Comparison of Clinical and Epidemiologic Characteristics of Young Febrile Infants with and without Severe Acute Respiratory Syndrome Coronavirus-2 Infection

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Objective To determine features that distinguish febrile young infants with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

Study design Retrospective single-center study included febrile infants <57 days of age evaluated in the emergency department of Cohen Children's Medical Center of Northwell Health, New Hyde Park, New York, from March 1 to April 30 of 2018, 2019, and 2020. Sociodemographic and clinical features were compared between those seen during the 2020 coronavirus disease-2019 pandemic and previous years, as well as between infants with SARS-CoV-2 infection and infants without SARS-CoV-2 infection (SARS-CoV-2 negative or evaluated during 2018 and 2019).

Results In all, 124 febrile infants <57 days of age were identified; 38 during the 2-month study period in 2018, 33 in 2019, and 53 in 2020. During 2020, fewer febrile infants had a serious bacterial infection or a positive respiratory viral panel than in prior years (6% vs 21% [$P = .02$]; 15% vs 53% [$P < .001$], respectively). SARS-CoV-2 was the most frequent pathogen detected in 2020; of 30 infants tested, 20 tested positive. Infants with SARS-CoV-2 were more likely to identify as Hispanic ($P = .004$), have public insurance or be uninsured ($P = .01$), exhibited lethargy ($P = .02$), had feeding difficulties ($P = .002$), and had lower white blood cell ($P = .001$), neutrophil ($P < .001$), and lymphocyte counts ($P = .005$) than the 81 infants without SARS-CoV-2 infection. None of the infants with SARS-CoV-2 had concurrent serious bacterial infection or detection of another virus. Overall, disease in infants with SARS-CoV-2 was mild.

Conclusions During the peak of the pandemic, SARS-CoV-2 was the predominant pathogen among febrile infants. Socioeconomic, historical, and laboratory features differed significantly between infants infected or not infected with SARS-CoV-2. None of the 20 infants with SARS-CoV-2 infection had an identified coviral or serious bacterial infection. *(J Pediatr 2021;229:41-7)*.

The first case of the novel coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was diagnosed in December of 2019 in Wuhan, China, and was designated as a worldwide pandemic in March 2020.[1,2] In January 2020, the first case in the US was identified, and in March 2020 a national emergency was declared.[3] Based on data from the Centers for Disease Control and Prevention through July 2020, infants <3 months of age accounted for 18.8% of hospitalized pediatric patients with COVID-19 in the US, and children <1 year of age accounted for 10% of fatalities associated with SARS-CoV-2 in US children; however, the proportion of children younger than 2-3 months of age was not specified.[4,5] Although an early study from Wuhan, China, reported 10.6% of COVID-19 cases in children <1 year of age to be critical or severe, of these cases, not all were laboratory confirmed SARS-CoV-2 infection and other viral etiologies of illness were not excluded.[6] Since then, a number of case reports and small series describing infants <2 months of age have been published, most reporting mild disease, with many infants coming to medical attention owing to fever, lethargy, and poor feeding, but without respiratory manifestations as seen in adult patients.[7-13] The largest case series to date describes 18 infants <90 days of age who tested positive for SARS-CoV-2, 14 of whom were febrile.[9]

ANC	Absolute neutrophil count
ALC	Absolute lymphocyte count
CCMC	Cohen Children's Medical Center
COVID-19	Novel coronavirus disease 2019
ED	Emergency department
NAA	Nucleic acid amplification
RVP	Respiratory viral panel
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
WBC	White blood cell count

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The objective of this study was to compare the clinical and demographic characteristics and hospital course of febrile infants who presented to Cohen Children's Medical Center (CCMC) during March and April of 2020, the time period of peak COVID-19 incidence in our region, with febrile infants treated in CCMC during March and April of previous years.[14] Particular emphasis was placed on infants in whom SARS-CoV-2 was detected to provide relevant clinical data for clinicians evaluating infants with fever during the pandemic.

