Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Community-Onset Severe Acute Respiratory Syndrome Coronavirus 2 Infection in Young Infants: A Systematic Review

Elyse G. Mark, MA[1], W. Christopher Golden, MD[1], Maureen M. Gilmore, MD[1], Anna Sick-Samuels, MD, MPH[2], Melanie S. Curless, MSPH, RN, CIC[3], Lawrence M. Nogee, MD[1], Aaron M. Milstone, MD, MHS[2], and Julia Johnson, MD, PhD[1]

Objective To summarize and evaluate current reports on community-onset severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in young infants.

Study design We performed a systematic review to identify reports published from November 1, 2019, until June 15, 2020, on laboratory-confirmed community-onset SARS-CoV-2 infection in infants younger than 3 months of age. We excluded studies reporting neonates with perinatal coronavirus disease 2019 (COVID-19) exposure and diagnosis before hospital discharge and hospital-onset disease, as well as clinically diagnosed cases without confirmation. Two independent reviewers performed study screening, data abstraction, and risk of bias assessment. Variables of interest included patient age, exposure to COVID-19, medical history, clinical symptoms, SARS-CoV-2 testing, laboratory findings, clinical course, and disposition.

Results In total, 38 publications met inclusion criteria, including 23 single case reports, 14 case series, and 1 cohort study, describing 63 infants younger than 3 months of age with laboratory-confirmed SARS-CoV-2 infection. Most cases were mild to moderate. Fever, respiratory, gastrointestinal, cardiac, and neurologic findings were reported. Laboratory abnormalities included neutropenia, lymphopenia, and elevated serum levels of inflammatory markers and aminotransferases. Fifty-eight (92%) infants were hospitalized, 13 (21%) were admitted to the intensive care unit, and 2 (3%) required mechanical ventilation. No death was reported.

Conclusions Among young infants with laboratory-confirmed SARS-CoV-2 infection, most cases were mild to moderate and improved with supportive care. Our results demonstrate a need for a high index of suspicion for SARS-CoV-2 infection in young infants presenting with generalized symptoms such as fever or decreased feeding, even in the absence of respiratory symptoms. *(J Pediatr 2021;228:94-100)*.

Since its identification in December 2019, severe acute respiratory coronavirus 2 (SARS-CoV-2) has proven highly contagious and globally devastating, causing 728 013 fatalities as of August 10, 2020.[1] Although coronavirus disease 2019 (COVID-19) is generally milder in children than in adults, infants have disproportionate risk of serious infection. In a retrospective study of 728 laboratory-confirmed pediatric cases in China, 97% presented with asymptomatic-to-moderate illness. Of confirmed severe or critically ill pediatric patients, however, one-third occurred in infants younger than 1 year of age.

As in adults, the most common pediatric symptoms of COVID-19 are fever and cough, with gastrointestinal and neurologic involvement in some patients.[2,3] In a retrospective study of 74 pediatric patients in China, Wu et al[4] noted a 51% prevalence of coinfection with other pathogens, including *Mycoplasma pneumoniae* (n = 16), respiratory syncytial virus (RSV) (n = 3), cytomegalovirus (n = 3), Epstein–Barr virus (n = 3), and influenza (n = 1). Moreover, recent evidence has emerged linking COVID-19 to multisystem inflammatory syndrome in children, including those as young as 6 months.[5] Published reports from the US and Italy describe increasing cases of SARS-CoV-2 infection in children manifesting with inflammatory symptoms similar to Kawasaki disease or toxic shock syndrome, frequently coming to medical attention with nonspecific gastrointestinal symptoms and elevation of cardiac biomarkers.[6,7]

SARS-CoV-2 spreads primarily through droplet and contact transmission, with a high incidence of familial clustering and significant proportion of asymptomatic infection.[8] Infants may be at greater risk of exposure to SARS-CoV-2 infection due to frequent contact with healthcare workers in the first few weeks of life, dependency on caretakers, and necessity for close contact during feeding and care that may increase exposure to respiratory secretions of infected persons. At present, studies of community-onset SARS-CoV-2 infection in young infants are primarily limited to case reports and small case series. This systematic review aims to consolidate reports of laboratory-confirmed, community-onset cases in infants younger than 3 months of age.

