was positive for rhinovirus/enterovirus on a respiratory viral panel. She had a *Staphylococcus epidermidis* positive blood culture, which was considered a contaminant. She was

discharged after four days. Of note, this infant's twin had no symptoms.

Of infants born to asymptomatic mothers, 23 (23%) reported symptoms at either or both follow-ups. The most common symptom was rash, followed by congestion and cough. Of these 23 infants, 14 presented to medical care, and two were tested for SARS-CoV-2 by PCR, both negative. The first infant presented to the ED with fever at 13 days old. He received a full sepsis evaluation revealing a urinary tract infection. He had an uneventful hospital course and was discharged after two days. The second infant presented to the ED at three days old due to parental concern for poor feeding and sluggishness. He was discharged from the ED with a reassuring exam and no other testing beyond his negative SARS-CoV-2 test. Of note, this child's mother was the only asymptomatic mother who later reported development of symptoms consistent with SARS-CoV-2 infection following hospital discharge. She reported cough at the 10–14 day follow-up call and was advised to seek a different caregiver for the infant until her symptoms resolved, which they had by the one month follow-up call. A third infant born to an asymptomatic mother received SARS-CoV-2 PCR testing at five days old solely because of parental request. No symptoms were reported at this visit or in subsequent telephone encounters or clinic notes. Two additional infants in the asymptomatic mothers cohort (both five days old) were referred to the ED with fevers diagnosed by

temporal thermometer at a clinic. Both had normal rectal temperatures in the ED and otherwise reassuring exams, so they were discharged without SARS-CoV-2 testing or any other work up.

Of 100 mothers who were asymptomatic and discharged to cohabitate with their newborn, 66% reported always adhering to recommended PPE usage, 25% reported occasional adherence, and 9% reported infrequent adherence to recommended PPE usage. Among 15 infants of symptomatic mothers who were discharged to another primary caregiver, 79% reported adherence to this care plan.

Medical record queries were performed for all 12 infants who were lost to phone follow-up. Of these, none had ED visits or sick clinic visits within our institution's three-hospital network.

Discussion

We present a large cohort of SARS-CoV-2-exposed infants followed longitudinally until one month of age. Our study adds to the growing body of literature that suggests that (1) perinatal transmission between mother and infant is unlikely and (2) horizontal transmission in the postnatal period leading to clinically significant disease is unlikely [4–7,18]. None of the 57 infants tested for SARS-CoV-2 prior to discharge from the WBN had positive results. In the follow-up period, while 25.6% of infants had some reported symptoms, all were mild and not suspected to be COVID-19 based on their clinical course. There were only two infant hospitalizations during the study period, neither of which was attributable to acute COVID-19 disease or MIS-C. On follow-up only three infants had symptoms that clinically warranted SARS-CoV-2 testing, and all were negative. These findings corroborate the results of recent studies of SARS-CoV-2-exposed infants that have found a low rate of symptomatology and positive testing after the perinatal period [5–7]. A recent article reported two infants born to SARS-CoV-2 positive mothers who tested positive for SARS-CoV-2 at seven days and one month of life [19]. Both infants were asymptomatic with normal development at follow-up clinic visits. A multi-center study in Spain found no cases of SARS-CoV-2 transmission during delivery and through the first month of life in a large cohort of newborns [20]. Finally, a large population-based study in the United Kingdom analyzing SARS-CoV-2-related hospital admissions in infants less than 29 days old estimated an incidence of 5.6 per 10,000 live births, suggesting the burden of clinically

significant disease transmission, while not zero, is exceedingly low [21].

Our study differs from previous cohort analyses in a few respects. Unlike earlier studies, infants of asymptomatic mothers were allowed to room-in with their mothers in an open crib rather than an isolette, though, as with those investigations, mothers were instructed to wear PPE whenever providing direct infant care [6–8]. In addition, unlike earlier studies, our hospital policy was to separate symptomatic mothers from their infants due to concern that these mothers would be more likely to transmit the virus [7,22]. Finally, our study uniquely used a combination of chart review, parental report of symptoms, and presentation to clinical care to determine if infants developed clinically significant illness attributable to COVID-19.

