Deaths in Children and Adolescents Associated With COVID-19 and MIS-C in the United States

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abstract

OBJECTIVES: To describe the demographics, clinical characteristics, and hospital course among persons <21 years of age with a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)–associated death.

METHODS: We conducted a retrospective case series of suspected SARS-CoV-2-associated deaths in the United States in persons <21 years of age during February 12 to July 31, 2020. All states and territories were invited to participate. We abstracted demographic and clinical data, including laboratory and treatment details, from medical records.

RESULTS: We included 112 SARS-CoV-2-associated deaths from 25 participating jurisdictions. The median age was 17 years (IQR 8.5–19 years). Most decedents were male (71, 63%), 31 (28%) were Black (non-Hispanic) persons, and 52 (46%) were Hispanic persons. Ninety-six decedents (86%) had at least 1 underlying condition; obesity (42%), asthma (29%), and developmental disorders (22%) were most commonly documented. Among 69 hospitalized decedents, common complications included mechanical ventilation (75%) and acute respiratory failure (82%). The sixteen (14%) decedents who met multisystem inflammatory syndrome in children (MIS-C) criteria were similar in age, sex, and race and/or ethnicity to decedents without MIS-C; 11 of 16 (69%) had at least 1 underlying condition.

CONCLUSIONS: SARS-CoV-2-associated deaths among persons <21 years of age occurred predominantly among Black (non-Hispanic) and Hispanic persons, male patients, and older adolescents. The most commonly reported underlying conditions were obesity, asthma, and developmental disorders. Decedents with coronavirus disease 2019 were more likely than those with MIS-C to have underlying medical conditions.

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WHAT'S KNOWN ON THIS SUBJECT: Pediatric mortality from SARS-CoV-2 is uncommon. Previous studies have reported risk factors associated with coronavirus disease 2019 and MIS-C. Case series describe clinical features of pediatric SARS-CoV-2-associated deaths.

WHAT THIS STUDY ADDS: SARS-CoV-2-associated deaths among persons <21 years of age during February to July 2020 occurred predominantly among older male adolescents and Black (non-Hispanic) and Hispanic persons. Obesity, asthma, and developmental disorders were the most commonly reported underlying conditions.

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In previously healthy individuals <21 years of age, infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19), is typically asymptomatic or mild, with recovery expected within 1 to 2 weeks.[1,2] An estimated 7% of children with COVID-19 are hospitalized,[3] and 28% to 33% of hospitalized children require intensive care.[3–6] Although individuals <21 years of age made up <2% of reported COVID-19 cases, as of April 13, 2021, >2.8 million cases and 377 deaths associated with SARS-CoV-2 in US children <18 years of age were reported to the US Centers for Disease Control and Prevention (CDC).[7]

Risk factors for death associated with COVID-19 among children are not well described.[8,9] In adults, risk factors include older age, male sex, and underlying medical conditions, including obesity, immunosuppression, chronic lung disease, cardiovascular disease, neurologic disorders, and diabetes.[10] In hospitalized children, the presence of underlying medical conditions increases the risk for severe illness from COVID-19.[4,11] In addition, children infected with SARS-CoV-2 can develop multisystem inflammatory syndrome in children (MIS-C), which predominantly affects previously healthy school-aged children.[12]

Given the low number of SARS-CoV-2-associated deaths among persons <21 years of age compared with adult deaths, limited information exists about the clinical course and underlying medical conditions among pediatric decedents. With the ongoing pandemic and increasing cases[13] and hospitalizations[14] in persons <21 years of age, we conducted an expanded review of data from an earlier study[15] to describe the demographics, clinical characteristics, and complications seen in children and adolescents with SARS-CoV-2 who died in the United States during February 12 to July 31, 2020.

METHODS

Case Definition

We defined a SARS-CoV-2-associated pediatric death as a death occurring in a person <21 years of age with confirmed or probable COVID-19 and/or MIS-C who died during February 12 to July 31, 2020. The interim COVID-19 case definition published by the Council of State and Territorial Epidemiologists on August 5, 2020, was used to classify cases as confirmed or probable.[16] Briefly, a case was classified as confirmed COVID-19 if there was a documented positive SARS-CoV-2 molecular amplification detection test result, and a case was classified as probable COVID-19 if the decedent (1) met clinical criteria and had epidemiological evidence without confirmatory laboratory testing, (2) met presumptive laboratory evidence and either clinical or epidemiological criteria, or (3) met vital records criteria without confirmatory laboratory testing performed. Cases met MIS-C criteria if they fulfilled the case definition published in the CDC Health Alert Network Health Advisory on May 14, 2020.[17]