Methods

Study Design and Population

We conducted a single centered, retrospective study of febrile infants evaluated in the emergency department (ED) of CCMC of Northwell Health (New Hyde Park, NY) who were <57 days of age and had a documented temperature of ≥38°C at home or in the ED within the previous 24 hours and were treated at CCMC during the initial COVID-19 pandemic period (March 1, 2020 to April 30, 2020) or during the corresponding months in the previous 2 years (March 1, 2018, to April 30, 2018, and March 1, 2019, to April 30, 2019). CCMC is located at the border of Nassau County and Queens in New York, which was the epicenter of COVID-19 in the US during the study period. The investigation included both infants who were evaluated and discharged from the CCMC ED and those admitted to an inpatient unit. Per institutional policy, all febrile infants <29 days are hospitalized, but for infants 29-56 days of age a decision to hospitalize is based on clinical criteria. For infants with an ED revisit or readmission to CCMC within 7 days, only the first visit was included in the study.

SARS-CoV-2 Testing

Patients were classified as having SARS-CoV-2 infection when a nasopharyngeal or combined nasopharyngeal/oropharyngeal swab tested positive by one of several nucleic acid amplification (NAA) assays for SARS-CoV-2 in Northwell Health Laboratories. As of March 24, 2020, all infants admitted to CCMC underwent SARS-CoV-2 testing; however, before March 24, testing for SARS-CoV-2 was not universal because of limited testing capacity. During the study period SARS-CoV-2 testing of febrile infants who were discharged from the ED was not universally applied.

Study Variables

Cases were ascertained through review of *International Classification of Diseases, 10th edition*, billing codes and discharge diagnosis in the electronic medical record. Clinical, laboratory, and sociodemographic data were abstracted from the electronic health record and managed with the use of a REDCap electronic database.[15] Collected data included age, sex, ethnicity, race, primary language, insurance, length of hospital stay, history of sick contacts or known COVID-19 exposure, history of prematurity or underlying medical condition, disposition from the ED (discharged home vs hospital admission), and need for admission to the pediatric intensive care unit. The presence or absence of symptoms such as fever, cough, rhinorrhea, feeding difficulties (defined as decreased oral intake), emesis, diarrhea, irritability, lethargy and rash, and vital signs and auscultatory lung examination were also recorded. Laboratory results included SARS-CoV-2 NAA test results, complete blood count, white blood cell differential, urinalysis, hepatic assays, cerebrospinal fluid parameters, bacterial cultures (urine, blood, cerebrospinal fluid), respiratory viral panel (RVP; GenMark Diagnostics, Carlsbad, California), erythrocyte sedimentation rate, C-reactive protein, stool assays (stool culture, rotavirus antigen, multiple pathogen gastrointestinal panel by NAA assay), and herpes simplex virus testing (NAA testing of cerebrospinal fluid, whole blood, surface specimens, and vesicles). Days of antimicrobial therapy, measured from date of first to last dose, and type and duration of respiratory support (eg, supplemental oxygen, noninvasive ventilation, or mechanical ventilation), measured from the date of initiation to discontinuation, were recorded. Neutropenia was defined as an absolute neutrophil count (ANC) of <1000 cells/μL, lymphopenia was defined as an absolute lymphocyte count (ALC) of <3000 cells/μL.[16,17] Serious bacterial infection was defined as the growth of a bacterial organism in the blood, urine, or cerebrospinal fluid that was deemed pathogenic.[18,19]

Febrile infants were classified based on the year of presentation (2018, 2019, or 2020). Febrile infants were also categorized based on their SARS-CoV-2 status: (1) infants who were SARS-CoV-2 test positive during March-April 2020 were classified as SARS-CoV-2 infected; (2) infants who were treated between March and April 2020 but were not tested for SARS-CoV-2 were categorized as SARS-CoV-2 indeterminate; (3) infants who were SARS-CoV-2 negative during March-April 2020 and febrile infants treated during March-April of 2018 and 2019 were classified as SARS-CoV-2 uninfected. SARS-CoV-2 indeterminate infants were included in the analyses of the March-April 2020 cohort vs March-April 2018-2019 cohort, but excluded from the analyses that compared SARS-CoV-2 infected and uninfected groups. Sixteen of the infants with SARS-CoV-2 infection were reported in previous studies.[13,14]

This study was approved by the Northwell Health Institutional Review Board.

