

# SARS-CoV-2 Among Infants <90 Days of Age Admitted for Serious Bacterial Infection Evaluation

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abstract

**OBJECTIVES:** To determine the prevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in infants hospitalized for a serious bacterial infection (SBI) evaluation and clinically characterize young infants with SARS-CoV-2 infection.

**METHODS:** A retrospective chart review was conducted on infants <90 days of age hospitalized for an SBI evaluation. The study was conducted at 4 inpatient facilities in New York City from March 15, 2020, to December 15, 2020.

**RESULTS:** We identified 148 SBI evaluation infants who met inclusion criteria. A total of 22 infants (15%) tested positive for SARS-CoV-2 by nasopharyngeal reverse transcription polymerase chain reaction; 31% of infants admitted during periods of high community SARS-CoV-2 circulation tested positive for SARS-CoV-2, compared with 3% when community SARS-CoV-2 circulation was low ( $P < .001$ ). The mean age of infants with SARS-CoV-2 was higher than that of SARS-CoV-2–negative infants (33 [SD: 17] days vs 23 [SD: 23] days, respectively;  $P = .03$ ), although no age difference was observed when analysis was limited only to febrile infants. An isolated fever was the most common presentation of SARS-CoV-2 ( $n = 13$ ; 59%). Admitted infants with SARS-CoV-2 were less likely to have positive urine culture results ( $n = 1$  [5%] versus  $n = 25$  [20%], respectively;  $P = .002$ ), positive cerebrospinal culture results ( $n = 0$  [0%] versus  $n = 5$  [4%], respectively;  $P = .02$ ), or be admitted to intensive care ( $n = 2$  [9%] versus  $n = 47$  [37%];  $P < .001$ ), compared with infants without SARS-CoV-2.

**CONCLUSIONS:** SARS-CoV-2 was common among young infants hospitalized for an SBI evaluation during periods of high but not low community SARS-CoV-2 circulation in New York City, although most infants did not require intensive care admission.

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Dr Paret participated in the concept and design of the study and coordinated and supervised data collection analysis, interpretation of data, drafting of the initial manuscript, and reviewing and revising of the manuscript; Dr Lalani participated in study design, data collection, analysis of data, and reviewing and revising of the manuscript; Drs Hedari, Jaffer, and Narayanan in provided feedback on the study design, participated in data collection, contributed to data interpretation, and reviewing and revising of the manuscript; Dr Noor contributed to providing feedback on the study design, contributed to data interpretation, and critically reviewed and revised the manuscript; Drs Lighter, Pellett Madan, Shust, and Ratner participated in the concept and design of the study, designed the data collection instruments, contributed to data interpretation, and critically reviewed and revised the manuscript; Dr Raabe conceptualized and designed the study, designed the data collection instruments, performed analysis and interpretation of data, drafted the initial manuscript, and critically reviewed and revised the

**WHAT'S KNOWN ON THIS SUBJECT:** Most infants <90 days of age with a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection have mild to moderate disease, but knowledge about SARS-CoV-2 infection in this age group is mostly limited to case reports and small case series.

**WHAT THIS STUDY ADDS:** SARS-CoV-2 infection is common among infants hospitalized for serious bacterial infection evaluation when there is high community SARS-CoV-2 circulation. The prevalence of SARS-CoV-2 infection among young infants varies with levels of community transmission.

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Since severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first described as the causative pathogen of coronavirus disease 2019 (COVID-19) in December 2019,<sup>1,2</sup> it has rapidly spread worldwide.<sup>3</sup> New York City (NYC) was the early epicenter of COVID-19 in the United States, with >190 000 reported infections and >15 000 deaths occurring during the peak of the NYC epidemic (March 2020 to May 2020).<sup>4</sup> Three percent of reported cases were in children <18 years of age during the peak of the NYC epidemic,<sup>4</sup> although these numbers may underestimate the true incidence given the lack of adequate testing capacity early in the pandemic. Most children infected with SARS-CoV-2 are asymptomatic or have mild to moderate symptoms, generally with more favorable outcomes compared with adults.<sup>5-16</sup> However, cases of severe illness have been described, and some reports suggest young infants may be at a higher risk for severe disease.<sup>5,6,17,18</sup>

Infants <90 days of age are frequently admitted for empirical broad-spectrum antibiotics until serious bacterial infections (SBIs) (eg, urinary tract infection, bacteremia, and/or meningitis) are excluded after potential exposure to maternal infection at delivery or because of symptoms concerning for bacterial infection, such as fever. Because fever is a common symptom of COVID-19 in children,<sup>19-21</sup> pediatricians must consider SARS-CoV-2 as a potential etiology of fever in young infants during the COVID-19 pandemic.<sup>12,22-24</sup> We conducted an observational, retrospective chart review of febrile and nonfebrile infants <90 days of age hospitalized primarily for SBI evaluation in 4 inpatient facilities in NYC to identify the prevalence of SARS-CoV-2

infection and describe the clinical characteristics of these infants.

