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SARS-CoV-2 Infection in Infants Less than 90 Days Old

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This is a single-center US case series of 18 infants <90 days old who tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). These infants had a mild febrile illness without significant pulmonary disease. One-half of the infants were hospitalized; 1 had bacterial urinary tract co-infection. Nasopharyngeal viral loads were notably high. Latinx ethnicity was overrepresented. (*J Pediatr* 2020;224:150-2).

Emerging data suggest that coronavirus disease 2019 (COVID-19) primarily affects adults, with children typically having no symptoms or mild course of illness.^{1,2} Although some case series report that children who come to medical attention with severe or critical illness² or require hospitalization³ are more likely to be <1 year of age, most initial reports from China and Europe²⁻⁷ suggest that infants are variably but generally mildly affected. Limited data have been published on infants in the US.^{3,8,9} We present a case series of US infants <90 days of age who tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA.

Methods

We included all infants younger than 90 days of age who had nasopharyngeal swabs positive for SARS-CoV-2 by reverse transcription polymerase chain reaction (RT-PCR) at the Ann and Robert H. Lurie Children's Hospital of Chicago, a freestanding tertiary care pediatric hospital with an associated outpatient network. We queried our clinical laboratory SARS-CoV-2 testing database for patients tested between 1 and 90 days of life between April 11, 2020 and May 12, 2020, which corresponded with a period of peak COVID-19 incidence in the Chicago area. SARS-CoV-2 testing was performed on all patients with suspected COVID-19 based on symptoms, as well as for screening all asymptomatic patients at the time of hospital admission and prior to procedures. Electronic medical records of infants with positive tests were reviewed for demographic, clinical, and laboratory data. This study was approved by the Institutional Review Board at Lurie Children's Hospital.

SARS-CoV-2 RT-PCR was performed by a Clinical Laboratory Improvement Amendments-certified laboratory on nasopharyngeal swab samples using a Food and Drug Administration-Emergency Authorization Use PCR assay

(Abbott Realtime SARS-CoV-2 performed on the m2000 instrument). A rapid assay, namely the XpertXpress SARS-CoV-2 assay (Cepheid/Danaher, Sunnyvale, California), was available in limited quantities during the study period for specific indications (eg, admission to intensive care units and preprocedural testing for an urgent surgery). Amplification cycle threshold (Ct) values were recorded from the Abbott assay results, with lower values indicating higher amounts of viral nucleic acid.

Results

Among 171 infants <90 days of age tested for SARS-CoV-2 within the designated 1-month period at Lurie Children's Hospital, testing locations were drive-through outpatient testing center (n = 35, 20.4%); emergency department (ED; n = 74, 43.3%); non-ED ambulatory setting (n = 3, 1.8%), during inpatient hospitalization (n = 14, 8.2%), cardiac intensive care unit with underlying heart disease (n = 15, 8.8%), and neonatal intensive care unit (n = 30, 17.5%; generally preprocedural or admission screening). Eighteen (10%) infants age 10-88 days tested positive (**Table I**), all by the Abbott assay; 39% were male, and none had significant past medical history. Fifteen infants were tested in the ED and 3 were tested as outpatients. Most infants (n = 14, 77.8%) had fever, 2 had cough as the only symptom, 1 had choking associated with feeding, and 1 was asymptomatic and was screened because parents had confirmed COVID-19 (**Table II**; available at www.jpeds.com).

Fifty percent of infants (9/18) (age 20-67 days at time of admission) were admitted to the hospital's general inpatient service; none required intensive care. Indications for admission were mainly clinical observation, monitoring of feeding tolerance, and ruling-out bacterial infection with empiric intravenous antibiotics in infants <60 days of age. Of those admitted, 8 of 9 had fever, 4 of 9 had cough or tachypnea,

COVID-19	Coronavirus disease 2019
Ct	Cycle threshold
ED	Emergency department
RT-PCR	Reverse transcription polymerase chain reaction
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
UTI	Urinary tract infection

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Table I. Summary of demographic and clinical characteristics

Patients	N = 18 n (%)
Age (d)	55.5 (40-75) med (IQR)
Sex	7 (39%) Male
Race	12 (67%) Other
Ethnicity (self-reported)	14 (78%) Latinx
Ct	4.39 (3.24-6.53) med (IQR)
ED visit	15 (83%)
Hospital admission	9 (50%)
Fever at home	14 (78%)
Fever at hospital	9 (50%)
Nasal congestion, rhinorrhea	5 (28%)
Cough	8 (44%)
Gastrointestinal symptoms (vomiting, diarrhea)	4 (22%)
Increased work of breathing	1 (6%)
Poor feeding	5 (28%)
Fussiness	4 (22%)
Other symptoms	eye redness (n = 2), rash (n = 1), choking with feeds (n = 1)
Hypoxemia	0
CBC obtained	12 (67%)
White blood cell count (thou/uL)	8.3 (6.1-10.1) med (IQR)
Absolute neutrophil count (thou/uL)	2639 (1590-4620) med (IQR)
Absolute lymphocyte count (thou/uL)	3750 (2645-5007) med (IQR)
Hemoglobin (g/dL)	11.35 (10.75-12.75) med (IQR)
Platelet count (thou/uL)	351 (253-411) med (IQR)
Chest radiograph obtained	5 (28%) initial visit, 1 follow-up ED visit
Intravenous fluids	5 (28%)
Respiratory support	0
Intravenous antibiotics	6 (33%)
Blood culture obtained	12 (67%)
Urinalysis/urine culture obtained	12 (67%)
Other viral PCR	5 obtained and resulted negative (28%)
Extended family lives in home	8 (44%)
Number of persons in home (including infant)	5.2 (1.6) mean (SD)
Symptomatic contact	14 (78%)
Confirmed COVID-19+ contact	8 (44%) positive, 2 tests pending