Case Ascertainment, Data Collection, and Data Entry

State and local health departments report confirmed or probable COVID-19 cases[16] to the CDC as an element of the integrated national pandemic response. We examined case-based data for persons <21 years of age with confirmed or probable COVID-19 and/or MIS-C who died during the study period. We contacted health departments in all 50 states, New York City, the District of Columbia, Puerto Rico, Guam, and the US Virgin Islands ($N = 55$) to review the identified deaths and to invite jurisdictions with at least 1 identified SARS-CoV-2-associated pediatric death to participate in this study (Fig 1). Classification of cases as SARS-CoV-2-associated deaths was determined by the individual jurisdictions.

Participating jurisdictions submitted demographic and clinical data on decedents abstracted from available medical records, death certificates, and autopsy reports. Clinical data included past medical history, presenting signs and symptoms, SARS-CoV-2 and other laboratory test results, clinical course and treatments received, location of death, and cause-of-death determination. Participating jurisdictions submitted information on all probable or confirmed SARS-CoV-2-associated deaths, as determined by the jurisdiction, in persons <21 years of age that occurred during the study period.

Information on decedents was collected and managed by using Research Electronic Data Capture[18,19] hosted at the CDC. Data were abstracted from available clinical charts and entered into a standardized Research Electronic Data Capture form by either the participating jurisdictions ($n = 84$) or CDC staff ($n = 28$).

Ethical Approval

This activity was reviewed by the CDC and was conducted consistent with applicable federal laws and CDC policy.[20–24]

Inclusion Criteria

All cases of SARS-CoV-2-associated deaths in persons <21 years of age who died during the study period were considered for inclusion.

Exclusion Criteria

Decedents were excluded if the jurisdiction elected not to

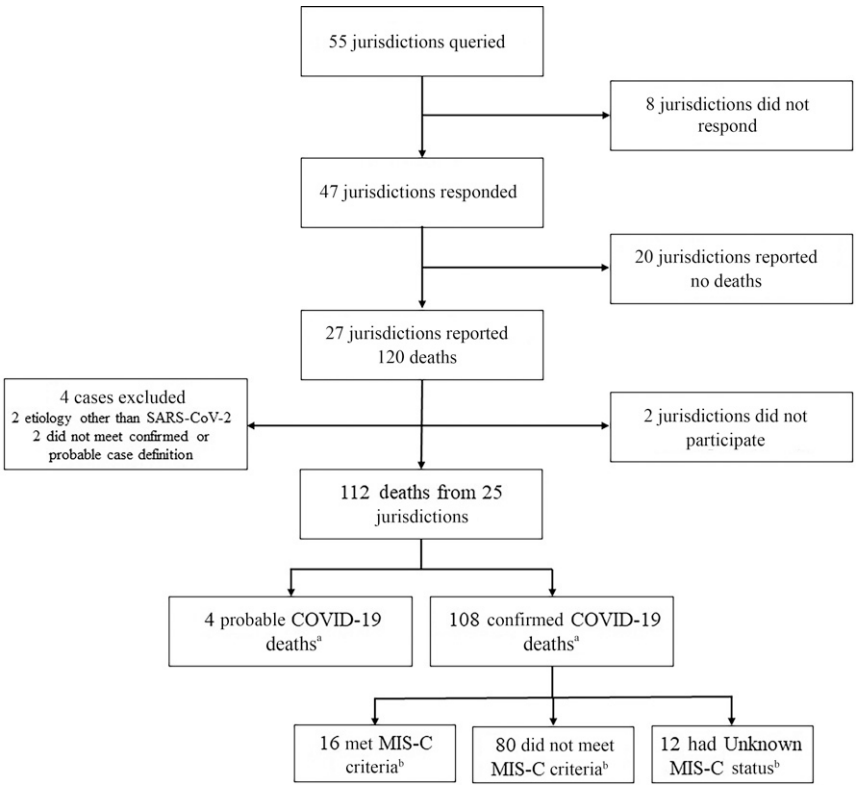

FIGURE 1

Study flow diagram. [a] The interim COVID-19 case definition published by the Council of State and Territorial Epidemiologists on August 5, 2020, was used to classify cases as confirmed or probable.[16] [b] Cases met MIS-C criteria if they fulfilled the case definition published in the CDC Health Alert Network Health Advisory on May 14, 2020.[17]

participate in the study ($n = 4$); if the clinical presentation, disease course, and pathologic findings after death were consistent with an etiology other than SARS-CoV-2 ($n = 2$); or if the decedents did not meet the confirmed or probable case definition ($n = 2$) (Fig 1).