## METHODS

Electronic medical records (EMRs) of infants <90 days of age admitted to any of 3 New York University Langone Health System inpatient facilities in Brooklyn, Long Island, and Manhattan, or NYC Health + Hospitals (NYCHHC) Bellevue Hospital between March 15, 2020, and December 15, 2020, were screened for eligibility. Records from the NYCHHC Bellevue Hospital were only available for review through October 1, 2020. The start date reflects when routine in-house SARS-CoV-2 nasopharyngeal reverse transcription polymerase chain reaction (RT-PCR) testing became available at 3 of the 4 study facilities. Because of the limited availability of SARS-CoV-2 testing supplies early in the NYC COVID-19 epidemic, SARS-CoV-2 RT-PCR testing was limited to hospitalized patients at the time of study initiation; therefore, infants undergoing SBI evaluation in the emergency department who were not hospitalized were not included.

Inclusion criteria included age <90 days at the time of hospitalization and admission for SBI evaluation. Admission for SBI evaluation was determined by investigator review of the emergency department and admitting history as to whether evaluation and treatment of bacterial infection was the main reason for admission. Febrile and nonfebrile infants, including newborns undergoing SBI evaluation because of exposure to maternal infection, were included in the overall study analysis, and separate subgroup analysis was performed on febrile infants. Infants without SARS-CoV-2 testing during admission were excluded. Abstracted data from the EMR were entered into a Health Insurance

Portability and Accountability Act of 1996-compliant database (Research Electronic Data Capture), including demographics (age, sex, ethnicity, and race), medical comorbidities, mode of birth delivery, history of exposure to ill contacts and confirmed COVID-19 cases, clinical symptoms at presentation (documented as negative if absent or not noted on admission notes), initial laboratory (white blood cell [WBC] count, absolute neutrophil count [ANC], absolute lymphocytic count [ALC], hemoglobin, platelets, C-reactive protein [CRP]) and chest radiograph findings (the presence of infiltrates or consolidations per radiology report, further categorized as focal or bilateral), microbiologic culture and/or BioFire FilmArray Respiratory Panel (BioFire Diagnostics, Salt Lake City, UT) results, respiratory and nonrespiratory interventions required, ICU admission status, clinical outcome, and hospital length of stay (LOS).

Categorical variables were analyzed via Pearson's  $\chi^2$  test. Continuous variables with normalized distributions (skewness:  $\leq 1$ ) are reported as a mean with the SD and were analyzed by using Student *t* tests with Welch's correction, and those with nonnormalized data distributions (skewness:  $> 1$ ) are reported as the median with the interquartile range (IQR) and were analyzed by using Mann-Whitney *U* tests. Prism 8.4 (GraphPad, San Diego, CA) was used for statistical analysis, and *P* values  $< 0.05$  were considered statistically significant. Classification of high and low community circulation periods were determined by examination of daily COVID-19 testing positivity data provided by the NYC Department of Health and Mental Hygiene, with high community circulation defined by 7-day rolling average testing positivity rates  $\geq 5\%$ .<sup>25</sup>

This study was approved by the New York University Grossman School of Medicine Institutional Review Board and NYCHHC System to Track and Approve Research with a waiver of consent and authorization for data collection.

## RESULTS

### Demographics, Medical History, and Exposures

Medical records of 1119 infants <90 days of age admitted to one of the study facilities during the study period were reviewed. Of these, 148 infants (13%) met the eligibility criteria. The majority were male ( $n = 86$ ; 58%), and the most frequently identified race and ethnicity were white ( $n = 71$ ; 48%) and non-Hispanic ( $n = 74$ ; 50%; Table 1). No differences in sex, racial, or ethnic distribution were observed between febrile and nonfebrile infants (Table 1). The mean age at admission was 25 (SD: 22) days (Fig 1) and was lower among nonfebrile infants (8 days [SD: 14]), compared with febrile infants (34 days [SD: 20];  $P < .001$ ). Most infants ( $n = 135$ ; 91%) had no pre-existing medical conditions. A total of 22 of the 148 infants (15%) admitted for SBI evaluation were positive for SARS-CoV-2 by using a nasopharyngeal RT-PCR.

By using the  $\geq 5\%$  7-day rolling average COVID-19 testing positivity threshold, March 15 to May 28, 2020, and November 28 to December 15, 2020, were defined as periods of high community circulation; the remainder of the study period was considered to have low community circulation. During high community circulation periods, 19 of 62 infants (31%) tested positive for SARS-CoV-2, whereas only 3 of 86 infants (3%) tested positive while community circulation was low ( $P < .001$ ).

Among all infants admitted for SBI evaluation, the mean age of infants with a positive SARS-CoV-2 RT-PCR was higher than that of infants who tested negative (33 [SD: 17] days, to 23 [SD: 23] days;  $P = .03$ ), although no age difference was observed between SARS-CoV-2-positive and SARS-CoV-2-negative infants in the febrile subgroup (33 days [SD: 14] to 35 days [SD: 22];  $P = .63$ ). Comorbidities were more common among infants negative for SARS-CoV-2 compared with those who were positive among all infants ( $n = 13$  [10%] to  $n = 0$  [0%];  $P < .001$ ) and the febrile subgroup ( $n = 7$  [9%] to  $n = 0$  [0%];  $P = .007$ ). Infants with SARS-CoV-2 were more likely to have any ill contact documented at admission, compared with those who tested negative, both among all infants ( $n = 9$  [41%] to  $n = 9$  [7%];  $P = .006$ ) and the febrile subgroup ( $n = 9$  [47%] to  $n = 6$  [9%];  $P = .006$ ). No differences were observed in admission documentation of confirmed COVID-19 contacts between all infants ( $P = .75$ ) or febrile infants ( $P = .48$ ) regardless of SARS-CoV-2 status ( $P = .75$ ) or community SARS-CoV-2 circulation level ( $P = .94$ ; Table 1).