Statistical Analyses

We categorized and analyzed the data according to the patients' SARS-CoV-2 status (infected or uninfected) and year of presentation. For the purposes of this analysis, we combined the 2018 and 2019 cohorts as a single cohort. We performed descriptive and bivariable analyses using Fisher exact test for categorical data, Student *t* test for continuous variables, and the Wilcoxon rank-sum test for ordinal data. All tests of significance were 2 sided with an α value of 0.05. Statistical analysis was performed by using SPSS 25 (IBM Corp, Armonk, New York).

Results

Characteristics of the Overall Study Population

A total of 124 infants were identified and included in the study: 38 during March-April 2018 (2018), 33 during March-April 2019 (2019), and 53 during March-April 2020 (2020). Overall, the age distribution was as follows: 12 (10%) were 0-14 days, 29 (23%) were 15-28 days, and 83 (67%) were 29-56 days; 69 (56%) were male; 80 (65%) were admitted to general inpatient unit, 2 (2%) to the pediatric intensive care unit, and 42 (34%) were discharged home from the ED. Patient demographics are summarized in Table I.

Comparison the of 2020 Cohort with the 2018-2019 Cohort

Compared with febrile infants presenting in 2018 and 2019, febrile infants in 2020 were similar in age and by sex, but were more likely to identify as Hispanic (P = .04) (Table I). In 2020, there were significantly fewer infants with a serious bacterial infection, as serious bacterial infection was detected in three of 53 (6%) infants in 2020 compared with 15 of 71 (21%) in 2018-2019 (P = .02). The 3 infants with a serious bacterial infection in 2020 had a urinary tract infection and in 2018-2019, 11 (15%) infants had a urinary tract infection, 3 (4%) had a urinary tract infection with bacteremia, and 1 (1%) had bacteremia. One infant was treated for mastitis in 2018-2019. There were significantly fewer infants with a positive RVP in 2020 than during 2018-2019: 15% during 2020 and 53% during 2018-2019 (P < .001) (Table I). Additional viral infections identified were 2 cases of rotavirus, 1 case each of enterovirus meningitis and herpes simplex virus meningitis in 2018-2019, and 1 case of meningitis with human herpes virus-6 detection in each of the 2018-2019 and in 2020 cohorts.

Characteristics of Infants with SARS-CoV-2 Infection

Thirty of the infants evaluated in the ED in 2020 were tested for SARS-CoV-2; 20 (67%) tested positive (95% CI, 48.8%-80.8%) with 4 of the 20 (20%) 0-14 days of age, 7 (35%) 15-28 days of age, and 9 (45%) 29-56 days of age. Of these 20 infants, 15 (75%) were admitted to hospital, including one who was admitted to the pediatric intensive care unit owing to a brief requirement for treatment with high flow-oxygen by nasal cannula. One hospitalized infant with SARS-CoV-2 infection was readmitted, and another infant was discharged from the ED and subsequently admitted. Mean length of hospital stay for admitted patients was 53.4 hours (range, 42.2-96.3 hours).

Comparison of Infants with SARS-CoV-2 Infection with Infants without SARS-CoV-2 Infection

Demographic and clinical variables of 20 infant who were SARS-CoV-2 positive were compared with 81 uninfected infants (71 seen 2018 and 2019 and the 10 infants who were SARS-CoV-2 negative seen in 2020) (Table II and Table III). A significantly higher proportion of infants in the COVID-19 group had public insurance or were uninsured and identified as Hispanic (P = .01 and P = .004, respectively). The racial distribution of the groups differed significantly with a higher proportion of patients identified as multiracial/other and a smaller proportion identified as Asian or Black in the SARS-CoV-2 group (P = .04). Infants with COVID-19 were significantly younger (P = .03), had a higher proportion with reported feeding difficulty (P = .002) and had a higher proportion with reported lethargy (P = .02) than the SARS-CoV-2 negative group. Infants with COVID-19 had a significantly lower mean white blood cell count (WBC) (P = .001), mean ANC (P < .001), and mean ALC (P = .005) than those who were SARS-CoV-2 uninfected. None of the infants with COVID-19 had a concurrent serious bacterial infection (0% [95% CI, 0-16.1]) or another respiratory viral infection