CBC, complete blood count.

and 6 of 9 had gastrointestinal symptoms (4 poor feeding, 3 vomiting, 1 diarrhea after admission). Upper respiratory tract symptoms of cough and congestion preceded onset of gastrointestinal symptoms. None of the infants was hypoxic or required respiratory support, 5 received intravenous fluids (4 admitted, 1 discharged from ED), and 6 infants (age 20-50 days) received intravenous antibiotics while undergoing evaluation for bacterial infection. Five infants had chest radiograph on initial presentation, all of which were normal. Twelve infants had complete blood count, blood culture, and urine culture sent. Five infants had lumbar puncture attempted. There was 1 bacterial infection identified, a urinary tract infection (UTI) with *Streptococcus agalactiae* and *Klebsiella oxytoca*, which was treated with antibiotics. Five infants were also tested for other respiratory viruses (respiratory syncytial virus/influenza or expanded respiratory panel) and no viral co-infection was identified. Two infants had low white blood cell count (3800-4300/ μ L), one of whom had bacterial UTI. Duration of hospitalization for

infants without bacterial infection was 1-3 days. Two infants discharged from the ED at time of testing returned to the ED after 1 and 4 days, respectively, because of poor feeding and due to persistent fever following concern for tachypnea during a telemedicine appointment in 1 infant.

Ct values were low (indicating high viral loads) for this cohort of infants with values ranging from 3.00 to 6.58 for 14 infants. One infant had exceptionally high viral load with sample necessitating 1:100 dilution to obtain Ct of 8.6. For reference, Ct values of 22.9 ± 0.4 resulted from a control standard of 1000 copies per mL included in each assay run. The remaining 3 infants had Ct of 10.3, 11.8, 22.4 (n = 1 each).

Fourteen infants (78%) had close contacts and/or household members who had symptoms consistent with COVID-19. Eight infants (44%) had confirmed SARS-CoV-2 positive contacts, and 2 infants had family members with ED visits and tests pending. Eight infants had extended family living in the same household. Average number of people in the household, including the reported infant, was 5 persons (SD 1.6). Infants were predominantly of self-reported Latinx ethnicity (14/18, 78%).

Discussion

This report presents a series of young infants <90 days of age with COVID-19 in the US. These SARS-CoV-2-infected patients were tested due to clinical concern; the majority was tested because of fever as the primary or only symptom. Remarkably, these infants were well, with little or no respiratory involvement. Many infants had a known positive or symptomatic contact which preceded the infant's illness, although notably 4 infants had no ill contacts, possibly suggesting asymptomatic transmission from a caregiver or other close contact. For young infants being evaluated because of fever, COVID-19 may be an important cause, particularly in a region with widespread community activity. At our institution, SARS-CoV-2 Abbott RT-PCR assay results generally are available within 24 hours, although a Cepheid rapid PCR is available in limited quantities for specific indications (eg, admission to intensive care units and preprocedural testing for an urgent surgery). It is unclear whether young infants with fever and a positive rapid test for SARS-CoV-2 require admission. Decision to admit to hospital is based on age, need to assess for bacterial infection, clinical assessment, feeding tolerance, and adequacy of follow-up. There was 1 significant bacterial co-infection, which highlights that infants with a positive SARS-CoV-2 PCR still may have another cause of fever. Thus, as in the case with respiratory syncytial virus, it remains prudent to evaluate for UTI and other foci as clinically indicated in young infants.¹⁰

We observed an overrepresentation of Latinx ethnicity among our infants who tested positive for SARS-CoV-2 (78%). The Latinx ethnicity in our ED patients was 49% in 2019 and 52% in 2020 (as of April). The proportion of patients seen in our ED overall has not changed with respect

to Latinx ethnicity. As of May 12, 2020, 41.6% of COVID-19 cases in Chicago were in persons of Latinx ethnicity, with Latinx having the highest case rate among race-ethnicity groups (1270 cases per 100 000 population).¹¹ Thus, although expected that there would be many infants of Latinx ethnicity with COVID-19, there may be additional factors contributing to the disproportionate majority of Latinx cases we observed in this age group. Access to sick-visit care in some primary care pediatric offices has been limited; with practices referring symptomatic children to the ED. Limited access to telemedicine care also may be a factor. In this age group of young infants with fever, however, in-person evaluation by an advanced care medical provider would be recommended. Finally, there may be a greater likelihood of exposure with extended Latinx family living in the home or family members working outside the home during this pandemic. These are important areas requiring further study.

The young infants in our cohort had low Ct values by our SARS-CoV-2 RT-RNA PCR test, indicating high viral load in comparison to other children and young adults who were tested at our laboratory (manuscript submitted and under revisions).¹² Possible explanations for this observation include that infants are presenting earlier in illness course than older patients or that infants have increased viral replication, higher viral loads, but generally mild symptoms. Further study of viral load kinetics, clinical symptoms, and transmissibility are needed and may have implications for isolation and child care settings. ■

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Data Statement

Data sharing statement available at www.jpeds.com.

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