### Clinical Presentation

Nearly all infants with SARS-CoV-2 presented with a fever ( $n = 20$ ; 91%), whereas less than two-thirds of infants without SARS-CoV-2 had a fever before admission ( $n = 74$  [59%];  $P < .001$ ; Table 2). An isolated fever was the most common presentation of SARS-CoV-2 ( $n = 13$ ; 59%), and an isolated fever was more frequent among infants with SARS-CoV-2 compared with those who tested negative ( $n = 17$ ; 13%;  $P < .001$ ), including in the febrile subgroup ( $P = .002$ ; Table 2). Hypothermia ( $n = 0$  [0%] to  $n = 8$  [6%];  $P = .004$ ), irritability and/or fussiness ( $n = 2$  [9%] to  $n = 37$  [29%];  $P = .01$ ), diarrhea ( $n = 0$  [0%] to  $n = 7$  [6%];  $P = .008$ ), and

lethargy ( $n = 0$  [0%] to  $n = 9$  [7%];  $P = .002$ ) were less frequently documented among all SBI evaluation infants who tested positive for SARS-CoV-2 than those with negative test results. Irritability and other symptoms were less frequently documented among febrile infants with SARS-CoV-2 compared with those without SARS-CoV-2 ( $n = 2$  [10%] to  $n = 35$  [47%];  $P < .001$  and  $n = 0$  [0%] to  $n = 7$  [9%];  $P = .007$ , respectively), but no differences in the frequency of other assessed symptoms was observed in the febrile subgroup (Table 2).

### Laboratory and Imaging Results

Infants with SARS-CoV-2 had significantly lower mean WBC counts (7.3 [IQR: 5.5–11.3]  $\times 10^3$  cells per  $\mu\text{L}$  to 13.0 [IQR: 8.8–17.7]  $\times 10^3$  cells per  $\mu\text{L}$ ;  $P < .001$ ), lower median ANC (1.7 [IQR: 1.4–3.1]  $\times 10^3$  cells per  $\mu\text{L}$  to 5.8 [IQR: 2.5–9.9]  $\times 10^3$  cells per  $\mu\text{L}$ ;  $P < .001$ ), lower median ALC (3.3 [IQR: 2.7–4.7]  $\times 10^3$  cells per  $\mu\text{L}$  to 4.6 [IQR: 3.0–6.6]  $\times 10^3$  cells per  $\mu\text{L}$ ;  $P = .04$ ), and lower mean hemoglobin levels (12.8 [SD: 2.1] g/dL to 14 [SD: 3.7] g/dL;  $P = .04$ ), compared with those without SARS-CoV-2 (Table 3). Lower WBC, ANC, and ALC counts were also observed in the febrile subgroup with SARS-CoV-2, although no differences in hemoglobin were observed (Table 3). Additionally, infants with SARS-CoV-2 infection had lower median CRP values than those without, both among all infants (0.8 [IQR: 0.4–2.5] mg/L to 5.7 [IQR: 1.5–49] mg/L;  $P = .005$ ) and the febrile subgroup (0.8 [IQR: 0.3–2.4] mg/L to 13.6 [IQR: 1.5–79.2];  $P < .001$ ).

Microbiologic samples obtained included blood cultures ( $n = 146$ ; 98%), urine cultures ( $n = 102$ , 69%), BioFire FilmArray respiratory panel testing ( $n = 97$ ; 66%), and cerebrospinal fluid (CSF) cultures ( $n = 92$ ; 62%). Twenty-two blood