Statistical Analysis

Continuous variables are expressed as medians and interquartile ranges (IQRs), and categorial data are expressed as counts and percentages. We did not impute missing data, and decedents with missing information on the variable of interest were excluded from any analyses of that variable of interest. The Mann–Whitney *U* test was used to compare age and illness duration, and the χ^2 test was used to compare all other variables. All statistical tests are 2-sided and an α value of .05 was considered significant. All statistical calculations were performed by using SAS software version 9.4 (SAS Institute, Inc, Cary, NC).

Laboratory measurements were converted to one standard unit of measure. Age- and sex-specific ranges for normal values and tachycardia were determined by using the Harriet Lane Handbook[25] and the Seattle Children's Hospital's Department of Laboratories online laboratory testing catalog.[26] We used the age-specific obesity cutoffs from the CDC's BMI-for-age charts[27] and the World Health Organization's age-specific cutoffs for tachypnea.[28]

Deaths that occurred at home or in the emergency department were classified as nonhospitalized, and deaths that occurred after hospital admission were classified as hospitalized.

RESULTS

Among the 55 jurisdictions invited to submit information, 47 responded. Twenty-five jurisdictions participated in the study, 20 jurisdictions reported no deaths, and 2 jurisdictions (representing 4 deaths) declined participation (Fig 1). We identified 112 deaths associated with COVID-19 and/or MIS-C in persons <21 years for inclusion in this study, of which 108 (96%) were confirmed and 4 (4%) were probable COVID-19 cases. Sixteen decedents (15%) met MIS-C criteria. The first death was reported the week of March 15, 2020 (Supplemental Fig 3).

Most decedents were male (71 of 112, 63%; Table 1). The median age at death was 17 years (IQR 8.5–19, range 1 month to 20 years; Fig 2; Table 1). Race and/or ethnicity was reported for 111 decedents (99%). Of these, there were 52 (47%) Hispanic, 31 (28%) Black (non-Hispanic), 16 (14%) White (non-Hispanic), 5 (5%) American Indian or Alaskan native (non-Hispanic), 5 (5%) Asian American or Pacific Islander (non-Hispanic), and 2 (2%) persons who identified as non-Hispanic of another race or of >1 race (Table 1). Decedents with MIS-C had similar age, sex, and race and/or ethnicity distributions as those without MIS-C (Table 2).

A death certificate was available for 74 (66%) decedents. COVID-19 was reported as the underlying cause of death in 48 (65%) and as a contributing factor in 21 (28%) decedents (Table 3). These decedents had similar age, sex, race and/or ethnicity, and underlying conditions as decedents without available information. The location

of death was reported for 111 decedents (99%); 69 (62%) died in the hospital, 23 (21%) decedents died in the emergency department, 18 (16%) died at home, and 1 (1%) died in hospice care. Among decedents with MIS-C, 1 of 16 (6%) died at home or in the emergency department, compared with 34 of 80 (43%) decedents without MIS-C ($P = .037$).

Information on underlying medical conditions was available for all decedents (Table 4, Supplemental Fig 4); 96 decedents (86%) had at least 1 underlying medical condition, including 50 (52%) with ≥3 underlying medical conditions and 25 (26%) with ≥5 underlying medical conditions. The most commonly documented conditions were obesity (47, 42%), asthma or reactive airway disease (33, 29%), and developmental disorders (25, 22%). Thirteen decedents (12%) had an active malignancy, of whom 8 (7%) were hematologic. Eighteen decedents (16%) were dependent on a gastrostomy tube for nutrition before illness onset. A higher proportion of decedents without MIS-C had at least 1 underlying condition (70 of 80, 87%) than decedents with MIS-C (11 of 16, 69%) ($P = .06$).