COVID-19	Coronavirus disease 2019
ICU	Intensive care unit
PCR	Polymerase chain reaction
RSV	Respiratory syncytial virus
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2

From the Divisions of [1]Neonatology and [2]Infectious Diseases, Department of Pediatrics, Johns Hopkins University; and [3]Department of Hospital Epidemiology and Infection Control, Johns Hopkins Hospital, Baltimore, MD

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Methods

We conducted a systematic review to identify studies published from November 1, 2019, until June 15, 2020, on laboratory-confirmed community-onset SARS-CoV-2 infection in infants younger than 3 months of age. We searched PubMed and Embase and only included peer-reviewed publications for which full-text articles could be retrieved (search strategy, **Table I** [available at www.jpeds.com]). Additional articles were identified via snowball search. Inclusion criteria were infant aged younger than 3 months, community onset of illness, and laboratory-based confirmation by at least 1 positive SARS-CoV-2 polymerase chain reaction (PCR) test. Exclusion criteria were perinatal COVID-19 exposure with positive PCR testing in infants before hospital discharge, nosocomial infection, and presentation of aggregate pediatric data that included age groups greater than 3 months.

Two independent reviewers performed screening of articles in Covidence (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia) and data abstraction in Microsoft Excel (Microsoft Corporation, Redmond, Washington). Risk of bias assessment was performed by 2 independent reviewers for all studies meeting inclusion criteria using The Joanna Briggs Institute Critical Appraisal Checklists (**Figure 1**; available at www.jpeds.com).[9-11] Discrepancies were resolved by discussion among the 2 reviewers with available third reviewer adjudication if needed. Descriptive analysis was performed to summarize infant demographic and clinical characteristics, laboratory findings, imaging studies, and clinical course, including hospital admission, intensive care unit (ICU) admission, need for respiratory support, antibiotic administration, COVID-specific therapy, and disposition. Categorical variables were expressed as numbers of cases (n), and percentages (%) and continuous variables were expressed as the median with IQR. Statistical analyses were performed using Microsoft Excel.

Results

Our search strategy identified 793 articles published between November 1, 2019, and June 15, 2020, along with 11 additional articles identified via snowball search (**Figure 2**).