**TABLE 1** Demographics, Medical History, and Exposures of Study Participants

	All SBI Evaluation Infants (n = 148)	SBI Evaluation Infants With SARS-CoV-2 (n = 22)	SBI Evaluation Infants Without SARS-CoV-2 (n = 126)	P	Febrile Infants With SARS-CoV-2 (n = 20)	Febrile Infants Without SARS-CoV-2 (n = 74)	P	SBI Evaluation Infants High Community Circulation Periods (n = 62)	SBI Evaluation Infants Low Community Circulation Period (n = 86)	P
Age at admission, mean (SD), d	25 (22)	33 (17)	23 (23)	.03	33 (14)	35 (22)	.63	23 (21)	26 (23)	.47
Sex, male, No. (%)	86 (58)	14 (64)	72 (57)	.57	13 (65)	47 (64)	.90	37 (60)	49 (57)	.74
Ethnicity, No. (%)				.11			.65			.002
Hispanic	43 (29)	7 (32) <sup>b</sup>	36 (29)		6 (30)	21 (28)		21 (34)	22 (26)	
Non-Hispanic	74 (50)	14 (64) <sup>b</sup>	60 (47)		13 (65)	36 (49)		36 (58)	38 (44)	
Unknown	31 (21)	1 (5) <sup>b</sup>	30 (24)		1 (5)	17 (23)		5 (8)	26 (30)	
Race, No. (%)				.61			.18			.62
American Indian or Alaskan native	3 (2)	0 (0) <sup>b</sup>	3 (2) <sup>b</sup>		0 (0)	2 (3)		1 (2)	2 (2)	
Asian	13 (9)	1 (5) <sup>b</sup>	12 (10) <sup>b</sup>		1 (5)	9 (12)		8 (13)	5 (6)	
Black or African American	10 (7)	1 (5) <sup>b</sup>	9 (7) <sup>b</sup>		1 (5)	7 (9)		3 (5)	7 (8)	
Native Hawaiian or Pacific Islander	7 (5)	0 (0) <sup>b</sup>	7 (6) <sup>b</sup>		0 (0)	2 (3)		2 (3)	5 (6)	
White	71 (48)	11 (50) <sup>b</sup>	60 (48) <sup>b</sup>		9 (45)	32 (43)		31 (50)	40 (47)	
Other or unknown	44 (29)	9 (41) <sup>b</sup>	35 (28) <sup>b</sup>		9 (45)	22 (30)		17 (27)	27 (31)	
Birth delivery method, No. (%)				.44			>.99			.49
Vaginal	97 (66)	15 (68)	82 (65)		14 (70)	52 (70) <sup>b</sup>		44 (71)	53 (62)	
Cesarean delivery	39 (26)	4 (18)	35 (28)		4 (20)	15 (20) <sup>b</sup>		14 (23)	25 (29)	
Unknown	12 (8)	3 (14)	9 (7)		2 (10)	7 (9) <sup>b</sup>		4 (6)	8 (9)	
Gestational age, Median (IQR), wk	39 (37–40)	39 (38–40)	39 (37–40)	.54	39 (39–40)	39 (37–40)	.34	39 (38–40)	39 (37–40)	.93
Any pre-existing medical comorbidities, <sup>a</sup> No. (%)	13 (9)	0 (0)	13 (10)	<.001	0 (0)	7 (9)	.007	6 (10)	7 (8)	.75
Cardiac	5 (3)	0 (0)	5 (4)		0 (0)	3 (4)		2 (3)	3 (3)	
Endocrine or metabolic	1 (1)	0 (0)	1 (1)		0 (0)	0 (0)		0 (0)	1 (1)	
Genetic, metabolic, or toxicological (confirmed or suspected)	3 (2)	0 (0)	3 (2)		0 (0)	3 (4)		1 (2)	2 (2)	
Neurologic or neuromuscular	3 (2)	0 (0)	3 (2)		0 (0)	1 (1)		2 (3)	1 (1)	
Pulmonary	1 (1)	0 (0)	1 (1)		0 (0)	0 (0)		0 (0)	1 (1)	
Renal	2 (1)	0 (0)	2 (2)		0 (0)	1 (1)		1 (2)	1 (1)	
Other <sup>c</sup>	1 (1)	0 (0)	1 (1)		0 (0)	1 (1)		0 (0)	1 (1)	
Reported with COVID-19 positive contacts, No. (%)	35 (24)	6 (27)	29 (23)	.75	4 (20)	9 (12)	.49	17 (27)	18 (21)	.94
Non-COVID-19 ill contact, No. (%)	18 (12)	9 (41)	9 (7)	.006	9 (45)	6 (8)	.006	12 (19)	6 (7)	.20

<sup>a</sup> Three study participants had a pre-existing medical comorbidity in >1 system.

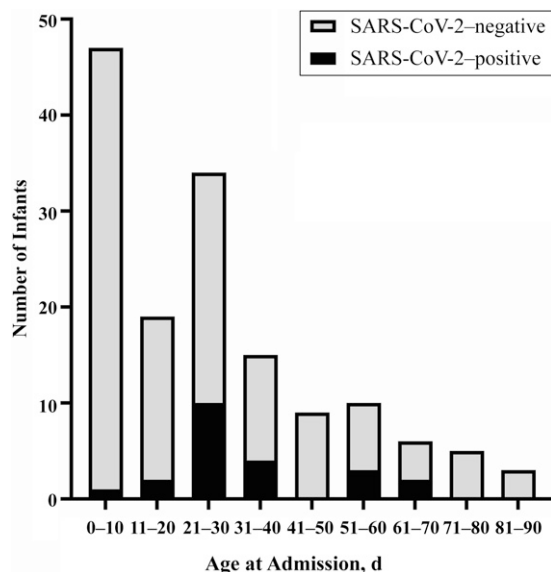
<sup>b</sup> Because of rounding, percentages do not add up precisely to 100%.

<sup>c</sup> Neonatal abstinence syndrome.

cultures were positive (15%), 9 of them (41%) were deemed by clinicians to represent true infections, whereas the remainder

(n = 13; 59%) were deemed to represent nonclinically significant contaminants. No difference was observed in overall blood culture

positivity (n = 3 [14%] to n = 19 [15%]; P = .83) or in the proportion of true infections compared with contaminants



**FIGURE 1**

The total number of eligible infants in each age group are shown. Infants with positive SARS-CoV-2 tests are shown in all black; infants with negative SARS-CoV-2 tests are shown in gray with a black outline.