Table I. Demographics and clinical features of febrile infants younger than 57 days: March-April 2018-2019 vs 2020

Characteristics	2018-2019			2020 (n = 53)	2020 vs 2018-2019, risk difference (95% CI)	*P* value
	2018 (n = 38)	2019 (n = 33)	2018-2019 (n = 71)			
Mean age, d	33.3	38.8	35.9 ± 15	35.3 ± 14	0.6 (−4.6 to 5.7)	.83
Sex, male	26 (68)	13 (39)	39 (55)	30 (57)	1.7% (−15.7 to 18.6)	.999
Ethnicity-Hispanic	2 (5)	2 (6)	4 (6)	9/52 (17)	11.7% (0.4 to 24.6)	.04
Race						
White	17 (45)	10 (30)	27 (38)	22 (42)	3.5%	.08
Black	8 (21)	5 (15)	13 (18)	5 (9)	−9.0%	
Asian	4 (11)	8 (24)	12 (17)	4 (8)	−9.3%	
Multi/other	9 (24)	10 (30)	19 (27)	20 (38)	11.0%	
Unknown	–	–	–	2 (4)	–	
Insurance—public*/no insurance	22 (58)	13 (39)	35 (49)	33 (62)	13.0% (−4.6 to 29.3)	.2
Admitted to hospital	29 (76)	19 (58)	48 (68)	34 (64)	−3.5% (−20.1 to 12.9)	.7
RVP positive†	14/36 (39)	22/32 (69)	36/68 (53)	8 (15)	−37.9% (−51.3 to −21.1)	<.001
Serious bacterial infection present	7 (18)	8 (24)	15 (21)	3 (6)	−15.5% (−26.9 to −3.0)	.02

Values are mean ± SD or number (%) unless otherwise noted.
*Medicaid or Children's Health Insurance Program.
†Tests for adenovirus, influenza A, AH1, AH1 2009, AH3, parainfluenza 1-4, respiratory syncytial virus, *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, Entero/rhinovirus, human metapneumovirus, coronavirus 229E, HKU1, NL63, and OC43.

Table II. Demographics of febrile infants younger than 57 days: Comparison by SARS-CoV-2 infection status

Characteristics	SARS-CoV-2 infected (n = 20)	SARS-CoV-2 uninfected (n = 81)	Risk difference (95% CI)	*P* value
Mean age, d	29.1 ± 12	36.6 ± 14	−7.5 (−14.4 to −0.6)	.03
Age <29 d	11 (55)	25 (31)	24.1% (1.0 to 45.3)	.07
Sex, male	10 (50)	45 (56)	−5.6% (−28.1 to 17.3)	.8
Race				
White	8 (40)	30 (37)	3.0%	.04
Black	1 (5)	13 (16)	−11.0%	
Asian	0	14 (17)	−17.3%	
Multiracial/other	10 (50)	23 (28)	22.6%	
Unknown	1 (5)	1 (1)	3.8%	
Ethnicity, Hispanic	6 (30)	4 (5)	25.1% (8.1 to 47.2)	.004
Insurance, public/no insurance	16 (80)	39 (48)	31.9% (7.7 to 47.8)	.01
Prematurity	3 (15)	4 (5)	10.1% (−2.0 to 31.3)	.14
Underlying medical condition	3 (15)	4 (5)	10.1% (−2.0 to 31.3)	.14

Values are mean ± SD or number (%) unless otherwise noted.