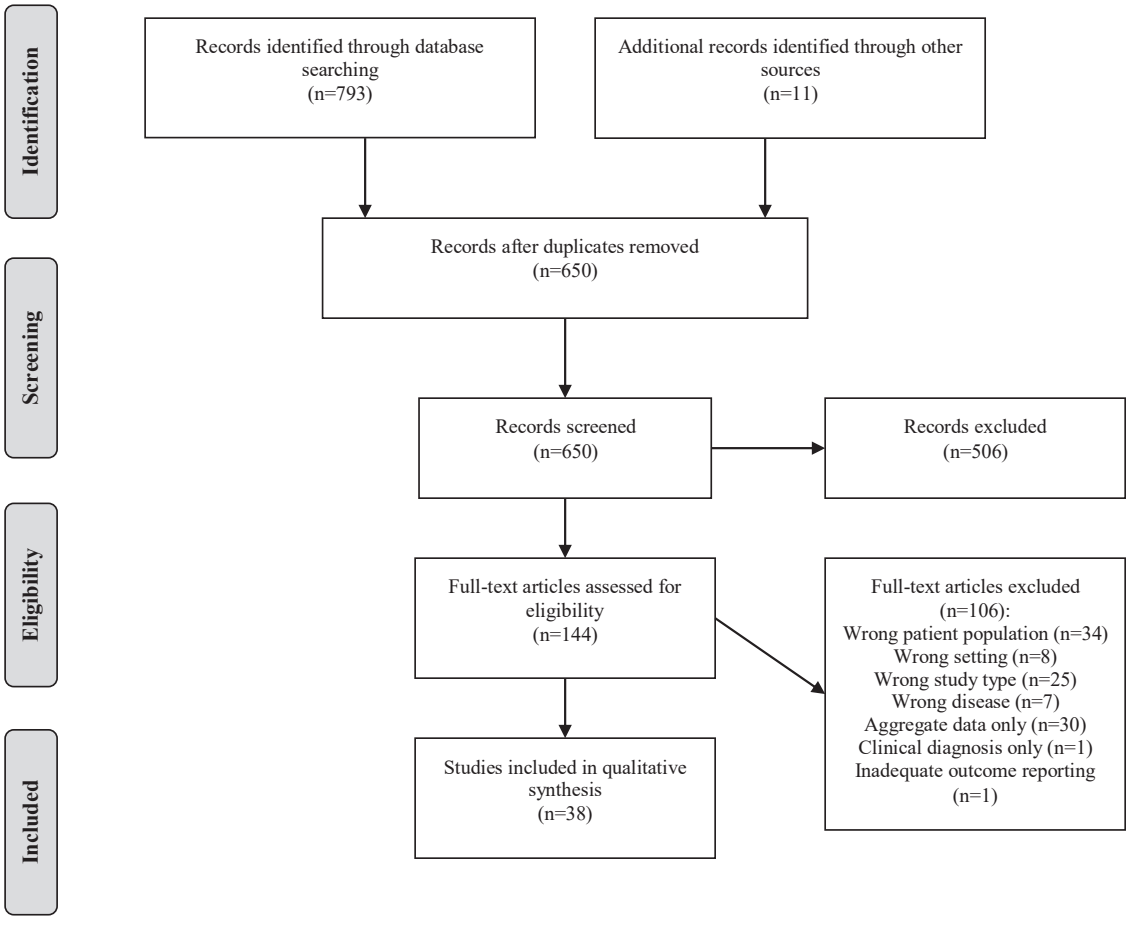

Figure 2. PRISMA study flow diagram. Flow diagram of study identification, screening, eligibility, and included studies.

Table II. Studies reporting community-onset COVID-19 among infants younger than 3 months of age by country, author, and study type

Countries	Authors	Date	Study type	Infants, n	SARS-CoV-2 PCR testing by source, n positive/total n tested (%)
Brazil	Carvalho et al[14]	6/3/2020	Case report	1	Nasopharyngeal, 1/1 (100)
China	Cai et al[35]	5/12/2020	Case series	1	Nasopharyngeal, 1/1 (100) Oropharyngeal, 1/1 (100)
China	Cui et al[18]	3/17/2020	Case report	1	Nasopharyngeal, 1/1 (100) Oropharyngeal, 0/1 Anal swab/stool sample, 1/1 (100)
China	Liu et al[49]	3/21/2020	Cohort study	1	Oropharyngeal, 1/1 (100)
China	Lu et al[37]	5/1/2020	Case report	1	Oropharyngeal, 1/1 Anal swab/stool sample, 0/1 Urine, 0/1
China	Shi et al[31]	4/15/2020	Case report	1	Oropharyngeal, 1/1 (100)
China	Wang et al[32]	3/25/2020	Case report	1	Oropharyngeal, 1/1 (100) Anal swab/stool sample, 1/1 (100)
China	Wei et al[45]	2/14/2020	Case series	1	Nasopharyngeal, 1/1 (100)
China	Xu et al[47]	3/13/2020	Case series	1	Nasopharyngeal, 1/1 (100) Anal swab/stool sample, 1/1 (100)
China	Zeng et al[33]	4/2/2020	Case report	1	Nasopharyngeal, 1/1 (100) Oropharyngeal, 1/1 (100) Anal swab/stool sample, 1/1 (100)
China	Zhang et al[48]	4/8/2020	Case series	2	Anal swab/stool sample, 2/2 (100)
France	Meslin et al[39]	5/2020	Case series	6	Nasopharyngeal, 6/6 (100)
France	Nathan et al[40]	4/27/2020	Case series	5	Nasopharyngeal, 5/5 (100) CSF, 0/4
Germany	Färber et al[21]	6/3/2020	Case report	1	Oropharyngeal, 1/1 (100) CSF, 1/1 (100)
Iran	Kamali Aghdam et al[25]	4/1/2020	Case report	1	Oropharyngeal, 1/1 (100)
Italy	Buonsenso et al[34]	5/2/2020	Case series	1	Nasopharyngeal, 1/1 (100) Oropharyngeal, 0/1
Italy	Calderaro et al[12]	5/14/2020	Case report	1	Nasopharyngeal, 1/1 (100)
Italy	Canarutto et al[13]	4/6/2020	Case report	1	Oropharyngeal, 1/1 (100)
Italy	Giacomet et al[22]	5/19/2020	Case report	1	Nasopharyngeal, 1/1 (100)
Italy	Poli et al[28]	4/13/2020	Case report	1	Nasopharyngeal, 1/1 (100)
Italy	Salvatori et al[43]	4/21/2020	Case series	2	Nasopharyngeal, 2/2 (100)
Italy	Venturini et al[44]	5/19/2020	Case series	2	Nasopharyngeal, 2/2 (100)
South Korea	Han et al[24]	4/16/2020	Case report	1	Nasopharyngeal, 1/1 (100) Oropharyngeal, 1/1 (100) Saliva, 1/1 (100) Anal swab/stool sample, 1/1 (100) Urine, 1/1 (100) Blood, 1/1 (100)
Spain	Chacón-Aguilar et al[15]	4/17/2020	Case report	1	Nasopharyngeal, 1/1 (100)
Spain	González-Brabin et al[23]		Case report	1	Nasopharyngeal, 1/1 (100)
United Kingdom	Cook et al[16]		Case report	1	Nasopharyngeal, 1/1 (100)
United Kingdom	Ng et al[41]	5/2020	Case series	3	Unspecified Nasopharyngeal/oropharyngeal, 3/3 (100)
US	Coronado Munoz et al[17]	4/22/2020	Case report	1	Nasopharyngeal, 1/1 (100)
US	Dugue et al[19]	4/23/2020	Case report	1	Nasopharyngeal, 1/1 (100) Anal swab/stool sample, 1/1 (100) Blood, 0/1 CSF, 0/1
US	Dumpa et al[20]	5/17/2020	Case report	1	Nasopharyngeal, 1/1 (100)
US	Feld et al[36]	5/13/2020	Case series	3	Nasopharyngeal, 3/3 (100)
US	Kan et al[26]	4/22/2020	Case report	1	Nasopharyngeal, 1/1 (100) Oropharyngeal, 1/1 (100)
US	McLaren et al[38]	6/11/2020	Case series (subset of cohort study)	7	Nasopharyngeal, 7/7 (100)
US	Paret et al[42]	4/17/2020	Case series	2	Nasopharyngeal, 2/2 (100)
US	Patek et al[27]	4/15/2020	Case report	1	Nasopharyngeal, 1/1 (100)
US	Precit et al[29]	5/22/2020	Case report	1	Nasopharyngeal, 1/1 (100) Blood, 0/1
US	Robbins et al[30]	6/2020	Case report	1	Unspecified, 1/1 (100)
US	White et al[46]	6/4/2020	Case series	3	Nasopharyngeal, 3/3 (100)
	Summary by sample type				Infant samples Nasopharyngeal, 48/48 (100) Oropharyngeal, 12/14 (83) Nasopharyngeal/oropharyngeal swab, 60/60 (100) Saliva, 1/1 (100) Anal swab/stool sample, 8/10 (80) Urine, 1/2 (50) Blood, 1/3 (33) CSF, 1/6 (17)