( $n = 1$  [33%] to  $n = 8$  [42%];  $P = .65$ ) between infants with and without SARS-CoV-2 infection, including the febrile subgroup ( $n = 3$  [15%] to  $n = 18$  [24%];  $P = .16$ ; and  $n = 3$  [15%] to  $n = 7$  [9%];  $P = .54$ ). Infants without SARS-CoV-2 were more likely than those with SARS-CoV-2 to have positive urine culture results ( $n = 25$  [20%] to  $n = 1$  [5%];  $P = .002$ ) and positive CSF culture results ( $n = 5$  [4%] to  $n = 0$  [0%];  $P = .02$ ). Among febrile infants, positive urine culture results were more likely among SARS-CoV-2-negative compared with positive infants ( $n = 22$  [33%] to  $n = 1$  [6%]  $P = .03$ ). No positive CSF cultures occurred among febrile infants. Detection of other viruses on the respiratory viral panel (RVP) was low ( $n = 9$ ; 6%) and no differences in RVP positivity rates were observed between those with and without SARS-CoV-2 in all infants ( $n = 2$  [9%] to  $n = 7$  [6%];  $P = .85$ ), febrile infants ( $n = 1$  [6%] to  $n = 6$  [10%];  $P = .69$ ), or between high or low community SARS-CoV-2 circulation periods ( $n = 2$  [3%] to  $n = 7$  [8%];  $P = .16$ ). Chest radiography was performed in 56 infants (38%); no differences in the presence or distribution of infiltrates

were present between all infants with and without SARS-CoV-2 or in the febrile subgroup (Table 3).

### Respiratory Interventions and Clinical Outcome

A minority of infants ( $n = 32$ ; 22%) required respiratory support during hospitalization (Table 4). The need for any respiratory support did not differ for infants with and without SARS-CoV-2 ( $n = 2$  [9%] to  $n = 20$  [24%];  $P = .16$ ). Infants with SARS-CoV-2 were significantly less likely to require an ICU admission ( $n = 2$  [9%] to  $n = 47$  [37%];  $P < .001$ ) but had a similar hospital LOS to infants without SARS-CoV-2 (2 [IQR: 2–3] days to 3 [IQR: 2–7] days;  $P = .08$ ). No differences in respiratory interventions, ICU admissions, or LOS were observed in the febrile subgroup (Table 4). All infants with SARS-CoV-2 survived to discharge.

### DISCUSSION

In this study, 15% of the 148 infants admitted for an SBI evaluation during the 9-month study period had positive SARS-CoV-2 nasopharyngeal RT-PCR tests. We

found SARS-CoV-2 positivity rates among infants hospitalized for an SBI evaluation significantly differed between periods of low (3%) and high (31%) community SARS-CoV-2 circulation. Our finding of 31% SARS-CoV-2 positivity during high community circulation periods is consistent with a 30% SARS-CoV-2 prevalence reported in a case series of febrile infants <60 days of age evaluated in a different facility in NYC during the peak of the epidemic.<sup>26</sup>

In adults and older children, COVID-19 can present with a wide variety of symptoms, including systemic, dermatologic, respiratory, and gastrointestinal symptoms.<sup>1,7,10–12,16,18,20,27</sup> However in this study, isolated fever was the most common presentation of SARS-CoV-2, with a higher percentage of infants in this study presenting with an isolated fever compared with the 40% reported in another study of infants.<sup>28</sup> A lower proportion of infants with SARS-CoV-2 in this study had dermatologic, respiratory, or gastrointestinal symptoms noted at admission, compared with other pediatric and young infant studies.<sup>5,9–14,20,26,27,29–32</sup>

The mean age of all infants with SARS-CoV-2 infection in our study was higher than that of SARS-CoV-2-negative infants but in line with mean or median ages (16 to 39 days) reported in other studies of infants undergoing SBI evaluation.<sup>9,12,26,28,30</sup> Although this could reflect longer exposure to the extrauterine environment and more opportunities for viral transmission, inclusion of asymptomatic newborns exposed to maternal infections may have decreased the average age of SARS-CoV-2-negative infants, which may explain why this age difference was not observed in the febrile subgroup. The lower age among infants without SARS-CoV-2 infection may confound the differences in hemoglobin observed

**TABLE 2** Presenting Symptoms of Study Participants

	All SBI Evaluation Infants (n = 148)	SBI Evaluation Infants With SARS-CoV-2 (n = 22)	SBI Evaluation Infants Without SARS-CoV-2 (n = 126)	P	Febrile Infants With SARS-CoV-2 (n = 20)	Febrile Infants Without SARS-CoV-2 (n = 74)	P	SBI Evaluation Infants High Community Circulation Periods (n = 62)	SBI Evaluation Infants Low Community Circulation Period (n = 86)	P
Fever	94 (64)	20 (91)	74 (59)	<.001	20 (100)	74 (100)	N/A	40 (65)	54 (63)	.83
Isolated fever	30 (20)	13 (59)	17 (13)	<.001	13 (65)	17 (23)	.002	22 (35)	8 (9)	<.001
Emesis	10 (7)	1 (5)	9 (7)	.61	1 (5)	5 (7)	.76	1 (2)	9 (10)	.02
Hypothermia	8 (5)	0 (0)	8 (6)	.004	0 (0)	0 (0)	N/A	4 (6)	4 (5)	.64
Irritability and/or fussy	39 (26)	2 (9)	37 (29)	.01	2 (10)	35 (47)	<.001	7 (11)	32 (37)	<.001
Conjunctivitis	2 (1)	0 (0)	2 (2)	.16	0 (0)	1 (1)	>.99	1 (2)	1 (1)	.82
Nasal congestion and/or rhinorrhea	12 (8)	2 (9)	10 (8)	.86	2 (10)	8 (11)	>.99	3 (5)	9 (10)	.19
Cough	9 (6)	3 (14)	6 (5)	.26	2 (10)	6 (8)	.80	4 (6)	5 (6)	.87
Cyanosis and/or hypoxia	13 (9)	1 (5)	12 (10)	.35	0 (0)	3 (4)	.60	6 (10)	7 (8)	.75
Respiratory distress	17 (11)	1 (5)	16 (13)	.14	0 (0)	2 (3)	>.99	6 (10)	11 (13)	.55
Decreased feeding	29 (20)	2 (9)	27 (21)	.10	2 (10)	24 (32)	.05	6 (10)	23 (27)	.006
Diarrhea	7 (5)	0 (0)	7 (6)	.008	0 (0)	7 (9)	.34	3 (5)	4 (5)	.96
Rash	4 (3)	2 (9)	2 (2)	.25	1 (5)	2 (3)	>.99	3 (5)	1 (1)	.22
Lethargy	9 (6)	0 (0)	9 (7)	.002	0 (0)	5 (7)	.36	4 (6)	5 (6)	.87
Asymptomatic, known exposure to infection	16 (11)	1 (5)	15 (12)	.18	0 (0)	0 (0)	N/A	9 (15)	7 (8)	.24
Other <sup>a</sup>	18 (12)	0 (0)	18 (14)	<.001	0 (0)	7 (9)	.007	4 (6)	15 (17)	.04