Table III. Clinical features of febrile infants younger than 57 days by SARS-CoV-2 infection status

Features	SARS-CoV-2 infected (n = 20)	SARS-CoV-2 uninfected (n = 81)	Risk difference (95% CI)	*P*
Historical features				
Sick contacts	9 (45)	33 (41)	4.4% (−17.8 to 27.4)	.32
Contact with COVID-19	3 (15)	0/10 (0)	15.0% (−14.4 to 38.0)	.53
History of cough	4 (20)	13 (16)	4.0% (−11.3 to 26.5)	.74
History of rhinorrhea	11 (55)	39 (48)	6.9% (−16.5 to 28.7)	.63
History of feeding difficulty	13 (65)	21 (26)	39% (15.0 to 57.9)	.002
History of emesis	4 (20)	10 (12)	7.7% (−7.2 to 30.0)	.47
History of diarrhea	0	6 (7)	−7.4% (−15.2 to 9.2)	.6
History of irritability	4 (20)	21 (26)	−5.9% (−21.8 to 17.2)	.77
History of lethargy	6 (30)	7 (9)	21.4% (3.9 to 43.7)	.02
History of rash	3 (15)	5 (6)	8.8% (−3.5 to 30.2)	.19
Physical examination				
Mean maximum temperature, °C*	38.5	38.6	−0.1 (−0.3 to 0.2)	.56
Respiratory distress at presentation†	1 (5)	3 (4)	1.3% (−6.5 to 20.1)	.999
Normal auscultatory lung examination	19 (95)	80 (99)	−3.8% (−22.4 to 3.1)	.36
Tachycardia at any point in hospital course‡	10 (50)	38 (47)	3.1% (−19.7 to 25.7)	.81
Tachypnea at any point in hospital course§	1 (5)	3 (4)	1.3% (−6.5 to 20.1)	.999
Lower respiratory tract infection¶	3 (15)	3 (4)	11.3% (−0.5 to 32.5)	.09
Laboratory test results				
Mean WBC × 10^9/L (SD)	7.8 (3.5)	11.2 (5.0)	−3.4 (−5.3 to −1.4)	.001
Mean ANC × 10^9/L (SD)	2.6 (1.5)	4.4 (3.0)	−1.8 (−2.8 to −0.9)	<.001
Mean ALC × 10^9/L (SD)	3.2 (1.9)	4.8 (3.2)	−1.6 (−2.7 to −0.5)	.005
Neutropenia**	4 (20)	2 (2)	17.5% (4.1 to 39.2)	.013
Lymphopenia††	12 (60)	25 (31)	29.1% (5.3 to 49.4)	.02
Serious bacterial infection	0	18 (22)	−22.2% (−32.4 to −4.4)	.02
RVP virus detected	0	37/78 (47)	−47.4% (−58.4 to −28.1)	<.001
Clinical course				
Admission to hospital	15 (75)	56/81 (69)	5.9% (−17.8 to 23.4)	.79
Admission to the pediatric intensive care unit	1 (5)	1/81 (1)	3.8% (−3.1 to 22.4)	.39
Mean hospital length of stay, h‡‡	53.4 ± 15.0§§	61.0 ± 65.0¶¶	−7.6 (−41.4 to 26.1)	.65
Required respiratory support	2 (10)	1 (1)	8.8% (−0.2 to 28.9)	.1

Values are mean ± SD or number (%) unless otherwise noted.
*At home or during hospitalization.
†Defined as the presence of tachypnea or retractions.
‡Defined as a heart rate of >180 beats per minute.
§Defined as a respiration rate of >60 breaths per minute.
¶Defined as the presence of any of the following: abnormal lung exam (crackles, rhonchi or wheeze), hypoxia, or parenchymal infiltrate on chest radiograph.
**Defined as an ANC of < 1.0 × 10^9/L.
††Defined as an ALC of < 3.0 × 10^9/L.
‡‡For patients to hospital only.
§§Range of 42.2-95.3 hours.
¶¶Range of 17.4-509.1 hours.