Summary of studies reporting community-onset COVID-19 among infants younger than 3 months of age with positive SARS-CoV-2 PCR testing.

After exclusion of duplicates, 650 records were screened; 506 were excluded after title and abstract screening and 106 were excluded after full-text review. We identified 38 studies for qualitative analysis, describing 63 infants younger than 3 months of age with community-onset SARS-CoV-2 infection. Among included studies, 23 were single case reports, 14 were case series, and 1 was a cohort study, with the majority of publications from the US (n = 11), China (n = 10), and Italy (n = 7) (**Table II**).[12-48]

Infant ages ranged from 5 days to less than 3 months (**Table III**). Among 59 infants with reported sex, 41 (69%) were male. Six (16%) infants with known gestational age were premature. Eight infants were reported as having a significant medical history, including extreme prematurity (n = 1), congenital heart disease (n = 3), cystic fibrosis (n = 1), and renal anomalies (n = 3). One neonate had a genetic syndrome associated with multiple congenital anomalies. Among the cases with a known contact history, 41 infants (69%) were exposed to a symptomatic person or person positive for COVID-19.

Among 62 infants with specified test site for SARS-CoV-2 PCR testing, 60 (97%) had at least 1 positive respiratory specimen (**Table II**). Two infants tested positive only from an anal swab.[48] All infected infants who had nasopharyngeal testing (n = 48) had a positive test, as did 12 (83%) infants who had an oropharyngeal sample tested. PCR testing of cerebrospinal fluid, blood, and urine was infrequently performed and was positive in 1 of 6 (17%), 1 of 3 (33%), and 1 of 2 (50%) samples, respectively. Eight (80%) of 10 infants tested had a positive PCR result from stool or an anal swab, with persistent viral shedding in stool reported in several infants. Han et al[24] reported serial quantitative PCR testing in an infant and her mother who also was hospitalized with COVID-19. The infant had positive PCR testing from nasopharyngeal, oropharyngeal, saliva, blood, urine, and stool samples, with gradual decline in viral load over a 3-week hospital admission. Her mother had detectable virus in nasopharyngeal/oropharyngeal, sputum, and stool samples; testing of blood and urine samples was negative.