N/A, not applicable.

<sup>a</sup> One infant each with abdominal distension, abnormal imaging, bleeding from a surgical site, decreased limb movement, decreased muscle tone, failure to thrive, jaundice, jitteriness, and tachycardia; 2 infants with skin erythema; 3 infants eye symptoms; and 4 infants with suspected or confirmed seizure.

between all infants with and without SARS-CoV-2, because hemoglobin may be elevated shortly after birth, and no hemoglobin differences were observed between SARS-CoV-2–positive and SARS-CoV-2–negative infants in the older, febrile subgroup. Lower WBC, ANC, and ALC values were observed among SARS-CoV-2 infants in all analysis groups, consistent with what has been reported in some pediatric COVID-19 studies.<sup>13,33–37</sup> No differences in chest imaging results were observed among infants with and without SARS-CoV-2, consistent with findings from older children described in the literature.<sup>29</sup> We recommend clinicians avoid using laboratory or imaging results to guide decision-making on whether to test hospitalized infants for SARS-CoV-2.

Case reports and series have identified concomitant urinary tract infections and bacteremia among young infants with COVID-19.<sup>9,13,26–28</sup> We found lower rates of positive urine and CSF cultures in infants with SARS-CoV-2 compared to those without SARS-CoV-2, but no difference in blood culture positivity rates. Given the potentially severe consequences of untreated bacterial infections, we recommend clinicians continue to assess young febrile infants for bacterial infections, regardless of SARS-CoV-2 status. We found a relatively low incidence (6%) of viral co-infection among infants with and without SARS-CoV-2. This likely reflects community-wide decreases in other respiratory viruses reported in New York during the study period<sup>38,39</sup> because of enhanced infection

control practices during the COVID-19 pandemic. Additional studies are warranted to determine the prevalence of viral coinfections when respiratory virus circulation resembles more typical, seasonal epidemiological patterns.

Overall illness among infants with SARS-CoV-2 infection in this study was mild to moderate, consistent with the severity of disease in this age group previously reported.<sup>26,28</sup> A minority of infants with SARS-CoV-2 required respiratory support or ICU admission, consistent with the reported literature,<sup>8,9,12,13,19,28–30,32</sup> although this may be confounded by our observed higher prevalence of comorbidities among infants without SARS-CoV-2 compared with infants with SARS-CoV-2. The