compared with the infants who were SARS-CoV-2 uninfected in whom serious bacterial infection and respiratory viral infection were detected in 22% and 47%, respectively (P = .02 and P < .001, respectively). Three infants required respiratory support; 2 with COVID-19 (1 required oxygen by high-flow nasal cannula for 2 days and 1 required supplemental oxygen for 2 days); 1 who was SARS-CoV-2 uninfected required 3 days of noninvasive ventilation and 1 day of oxygen by high-flow nasal cannula. Twenty-three infants from 2020 were not tested for SARS-CoV-2 (COVID-19 indeterminate) and were excluded from this analysis, but selected demographic factors and clinical parameters are summarized in **Table IV** (available at www.jpeds.com).

The clinical features of the 44 infants in whom a respiratory virus (other than SARS-CoV-2) was detected were compared with the 20 infants with COVID-19 (all of whom had a negative RVP). Of the 44 infants with a positive RVP, 25 were positive for entero/rhinovirus, 2 for respiratory syncytial virus, 2 for entero/rhinovirus as well as respiratory syncytial virus, 7 for influenza A, 1 for influenza B, 5 for parainfluenza, 1 for coronavirus plus 1 for human-metapneumovirus. The infants with COVID-19 were younger (mean age, 29.1 days vs 41.1 days; P = .01), more likely to report feeding difficulties (35% vs 21%; P = .001), had a lower mean WBC (7800 vs 10 100 cells/μL; P = .04), and a lower ALC (3200 vs 4800 cells/μL; P = .015) than infants in the respiratory virus group. Three of the 44 (6.8%; 95% CI, 2.4-18.2) infants with positive RVP had concurrent serious bacterial infection compared with none of the 20 (0%; 95% CI, 0-16.1) infants infected with SARS-CoV-2 (P = .55).

Discussion

The key findings of our study are that during the peak of the COVID-19 pandemic in New York, SARS-CoV-2 was the predominant pathogen identified among febrile infants <57 days of age, and the disease was self-limited in all infants with COVID-19. None of the infants infected with SARS-CoV-2 had an additional pathogen identified. Febrile young infants with SARS-CoV-2 infection differ from other febrile infants in that they are younger; are more likely to be lethargic or exhibit feeding difficulties; have lower mean WBC, ANC, and ALC; and have a higher likelihood of neutropenia and lymphopenia.

Despite performing SARS-CoV-2 testing on only 57% of the 2020 cohort of febrile infants owing to limitations on availability of testing during this time, SARS-CoV-2 was detected in 38% of the entire cohort and 67% of those tested. In contrast, although the entire 2020 cohort was tested for other respiratory viruses, a virus was detected in only 15% of febrile infants, similar to a study that demonstrated a decrease in influenza rates while COVID-19 was prevalent and while local school closures and stay-at-home orders were in place.[20] The shutdown of schools and businesses in our community during this time and the resultant decrease in interpersonal contact may have contributed to a lower prevalence of respiratory viruses other than SARS-CoV-2. The larger number of febrile infants seen during 2020 compared with the 2018 and 2019 study periods as well as the high prevalence of SARS-CoV-2 among this cohort attest to the high contagion of SARS-CoV-2 during this time period.

The majority of febrile infants with COVID-19 had a relatively mild infections, with only 2 of 20 infants requiring supplemental oxygen, one of whom also required high-flow nasal cannula, findings similar to those described in other case reports and small case series.[8-12] However, severe disease with respiratory failure has been reported in a 4-week-old infant with COVID-19 who was born after a 33-week gestation and in previously healthy infants with COVID-19 who developed pneumonia and evidence of myocardial involvement.[21-23]

The significantly higher proportion of infants with SARS-CoV-2 infection of Hispanic ethnicity and with public health insurance compared with infants who were SARS-CoV-2 uninfected may reflect the more pronounced impact of COVID-19 in Hispanic persons than those of other ethnicities and in persons from lower socioeconomic groups that has been observed in adults.[24,25]