Fever was the most common symptom reported among infants (n = 46, 73%), followed by respiratory symptoms (rhinitis, cough, or respiratory distress) (n = 40, 66%) (**Table III**). Reported gastrointestinal symptoms included diarrhea (n = 9) and emesis (n = 9). Two infants (3%) presented with seizures. Three infants (5%) were asymptomatic, including 1 infant with cystic fibrosis who had been tested due to known exposure to a family member with COVID-19.[28]

Laboratory tests were performed and reported in up to two-thirds of cases. Reported hematologic abnormalities included neutropenia (n = 22/39, 56%), lymphopenia (n = 7/45, 16%), and thrombocytopenia (n = 2/27, 7%). Median C-reactive protein was 2.1 mg/L (IQR 0.9-4.5; range, below limit of detection to 172); 5 (19%) infants had an elevated C-reactive protein ≥10 mg/L. Median procalcitonin was 0.13 ng/mL (IQR 0.10-0.22; range, 0.01-9.3); 4 (20%) infants had an elevated procalcitonin (≥0.5 ng/mL). Elevated aminotransferases were documented in 9 of 11 infants tested (82%), although only 1 infant was reported to have substantial elevation of hepatic enzymes with aspartate aminotransferase >500 units/L. Two of the infants with abnormal aminotransferase values also had elevated cardiac biomarkers.[18,35] An additional infant with suspected myocarditis had elevated inflammatory markers and markers of cardiac dysfunction in the absence of either respiratory or hepatic involvement.[22] Chest imaging was performed in 34 infants. Of 28 infants for whom chest radiography was performed, 13 (46%) had abnormal findings. Among infants who had chest computed tomography performed (n = 9), all had noted abnormal findings.

Forty-three infants (68%) were evaluated for bacterial infection. Of 37 reported blood cultures, 3 (8%) were positive, although 2 cultures positive for *Staphylococcus epidermidis* and *Streptococcus salivarius* were thought to be due to contamination.[29,36] One critically ill infant with septic shock and an admission blood culture positive for *S epidermidis* was treated.[16] Among 28 infants with a reported urine culture, 3 (11%) were found to have a urinary tract infection. Urinary tract infection pathogens included *Escherichia coli* (n = 2) and *Klebsiella oxytoca* (n = 1).[23,38] None of the 26 reported cerebrospinal fluid cultures was positive. Testing for viral coinfection was reported in 30 infants, of whom 5 (17%) had positive testing; identified pathogens included RSV (n = 2), rhinovirus/enterovirus (n = 2), and seasonal coronavirus (n = 1).[17,19,31,41,49] One neonate was diagnosed with human metapneumovirus coinfection after initial SARS-CoV-2 hospital admission; this neonate presented 5 days after initial discharge with poor feeding and respiratory distress and was readmitted.[29]

Fifty-eight (92%) infants were hospitalized with 13 (21%) requiring ICU admission. Fourteen (24%) infants required respiratory support, but only 3 (5%) required continuous positive airway pressure and 2 (3%) required invasive mechanical ventilation. One neonate presenting with clinical sepsis required mechanical ventilation and vasopressor support, with course complicated by pneumothorax and thoracostomy tube placement.[17] The neonate recovered quickly and was discharged home without respiratory support 9 days after admission. Cook et al[16] reported a neonate with a history of extreme prematurity at 27 weeks gestation who had been discharged from the neonatal ICU 10 days before hospitalization with respiratory failure and SARS-CoV-2 infection. The neonate was successfully extubated but remained hospitalized at the time of publication. Most infants received supportive care only; COVID-specific pharmacotherapies employed included hydroxychloroquine/azithromycin (n = 2), inhaled interferon (n = 5), and remdesivir (n = 1). Two neonates were treated with intravenous immunoglobulin, one in the setting of suspected myocarditis and the other with RSV coinfection and severe pneumonia requiring continuous positive airway pressure.[22,31]

Among admitted infants, length of hospital stay ranged from 1 to 30 days. Almost all infants with known

Table III. Clinical and demographic characteristics of infants younger than 3 months of age with community-onset SARS-CoV-2 infection