**TABLE 3** Laboratory and Radiologic Findings Among Study Participants

	All SBI Evaluation Infants (n = 148)	SBI Evaluation Infants With SARS-CoV-2 (n = 22)	SBI Evaluation Infants Without SARS-CoV-2 (n = 126)	P	Febrile Infants With SARS-CoV-2 (n = 20)	Febrile Infants Without SARS-CoV-2 (n = 74)	P	SBI Evaluation Infants High Community Circulation Periods (n = 62)	SBI Evaluation Infants Low Community Circulation Period (n = 86)	P
CBC performed, No. (%)	146 (99)	22 (100)	124 (98)	.16	20 (100)	73 (99)	.32	62 (100%)	84 (98)	.16
WBC, median (IQR), 10 <sup>3</sup> /μL	12.1 (7.7–16.7)	7.3 (5.5–11.3)	13.0 (8.8–17.7)	<.001	6.9 (5.2–8.7)	11.2 (8.5–14.3)	<.001	10.7 (7.1–16.0)	12.9 (8.7–17.7)	.05
ANC, Median (IQR), 10 <sup>3</sup> /μL	4.9 (2.3–9.2)	1.7 (1.4–3.3)	5.8 (2.5–9.9)	<.001	1.7 (1.3–3.2)	5 (2.1–7)	<.001	4.0 (1.8–7.6)	5.2 (2.4–9.7)	.13
Absolute lymphocyte count, median (IQR), 10 <sup>3</sup> /μL	4.4 (2.9–6.5)	3.3 (2.7–4.7)	4.6 (3.0–6.6)	.04	3.2 (2.6–4.0)	4.9 (3.0–7.0)	.009	3.9 (2.9–5.3)	4.8 (3.0–7.2)	.04
Hemoglobin, mean (SD), g/dL	13.8 (3.5)	12.8 (2.1)	14.0 (3.7)	.04	12.6 (1.8)	12.4 (2.9)	.69	13.8 (3.3)	13.8 (3.7)	.97
Platelet count, mean (SD), 10 <sup>3</sup> /μL	319 (127)	333 (88)	317 (133)	.48	328 (85)	354 (136)	.29	320 (113)	319 (138)	.96
CRP performed, No. (%)	72 (49)	13 (59)	59 (47)	.30	12 (60)	43 (58)	.88	33 (53)	39 (45)	.35
CRP, median (IQR), mg/L	2.7 (1.0–29.3)	0.8 (0.4–2.5)	5.7 (1.5–49.0)	.005	0.8 (0.3–2.4)	13.6 (1.5–79.2)	<.001	2.5 (0.7–33)	2.8 (1.3–30.4)	.69
Blood culture performed, No. (%)	145 (98)	22 (100)	123 (98)	.08	20 (100)	72 (97)	.32	61 (98)	84 (98)	.76
Blood culture result positive, <sup>a</sup> No. (%)	22 (15)	3 (14)	19 (15)	.83	3 (15)	18 (24)	>.16	7 (11)	15 (17)	.28
Urine culture performed, No. (%)	102 (69)	18 (82)	84 (67)	.12	17 (85)	66 (89)	.70	43 (69)	59 (69)	.92
Urine culture results positive, No. (%)	26 (18)	1 (5)	25 (20)	.002	1 (5)	22 (30)	.03	10 (16)	16 (19)	.66
CSF collected, No. (%)	92 (62)	17 (77)	75 (60)	.09	16 (80)	57 (77)	>.99	39 (63)	53 (62)	.88
CSF WBC count, median (IQR), cells	4 (2–12)	3 (1–7)	6 (2–27)	.14	4 (1–7)	6 (2–30)	.10	6 (2–13)	3 (2–15)	.59
CSF neutrophils, median (IQR), %	8 (0–36)	2.5 (0–22)	8 (2–40)	.11	3 (0–22)	8 (2–39)	.13	6 (0–24)	10 (2–44)	.08
CSF lymphocytes, mean (SD), %	34 (24)	10 (12)	33 (23)	.44	40 (27)	32 (25)	.41	37 (24)	32 (23)	.36
CSF protein, median (IQR), mg/dL	77 (60–106)	57 (42–88)	82 (65–108)	.04	58 (44–98)	78 (60–105)	.18	77 (57–115)	77 (61–105)	.90
CSF glucose, median (IQR), mg/dL	49 (43–54)	48 (44–54)	49 (43–53)	.78	48 (43–54)	49 (41–53)	.98	47 (40–52)	49 (43–60)	.29
CSF culture result positive, No. (%)	5 (3)	0 (0)	5 (4)	.02	0 (0)	5 (7)	.35	0 (0)	5 (6)	.02
RVP performed, No. (%)	97 (66)	19 (86)	78 (62)	.007	18 (90)	61 (82)	.51	42 (68)	55 (64)	.63
RVP positive, No. (%)	9 (6)	2 (9)	7 (6)	.85	1 (5)	6 (8)	.69	2 (3)	7 (8)	.16
Chest radiograph performed, No. (%)	56 (38)	8 (36)	48 (38)	.88	7 (35)	24 (32)	.84	18 (29)	38 (44)	.06
Chest radiography findings				.25			.43			.39
No lung infiltrates, No. (%)	27 (18)	2 (9)	25 (20)		2 (10)	11 (15)		7 (11)	20 (23)	
Unilateral lung infiltrate, No. (%)	2 (1)	0 (0)	2 (2)		0 (0)	1 (1)		0 (0)	2 (2)	
Bilateral lung infiltrates, No. (%)	27 (18)	6 (27)	21 (17)		5 (25)	12 (16)		11 (18)	16 (19)	

CBC, complete blood cell count.

<sup>a</sup> Inclusive of all positive blood culture results, regardless of clinical significance.

median hospital LOS for SARS-CoV-2-positive infants in this study was shorter than previously reported,<sup>10,30</sup> and all infants with SARS-CoV-2 survived to discharge, consistent with good outcomes

reported across other studies.<sup>10–12,17,26</sup>

Our study has several limitations. The number of infants with SARS-CoV-2 in our sample is small, and

most participants were not identified in the EMR as belonging to a racial or ethnic minority group. Therefore, our results may not accurately reflect the prevalence and/or severity of infection among