At the outset of this study, many organizations, including the Centers for Disease Control (CDC) and the American Academy of Pediatrics (AAP), recommended isolating SARS-CoV-2 positive mothers, regardless of symptomatology, and suggested that infants avoid direct breastfeeding [10,11,23]. Separation of mothers and infants postpartum is known to negatively affect maternal-infant bonding and the establishment and continuation of breastfeeding [24]. Indeed, SARS-CoV-2 positive mothers separated from their infants have a lower rate of breastfeeding at hospital discharge as well as on follow-up [25]. Our study suggests that infants of asymptomatic mothers can likely room-in safely and is in line with the revised CDC and AAP guidelines which encourage shared decision-making regarding rooming-in [10,11]. Our hospital policy did not allow symptomatic mothers to room-in with their infants. However, recent studies have shown that this practice may be safe, and revised AAP guidelines suggest that timing of maternal symptom onset, rather than presence of symptoms alone, may more accurately reflect risk of transmission to a neonate [11].

While we did not specifically investigate antibody status, two infants of asymptomatic mothers had positive SARS-CoV-2 IgG antibodies at follow-up clinical appointments, indicating immunologic evidence of immunity without clinical symptoms to suggest the infants themselves were infected. Zeng et al. showed evidence of IgG and IgM antibodies among infants born to SARS-CoV-2 positive, symptomatic mothers. Testing was sent in the perinatal period, and all infants were asymptomatic upon follow-up [26]. Gao et al. documented the declining level of SARS-CoV-2 IgG antibodies over time in a cohort of infants born to mothers with COVID-19 [27]. 63% of exposed infants had IgG antibodies at birth, and all had continued

evidence of antibodies 28 to 75 days postpartum. In addition, some reports demonstrated SARS-CoV-2 antibodies in maternal breast milk [28,29]. The clinical implications of such antibodies remain unknown, and more investigation is needed to determine whether positive antibodies in infants represent transplacental passage, passage through breast milk, or an immunologic response from SARS-CoV-2 infection that confers temporary or long-term immunity.

Our study has several limitations. We excluded infants admitted to the NICU, limiting the generalizability of our findings regarding vertical transmission, particularly among premature infants. However, chart review revealed that none of the 11 exposed NICU infants tested positive or had clinical illness attributable to SARS-CoV-2 during their initial hospitalization. We relied on maternal self-report of infant symptoms following hospital discharge, which introduces the possibility of recall bias. To some degree, this bias was mitigated by our chart review; however, not every infant born at our hospital followed up in our hospital system, so we may have missed presentations to other institutions. Maternal self-report by phone also allowed us to have an excellent follow-up rate of greater than 90% while avoiding unnecessary in-person visits that would place patients at risk for additional exposure. Furthermore, as we did not conduct follow-up PCR testing on infants, we cannot say with certainty whether they acquired infection. However, we reasoned that other studies have already investigated rates of positive testing among exposed infants, and thus we purposefully selected clinically significant COVID-19 disease as our outcome of interest rather than positive SARS-CoV-2 testing in general [6,7,19].

Despite the promise of new vaccines for COVID-19, pregnant women were excluded from initial trials and may not be routinely vaccinated [30,31]. As such, hospitals will continue to care for numerous expectant mothers who test positive for SARS-CoV-2, particularly if an institution practices universal screening. While multicenter, large cohort studies are needed to determine the exact risk of transmission of SARS-CoV-2 from mothers to infants, our results add to the growing body of literature that suggests maternal SARS-CoV-2 infection is unlikely to cause clinically significant disease among healthy newborns in the 30-day perinatal and postnatal period.

Authors' contributions

Dr. Moffat conceptualized and designed the study, designed the data collection instruments, collected

data, drafted the initial manuscript, and reviewed and revised the manuscript.

Dr. Dessie conceptualized and designed the study and reviewed and critically revised the manuscript.

Ms. O'Leary contributed to data acquisition and reviewed and critically revised the manuscript.

Dr. Lumba contributed to data analysis and interpretation and reviewed and critically revised the manuscript.

Dr. Rhee conceptualized and designed the study, contributed to data analysis and interpretation, and reviewed and critically revised the manuscript.

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

Disclosure statement

No potential conflict of interest was reported by the author(s).

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