Characteristics	Total N = 63
Age, range	5 d to <3 mo
Male, n/total (%)	42/61 (69)
Gestational age at birth in completed weeks, median (IQR)	39 (37-39) (n = 26)
History of prematurity, n/total (%)	6/37 (16)
Significant medical history, n/total (%)	8/42 (19)
Contact with individual symptomatic or positive for COVID-19, n/total (%)	41/59 (69)
Clinical presentation	
Fever, n (%)	46 (73)
Cough, n (%)	23 (38)
Rhinitis, n (%)	22 (36)
Respiratory distress, n (%)	16 (26)
Poor feeding, n (%)	15 (24)
Emesis, n (%)	9 (14)
Diarrhea, n (%)	9 (14)
Hypoxia, n (%)	9 (16)
Hypothermia, n (%)	3 (5)
Rash, n (%)	3 (5)
Hypotension, n (%)	2 (3)
Apnea, n (%)	2 (3)
Seizure, n (%)	2 (3)
Asymptomatic, n (%)	3 (5)
Laboratory and imaging studies	
WBC count, cells × 10^9/L, median (IQR)	7.04 (4.80-8.94) (n = 44)
Neutrophil count, cells × 10^9/L median (IQR)	1.20 (0.87-1.99) (n = 36)
Neutropenia, n/total (%)	22/36 (56)
Lymphocyte count, cells × 10^9/L, median (IQR)	2.92 (1.83-4.87) (n = 42)
Lymphopenia, n/total (%)	7/45 (16)
Platelet count, cells/μL, median (IQR)	348 500 (284 750-408 500)* (n = 24)
Thrombocytopenia, n/total (%)	2/27 (7)
CRP, mg/L, median (IQR)	2.1 (0.9-4.5)† (n = 27)
Procalcitonin, ng/mL, median (IQR)	0.13 (0.10-0.22)† (n = 20)
AST, U/L, median (IQR)	61.5 (46.25-66.5)‡ (n = 11)
ALT, U/L, median (IQR)	26.5 (18-38.25) (n = 10)
Elevated cardiac biomarkers, n (%)	3 (5)
Chest radiograph abnormal, n/n obtained (%)	13/28 (46)
Chest CT abnormal, n/n obtained (%)	9/9 (100)
Blood culture, n positive/n obtained (%)	3/37 (8)
Urine culture, n positive/n obtained (%)	3/28 (11)
CSF culture, n positive/n obtained (%)	0/26
Viral coinfection, n (%)	5 (8)
Treatment and disposition	
Hospital admission, n (%)	58 (92)§
ICU admission, n/total (%)	13/61 (21)
Supplemental oxygen via nasal cannula, n/total (%)	12/55 (22)
CPAP, n/total (%)	3/59 (5)
Mechanical ventilation, n/total (%)	2/62 (3)
Vasopressor, n/total (%)	1/59 (2)
Antibiotic therapy, n/total (%)	25/39 (64)
COVID-19–specific treatment, n (%)	8/56 (14)
Hospital length of stay, d, median (IQR)	3 (2, 8) (n = 46)
Death, n (%)	0/63

ALT, alanine aminotransferase; *AST*, aspartate aminotransferase; *CPAP*, continuous positive airway pressure; *CRP*, C-reactive protein; *CSF*, cerebrospinal fluid; *CT*, computed tomography; *WBC*, white blood cell.

Clinical and demographic characteristics of infants younger than 3 months of age with community-onset SARS-CoV-2 infection. Not all variables of interest were reported for all infants; denominators reported for individual variables as appropriate. Age was reported with variable units and degree of precision; summary statistics were therefore not performed. Neutropenia was defined as a neutrophil count <1500/μL. Lymphopenia was defined as a lymphocyte count <1500/μL. Thrombocytopenia was defined as a platelet count <150 000/μL. For WBC count, lymphocytes, neutrophils, and platelet count, if multiple values were reported, the lowest value was included.

*Two infants were described as thrombocytopenic without reported platelet count.

†Values reported in 1 study were excluded as they represented significant outliers, with concern for possible incorrect reporting of units. Study authors were contacted for clarification with no response.

‡One infant was reported to have significant aminotransferase elevation with an AST >500 U/L. Precise value was not provided and therefore not included in statistical analysis.

§One infant did not require admission on initial presentation but was admitted after blood culture was positive, ultimately determined to be a contaminant. Infant not included in n of infants requiring hospitalization.

disposition were discharged home; 1 infant was transferred to another hospital and 2 remained admitted at time of publication. Among infants discharged after hospital admission, 2 required readmission, 1 with newly diagnosed human metapneumovirus infection and the other due to persistent fever.[29,38] Feld et al[36] reported an infant who initially did not require hospital admission but was subsequently admitted due to a positive blood culture, determined to be a contaminant. There were no reported deaths among infants with community-onset SARS-CoV-2 infection.

Discussion

Although the spectrum of clinical disease of community-onset SARS-CoV-2 infection among young infants ranges from asymptomatic to critical illness, most identified infants appear to have mild-to-moderate illness and to recover quickly with supportive treatment alone. We were unable to draw conclusions regarding prevalence of infant disease, given the preponderance of case reports among publications to date. Larger pediatric studies have reported epidemiologic data of interest; however, aggregate reporting of data in broader age groups (ie, children <12 months of age or children <5 years) prohibits commentary on prevalence among young infants. There was a notable male predominance among reported infants, mirroring observations in other groups.[50,51] It is unclear whether male sex could predispose infants to infection or to more significant clinical symptomatology, increasing likelihood of seeking care and of SARS-CoV-2 testing.