The infants with SARS-CoV-2 infection were younger than the infants who were SARS-CoV-2 uninfected, and were also younger than the subgroup with other respiratory viral infections. This finding may in part be an artifact of our practice of admitting infants <29 days of age to the hospital and preferential testing of admitted patients over ambulatory patients. This finding also could reflect the high prevalence of SARS-CoV-2 among women presenting in labor during this pandemic with transmission from the infant's mother or another household member.[26] Infants with COVID-19 presented with lethargy and feeding difficulty more frequently than their SARS-CoV-2 uninfected counterparts; additionally, feeding difficulty was reported more frequently in infants with COVID-19 than infants infected with other respiratory viruses. The presence of these symptoms may be a useful clue to suspect SARS-CoV-2 infection.

Differences in the complete blood count results may help to differentiate febrile young infants with SARS-CoV-2 infection because these infants had significantly lower values of WBC, ANC, and ALC, and a higher proportion had neutropenia or lymphopenia compared with febrile infants without SARS-CoV-2 infection. Infants with SARS-CoV-2 infection also had lower WBC and ALCs compared with the subgroup who had other documented respiratory viral infections. Similarly, Mithal et al reported 2 infants with COVID-19 with a low WBC, Kan et al reported an infant with lymphopenia and neutropenia, and White et al reported 3 infants, all of whom had neutropenia detected during hospitalization.[9,11,27] Although lymphopenia has been observed commonly in adults and older children with COVID-19, neutropenia has not been reported commonly in these older populations.[1,14,28]

There was a significantly smaller proportion of febrile infants with a serious bacterial infection during March-April 2020 compared with infants evaluated in March-April 2018

and in March-April 2019, and among infants with SARS-CoV-2 infection compared with those without. The absence of serious bacterial infection among 20 infants with SARS-CoV-2 infection was notable, because the overall incidence of serious bacterial infection in febrile infants was 15.2% from 2017 through 2019 at CCMC (J Leibowitz, unpublished observation). Serious bacterial infection in febrile infants with COVID-19 may be uncommon, similar to findings of a low risk of serious bacterial infection in infants with other viral infections.[29] However, the small sample size precludes conclusions about the risk for serious bacterial infection in infants with SARS-CoV-2 infection. Furthermore, serious bacterial infection has been reported in infants with COVID-19 by McLaren et al, who found a urinary tract infection in 2 of 7 febrile infants with SARS-CoV-2 infection and by Mithal et al who found 1 serious bacterial infection in 12 infants with SARS-CoV-2 infection among infants younger than 90 days of age.[9,12] The uncommon occurrence of serious bacterial infection or a second viral pathogen strongly support the assertion that SARS-CoV-2 infection is the cause of the febrile illness in most or all of these infants rather than that detection reflects an asymptomatic infection.

There were several limitations to this study. This analysis was from a single-center study, and the findings may not be generalizable. Additionally, because the initial phase of the COVID-19 pandemic in the US took place in March and April of 2020, we compared febrile infants seen during this time period with febrile infants evaluated in the ED during corresponding months of 2018 and 2019, so generalizability to other time periods is not possible. Last, owing to variable testing for SARS-CoV-2 at the initial stages of the pandemic, 23 of 53 infants evaluated in the ED because of fever were not tested; therefore, we may have underestimated the prevalence of COVID-19 in this patient population during this time period.

SARS-CoV-2 should be considered as a cause of fever in young infants, particularly when the infant has poor feeding and/or lethargy and when leukopenia, lymphopenia, or neutropenia is present. The infection generally is self-limited and has a relatively rapid clinical resolution. ■

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Table IV. Demographics of febrile infants younger than 57 days with an indeterminate SARS-CoV-2 infection status (n = 23)

Characteristics	No. (%)
Mean age ± SD	38.0 ± 14.6
Male sex	14 (61)
Ethnicity, Hispanic	3 (13)
Race	
White	11 (48)
Black	4 (17)
Asian	2 (9)
Multiracial/other	6 (26)
Insurance-public/self-pay	13 (57)
COVID + contact	1 (4)
RVP+	7 (30)
Serious bacterial infection detected	0
Admitted to hospital	11 (48)