Among the 16 decedents with no underlying medical conditions, 12 (75%) were male; 8 (50%) were Hispanic, 5 (31%) were Black (non-Hispanic), 2 (13%) were White (non-Hispanic), and 1 (6%) was Hawaiian, Pacific Islander, or Asian American (non-Hispanic). These decedents were younger than decedents with underlying medical conditions (median age 2 years [IQR 0.75–12 years] versus median age 17 years [IQR 12–19 years]; $P < .001$). Five had MIS-C (31%) compared with 11 of 96 (11%; $P = .13$) among all other decedents, and 11 (69%) died at home or in the emergency department compared with 30 of 96 (31%; $P = .02$) among all other decedents. Four (25%) had been seen in an ambulatory or urgent care setting before death. The location of exposure to COVID-19 was available for 46 decedents (41%). The most common location for reported exposure was the decedent's household (33, 72%).

Data on reported symptoms were available for 67 of 80 (84%) decedents without MIS-C and 14 of 16 (88%) decedents with MIS-C (Supplemental Table 6). The most commonly reported symptoms for decedents without MIS-C were fever (44 of 67, 66%), dyspnea (36 of 67, 54%), cough (34 of 67, 51%), nausea or vomiting (18 of 67, 27%), and fatigue (17 of 67, 25%); the most commonly reported symptoms for decedents with MIS-C (besides fever, which is part of the case definition for MIS-C) were cough (10 of 14, 71%), nausea or vomiting (10 of 14, 71%), dyspnea (6 of 14, 43%), loss of appetite (6 of 14, 43%), dehydration (6 of 14, 43%), and nasal congestion (5 of 14, 36%).

Among 98 (88%) decedents with a recorded symptom onset date, the median illness duration (time from symptom onset to death) was 11 days (IQR 7–23 days). Among 99 decedents with a recorded SARS-CoV-2 viral detection test date, the median time from a first positive test result to death was 8 days (IQR 3–20 days). Decedents with MIS-C had a similar illness duration as those without MIS-C (median 11 days [IQR 6–27 days] versus median 11 days [IQR 7–23 days], respectively) and had a similar time from first positive SARS-CoV-2 test result to death compared with those without MIS-C (median 7 days [IQR 3–24 days] versus median 8 days [IQR 7–23 days], respectively).

Nonhospitalized decedents (41, 37%) had similar age, sex, and race distributions compared with hospitalized decedents (69, 63%) (Supplemental Table 7). Nonhospitalized decedents had a shorter illness duration than hospitalized decedents (nonhospitalized: median 7 days, IQR 1–12 days; hospitalized: median 13 days, IQR 9–27 days; $P < .0001$).

Among the 69 hospitalized decedents, the median number of days from symptom onset to hospital admission was 4 (IQR 2–7 days) and the median number of days from initial hospitalization to death was 9 (IQR 4–9 days). Fifteen (22%) met MIS-C criteria, 44 (64%) did not meet MIS-C criteria, and MIS-C status was unknown for 10 (14%) decedents. Fifty-five (80%) were admitted to the ICU at a median of 0 days (IQR 0–1 day) after hospitalization; the median duration from ICU admission to death was 8 days (IQR 3–13 days).

Vital signs at the time of presentation were available for 53 of 69 decedents (77%) who died after hospitalization (Supplemental Table 8), including 37 of 44 (84%) without MIS-C, 13 of 15 (87%) with MIS-C, and 3 of 10 (30%) with unknown MIS-C status. The prevalence of fever, tachycardia, and tachypnea was similar between decedents with MIS-C and those without MIS-C.

Laboratory studies were available for 40 of 69 (58%) decedents who died after hospitalization (Supplemental Table 9). Common findings included thrombocytopenia (32 of 40, 80%), elevated procalcitonin levels (18 of 40, 45%), and elevated ferritin levels (21 of 40, 53%). Laboratory studies for decedents with MIS-C were similar to those for decedents without MIS-C. Among the 60 decedents who died after hospitalization with available information on hospital course and therapeutics, 45 were intubated and required mechanical ventilation (75%)

TABLE 1 Demographic Characteristics of All Decedents ($N = 112$)

	Value
Sex, *n* (%)	
Male	71 (63)
Female	41 (37)
Age, median (IQR), y	17 (8.5–19)
Age, y, *n* (%)	
<1	8 (7)
1–4	11 (10)
5–9	12 (11)
10–13	12 (11)
14–17	21 (19)
18–20	48 (43)
Race and/or ethnicity, *n* (%)	
White (non-Hispanic)	16 (14)
Black, non-Hispanic	31 (28)
Hispanic	52 (46)
American Indian or Alaskan native (non-Hispanic)	5 (5)
Asian American or Pacific Islander (non-Hispanic)	5 (5)
Other	2 (2)
Unknown	1 (1)
Geographic region, *n* (%)[a]	
Midwest	13 (12)
Northeast	35 (31)
South	41 (37)
West	23 (21)