Clinical presentation in infants largely was nonspecific, with predominance of fever and respiratory symptoms

among ill infants. Laboratory abnormalities such as neutropenia, leukopenia, and elevated inflammatory markers seen in these cases also can be observed in a number of common illnesses in this age group. In infants diagnosed with coinfection, such as urinary tract infection or other concomitant respiratory viral disease, it is unclear whether presentation and observed laboratory anomalies were primarily reflective of SARS-CoV-2 infection.

Unusual but noteworthy presentations reported among infants included cardiac and neurologic manifestations. Elevated cardiac biomarkers were reported in only 3 infants; however, these studies were not obtained routinely in infants presenting with community-onset disease.[18,22,35] Cardiac manifestations have been reported in other age groups, including myocarditis in older children during SARS-CoV-2 infection.[52,53] Among children with multisystem inflammatory syndrome in children, cardiac manifestations including elevated cardiac biomarkers, diminished cardiac function, arrhythmias, and coronary artery aneurysms can occur.[6]

Clinical seizures were reported only in 2 infants, only one of whom had an abnormal electroencephalogram.[15,19] Bhatta et al[54] reported new-onset seizures as the only manifestation of SARS-CoV-2 infection in a school-aged child. Neurologic manifestations of SARS-CoV-2 infection also have been reported in older age groups, including in more than one-third of patients in a large case series of adults with COVID-19 admitted to 3 hospitals in Wuhan, China.[55]

There are important limitations of this systematic review, including the quality of the available evidence (with a preponderance of case reports), the potential impact of publication bias, and variable reporting of outcomes of interest among included studies. In addition, we cannot exclude perinatal COVID-19 transmission among young neonates who presented from the community and who had symptomatic mothers; however, only 2 of the infants included in this systematic review came to medical attention in the first week of life.

Given the variability of manifestations described in reports, clinicians should have a high index of suspicion for SARS-CoV-2 infection in young infants presenting from the community with systemic symptoms, even in the absence of fever. Evaluation for serious bacterial illnesses should continue based on community guidelines, especially among febrile neonates. Diagnosis of SARS-CoV-2 infection does not preclude coinfection with other respiratory pathogens. We suggest that a thorough evaluation include PCR testing by a respiratory viral panel in children with respiratory symptoms. There are no studies to date reporting efficacy of COVID-specific therapies in this age group; however, critical illness in this age group is rare and infants appear to recover well with supportive care. ■

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Reprint requests: Julia Johnson, MD, PhD, Department of Pediatrics, Division of Neonatology, 1800 Orleans St, Suite 8534, Baltimore, MD 21287. E-mail: jjohn245@jhmi.edu

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Table I. Electronic search strategy

Databases	Search terms
PubMed	(Coronavirus[tw] OR COVID[tw] OR "SARS-CoV-2"[tw]) AND (Neonat*[tw] OR infant[tw]) AND (2019/11/01:2020/06/15[dp])
Embase	'Coronavirus infection' OR 'Severe acute respiratory syndrome coronavirus 2' AND Infant OR Newborn

Electronic search strategy for PubMed and Embase. The electronic search identified 415 records via PubMed and 378 records via Embase.

A **Risk of bias assessment of included case reports**

Q1	Were patient's demographic characteristics clearly described?
Q2	Was the patient's history clearly described and presented as a timeline?
Q3	Was the current clinical condition of the patient on presentation clearly described?
Q4	Were diagnostic tests or assessment methods and the results clearly described?
Q5	Was the intervention(s) or treatment procedure(s) clearly described?
Q6	Was the post-intervention clinical condition clearly described?
Q7	Were adverse events (harms) or unanticipated events identified and described?
Q8	Does the case report provide takeaway lessons?

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8
Calderado[12]	?	?	✓	✓	X	✓	?	✓
Canarutto[13]	✓	✓	✓	✓	✓	✓	✓	✓
Carvalho[14]	✓	✓	✓	✓	✓	✓	✓	✓
Chacón Aguilar[15]	✓	✓	✓	✓	✓	✓	✓	✓
Cook[16]	✓	✓	✓	✓	✓	✓	✓	✓
Coronado Munoz[17]	✓	✓	✓	✓	✓	✓	✓	✓
Cui[18]	✓	✓	✓	✓	✓	✓	✓	✓
Dugue[19]	✓	✓	✓	✓	✓	?	✓	✓
Dumpa[20]	✓	X	✓	✓	✓	?	X	✓
Färber[21]	✓	✓	✓	✓	✓	✓	✓	✓
Giacomet[22]	✓	✓	✓	✓	✓	✓	✓	✓
González-Brabin[23]	✓	✓	✓	✓	✓	✓	✓	✓
Han[24]	✓	✓	✓	✓	✓	✓	✓	✓
Kamali Aghdam[25]	✓	✓	✓	✓	✓	✓	✓	✓
Kan[26]	✓	✓	✓	✓	✓	✓	✓	✓
Patek[27]	✓	✓	✓	✓	✓	✓	✓	✓
Poli[28]	✓	✓	✓	✓	N/A	N/A	✓	✓
Precit[29]	✓	✓	✓	✓	✓	✓	✓	✓
Robbins[30]	✓	✓	✓	✓	✓	✓	✓	✓
Shi[31]	✓	✓	✓	✓	✓	✓	✓	✓
Wang[32]	✓	✓	✓	✓	✓	✓	✓	✓
Zeng[33]	✓	✓	✓	✓	✓	✓	✓	✓