**TABLE 4** Respiratory Interventions and Clinical Outcomes Among Study Participants

	All SBI Evaluation Infants (n = 148)	SBI Evaluation Infants With SARS-CoV-2 (n = 22)	SBI Evaluation Infants Without SARS-CoV-2 (n = 126)	P	Febrile Infants With SARS-CoV-2 (n = 20)	Febrile Infants Without SARS-CoV-2 (n = 74)	P	SBI Evaluation Infants High Community Circulation Periods (n = 62)	SBI Evaluation Infants Low Community Circulation Period (n = 86)	P
Requiring respiratory support, No. (%)	32 (22)	2 (9)	30 (24)	.16	1 (5)	6 (8)	>.99	9 (15)	23 (27)	.10
Nebulizers <sup>a</sup>	1 (1)	0 (0)	1 (1)	.32	0 (0)	0 (0)	N/A	0 (0)	1 (1)	.32
Oxygen <sup>a</sup>	27 (18)	2 (9)	25 (20)	.26	1 (5)	4 (5)	>.99	9 (15)	18 (21)	.39
Noninvasive pressure support <sup>a</sup>	12 (8)	0 (0)	12 (10)	.21	0 (0)	1 (1)	>.99	4 (6)	8 (9)	.56
Mechanical ventilation <sup>a</sup>	5 (3)	1 (5)	4 (3)	>.99	0 (0)	1 (1)	>.99	2 (3)	3 (3)	.93
Admitted to ICU, No. (%)	49 (33)	2 (9)	47 (37)	<.001	0 (0)	10 (14)	.11	20 (32)	29 (34)	.85
Requiring pressors, No. (%)	3 (2)	0 (0)	3 (2)	.08	0 (0)	0 (0)	N/A	0 (0)	3 (3)	.26
Requiring ECMO, No. (%)	0 (0)	0 (0)	0 (0)	N/A	0 (0)	0 (0)	N/A	0 (0)	0 (0)	0 (0)
Admission duration, median (IQR), d	3 (2–6)	2 (2–3)	3 (2–7)	.08	2 (2–3)	3 (2–7)	.06	2 (2–4)	3 (2–7)	.09
Clinical outcome, No. (%)				.91			>.60			.53
Discharged from the hospital	145 (98) <sup>b</sup>	22 (100)	123 (98) <sup>b</sup>		20 (100)	73 (99)		62 (100)	83 (97)	
Discharged to rehabilitation center	1 (1) <sup>b</sup>	0 (0)	1 (1) <sup>b</sup>		0 (0)	1 (1)		0 (0)	1 (1)	
Transferred to different inpatient facility	1 (1) <sup>b</sup>	0 (0)	1 (1) <sup>b</sup>		0 (0)	0 (0)		0 (0)	1 (1)	
Deceased	1 (1) <sup>b</sup>	0 (0)	1 (1) <sup>b</sup>		0 (0)	0 (0)		0 (0)	1 (1)	

ECMO, extracorporeal membrane oxygenation; N/A, not applicable.

<sup>a</sup> Respiratory interventions were not considered mutually exclusive.

<sup>b</sup> Because of rounding, percentages do not add up precisely to 100%.

infants of racial or ethnic backgrounds that have been associated with more severe COVID-19. Because of limited SARS-CoV-2 testing capacity at the beginning of the NYC epidemic, testing was only available for hospitalized patients at the start of this study; therefore, the study population was limited to hospitalized infants and is not representative of all SARS-CoV-2 infections among infants <90 days of age undergoing SBI evaluation in an emergency care setting. We anticipate that the exclusion of infants evaluated for an SBI in the emergency department but subsequently discharged may bias our results in favor of reflecting illness among younger infants and capture more moderate to severe cases, potentially underrepresenting infants 60-89 days of age and those with mild infections. However, despite a potential bias toward enrolling sicker infants, we found a low incidence of ICU admission and

need for respiratory support among hospitalized infants with SARS-CoV-2.

We used 7-day rolling average testing positivity rates, with a cutoff threshold of 5% as a surrogate marker for levels of community SARS-CoV-2 circulation, although use of this measure has limitations. Changes in testing capacity throughout the NYC COVID-19 epidemic, from initially being limited to hospitalized patients to widespread outpatient testing, makes this an imprecise surrogate marker of community circulation because of differences in the population receiving testing over time. However, these testing limitations also affect other markers of community SARS-CoV-2 circulation, such as the total number of confirmed cases or case rates in the NYC population. We opted to use testing positivity because of the availability of data from the NYC Department of Health and Mental

Hygiene during the entire study period without any data gaps. The cutoff threshold of 5% testing positivity was chosen on the basis of agreement between the timing of this testing positivity value with significant inclines or declines on the NYC COVID-19 epidemic curve.

## CONCLUSIONS

Enhancing our knowledge of how SARS-CoV-2 infection affects young infants is important for informing clinical practice, planning public health measures (such as COVID-19 vaccine distribution), and furthering our understanding of COVID-19 in this age group. The prevalence of SARS-CoV-2 infection among hospitalized young infants in 2020 varied with levels of community transmission. Although the transmissibility of SARS-CoV-2 from infants at this age is unknown, identification of infants with SARS-CoV-2 infection has important



implications for hospital and local community infection control. Additional research is needed on young infants evaluated in a wider range of settings, including the emergency department and outpatient clinics, to truly understand the full impact of SARS-CoV-2 infection in this age group. During the 9-month study period, we witnessed rapidly evolving changes in SARS-CoV-2 epidemiology and variations in

testing capacity from limited inpatient testing only to broad-scale outpatient availability. As the epidemiology of COVID-19 continues to evolve with the emergence of variant viruses and vaccination implementation, continued monitoring of infection in this age group is warranted to determine if, when, and in what settings a selective testing strategy, as opposed to universal testing, may be appropriate in the future.

## ABBREVIATIONS

ALC: absolute lymphocytic count  
ANC: absolute neutrophil count  
COVID-19: coronavirus disease 2019  
CRP: C-reactive protein  
CSF: cerebrospinal fluid  
EMR: electronic medical record  
IQR: interquartile range  
LOS: length of stay  
NYC: New York City  
NYCHHC: New York City Health + Hospitals  
RT-PCR: reverse transcription polymerase chain reaction  
SARS-CoV-2: severe acute respiratory syndrome coronavirus 2  
SBI: serious bacterial infection  
WBC: white blood cell count

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

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