[a] Regions are based on US Census Bureau regions (US Census Bureau. Census regions and divisions of the United States. Available at: https://www2.census.gov/geo/pdfs/maps-data/maps/reference/us_regdiv.pdf. Accessed May 27, 2021). US territories are assigned to Census regions on the basis of their geographic proximity to states assigned to those regions and on the basis of their assignment to standard federal regions (US General Services Administration. GSA Regions. Available at: https://www.gsa.gov/about-us/gsa-regions. Accessed May 27, 2021).

and 8 received extracorporeal membrane oxygenation therapy (13%) (Table 5). One-quarter of decedents (15) who died after hospitalization received immunomodulatory therapy, and 21 (35%) received remdesivir.

Information on complications was available for 62 (90%) hospitalized decedents. The most commonly reported complications were acute respiratory failure (51, 82%), shock (35, 56%), acute respiratory distress syndrome (31, 50%), sepsis (25, 40%), and acute renal failure (21, 34%) (Table 5).

DISCUSSION

Deaths associated with SARS-CoV-2 among individuals <21 years of age during February to July 2020 occurred predominantly among older adolescents, male patients, Black (non-Hispanic) and Hispanic persons, and persons with underlying medical conditions. Persons >15 years of age constituted 58% of deaths in this study, whereas persons <1 year of age constituted only 7% of deaths, which contrasts with other studies that have shown the highest numbers of deaths in both infants and older adolescents.[9,11,29,30] The predominance of male patients among the decedents in this study is consistent with previous studies that found male sex as a risk factor for more severe illness among both children and adults with COVID-19.[31]

The COVID-19 pandemic has amplified racial and ethnic disparities in health, with Black (non-Hispanic) and Hispanic adults having higher rates of hospitalization due to COVID-19 than White (non-Hispanic)

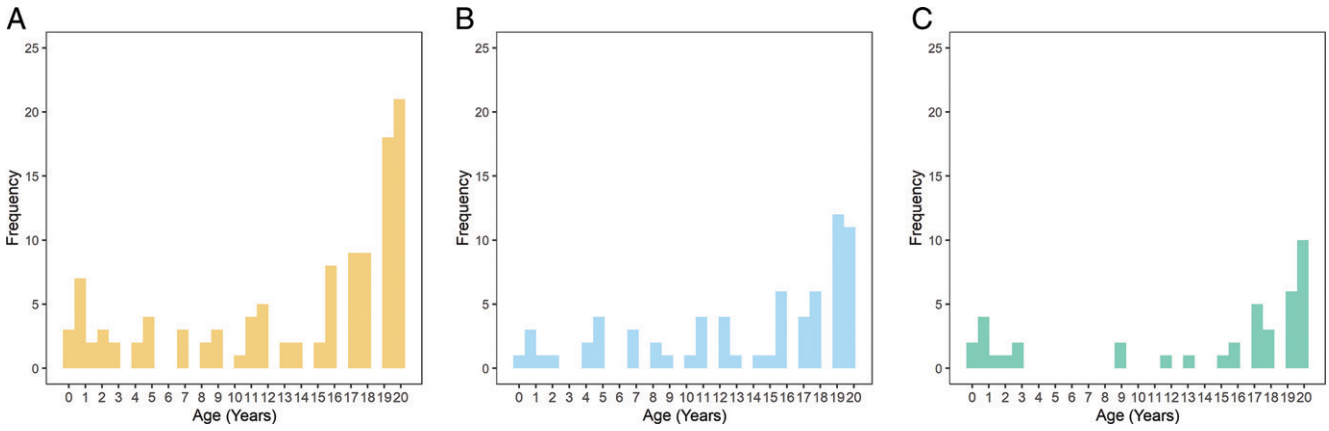

FIGURE 2
Histogram showing the age distribution for all decedents, those who died in the hospital, and those who died at home or in the emergency department. A, All cases ($N = 112$). B, Death at hospital ($n = 69$). C, Death at emergency department or home ($n = 41$).