Figure 1. Risk of bias assessment of studies reporting community-onset COVID-19 among infants younger than 3 months of age. **A,** Risk of bias assessment of included case reports. **B,** Risk of bias assessment of included case series. **C,** Risk of bias assessment of included cohort studies. Risk of bias assessment of case reports using The Joanna Briggs Institute (JBI) Critical Appraisal Tools: **A,** Checklist for Case Reports; **B,** Checklist for Case Series; and **C,** Checklist for Cohort Studies. Original study design was used for determining the appropriate critical appraisal tool. If a single case of a case series met inclusion criteria for the review, the Checklist for Case Series was used to assess risk of bias. [a]McLaren et al[38] described the overarching study design as a mixed retrospective/prospective cohort study but stated that the preliminary data presented was a case series. The Checklist for Case Series was used for risk of bias assessment. Key: ✓ indicates yes; ? indicates unclear; X indicates no; *N/A*, not applicable. *(Continues)*

B **Risk of bias assessment of included case series**

Q1	Were there clear criteria for inclusion in the case series?
Q2	Was the condition measured in a standard, reliable way for all participants included in the case series?
Q3	Were valid methods used for identification of the condition for all participants included in the case series?
Q4	Did the case series have consecutive inclusion of participants?
Q5	Did the case series have complete inclusion of participants?
Q6	Was there clear reporting of the demographics of the participants in the study?
Q7	Was there clear reporting of clinical information of the participants?
Q8	Were the outcomes or follow up results of cases clearly reported?
Q9	Was there clear reporting of the presenting site(s)/clinic(s) demographic information?
Q10	Was statistical analysis appropriate?

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10
Buonsenso[34]	✓	✓	✓	✓	✓	✓	✓	✓	X	N/A
Cai[35]	✓	✓	✓	✓	✓	✓	?	✓	✓	N/A
Feld[36]	✓	✓	✓	?	?	✓	✓	✓	✓	N/A
Lu[37]	✓	✓	✓	✓	✓	✓	?	X	✓	N/A
McLaren[a38]	✓	✓	✓	✓	✓	✓	✓	✓	✓	N/A
Meslin[39]	✓	✓	✓	✓	✓	✓	✓	✓	✓	N/A
Nathan[40]	✓	✓	✓	✓	✓	✓	✓	✓	✓	N/A
Ng[41]	✓	✓	✓	✓	✓	✓	✓	✓	X	N/A
Paret[42]	✓	✓	✓	✓	✓	✓	✓	✓	✓	N/A
Salvatori[43]	✓	✓	✓	✓	✓	✓	✓	✓	✓	N/A
Venturini[44]	✓	✓	✓	X	?	?	✓	?	✓	N/A
Wei[45]	✓	✓	✓	✓	✓	?	?	?	?	N/A
White[46]	✓	✓	✓	✓	✓	✓	✓	✓	✓	N/A
Xu[47]	✓	✓	✓	✓	✓	?	✓	✓	✓	N/A
Zhang[48]	✓	✓	✓	✓	✓	✓	?	?	?	N/A

C **Risk of bias assessment of included cohort studies**

Q1	Were the two groups similar and recruited from the same population?
Q2	Were the exposures measured similarly to assign people to both exposed and unexposed groups?
Q3	Was the exposure measured in a valid and reliable way?
Q4	Were confounding factors identified?
Q5	Were strategies to deal with confounding factors stated?
Q6	Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?
Q7	Were the outcomes measured in a valid and reliable way?
Q8	Was the follow up time reported and sufficient to be long enough for outcomes to occur?
Q9	Was follow up complete, and, if not, were the reasons to loss to follow up described and explored?
Q10	Were strategies to address incomplete follow up utilized?
Q11	Was appropriate statistical analysis used?

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11
Liu[49]	?	?	✓	✓	?	?	✓	✓	?	X	✓

Figure 1. Continues