TABLE 2 Demographic Characteristics for Decedents With Known MIS-C Status ($n = 96$)

	Met MIS-C Criteria[a] ($n = 16$)	Did Not Meet MIS-C Criteria ($n = 80$)
Sex, *n* (%)		
Male	9 (56)	51 (64)
Female	7 (44)	29 (36)
Age, median (IQR), y	16 (6–19)	17 (11–19)
Age, y, *n* (%)		
<1	1 (6)	7 (9)
1–4	2 (13)	6 (8)
5–9	3 (19)	6 (8)
10–13	1 (6)	9 (11)
14–17	4 (25)	15 (19)
18–20	5 (31)	37 (46)
Race and/or ethnicity, *n* (%)		
White (non-Hispanic)	1 (6)	13 (16)
Black (non-Hispanic)	4 (25)	24 (30)
Hispanic	9 (56)	32 (40)
American Indian or Alaskan native (non-Hispanic)	0 (0)	5 (6)
Asian American or Pacific Islander (non-Hispanic)	1 (6)	4 (5)
Other	1 (6)	1 (1)
Unknown	0 (0)	1 (1)
Geographic region,[b] *n* (%)		
Midwest	1 (6)	12 (15)
Northeast	3 (19)	26 (33)
South	9 (56)	23 (29)
West	3 (19)	19 (24)
Underlying medical conditions, *n* (%)		
None (0)	5 (31)	10 (13)
Any (≥1)	11 (69)	70 (87)

[a] Cases met MIS-C criteria if they fulfilled the case definition published in the CDC Health Alert Network Health Advisory on May 14, 2020.[17]

[b] Regions are based on US Census Bureau regions (US Census Bureau. Census regions and divisions of the United States. Available at: https://www2.census.gov/geo/pdfs/maps-data/maps/reference/us_regdiv.pdf. Accessed May 27, 2021). US territories are assigned to Census regions on the basis of their geographic proximity to states assigned to those regions and on the basis of their assignment to standard federal regions (US General Services Administration. GSA Regions. Available at: https://www.gsa.gov/about-us/gsa-regions. Accessed May 27, 2021).

adults[10,32,33] and Black (non-Hispanic) and Hispanic children and adolescents having increased risk of severe COVID-19 illness and MIS-C compared with White (non-Hispanic) children and adolescents.[34–36] The majority of decedents in this study were Black (non-Hispanic) or Hispanic, providing further evidence of these disparities. Improving the health outcomes of populations disproportionately affected will require focused and ongoing strategies to address historical and contemporary injustices and to eliminate health and health care disparities.[37]

The proportion of decedents in this study with at least 1 underlying condition is much higher than in the general pediatric population.[38–41] Developmental disorders are more prevalent among White (non-Hispanic) children compared with other racial and ethnic groups,[38] and obesity is more prevalent among Hispanic children than White (non-Hispanic) or Black (non-Hispanic) children.[39] Children and adolescents with multiple underlying medical conditions, including those with complex medical needs, are at increased risk for severe disease, hospitalization, and death due to COVID-19.[9,11,42] Obesity and neurologic and developmental conditions were common in this study; previous studies have revealed that children with obesity and children with intellectual disabilities and seizure disorders have increased risk of both requiring critical care[29,30] and death associated with COVID-19.[43,44]

Most reported exposures among decedents in this study occurred in the household, which is consistent with transmission studies conducted outside the United States.[45] Notably, this study occurred during the first 6 months of the pandemic in the United States, when many students were enrolled in remote learning and stay-at-home orders were in place in some locations around the country.[46] Although classrooms appear to be a low-risk setting for SARS-CoV-2 transmission,[47–50] some studies have suggested an increased role for transmission in children and adolescents outside the home because they have resumed other activities and stay-at-home orders are lifted in some jurisdictions.[51,52] However, returning to face-to-face instruction may increase the risk of infection with SARS-CoV-2 and death in this population because in-person contact increases the risk of SARS-CoV-2 transmission.

Only 14% of decedents in this study met MIS-C criteria. Non-MIS-C COVID-19 represents a much higher contribution to SARS-CoV-2-associated mortality in this age group. Among those with MIS-C, a higher proportion were previously healthy decedents compared with those without MIS-C, consistent with other studies.[9,12] However, it is important to note that MIS-C criteria at the time of this study included severe illness requiring hospitalization, which likely contributes to the high proportions of persons with MIS-C who died after hospitalization.

Acute respiratory failure, shock, and acute renal failure were relatively common complications among

TABLE 3 Disease Classification and Hospitalization Status for Decedents With Clinical Information ($N = 112$)

	n	%
COVID-19 classification[a]		
Confirmed	108	96
Probable	4	4
MIS-C classification[b]		
Met MIS-C criteria	16	14
Did not meet MIS-C criteria	80	71
Unknown MIS-C status	16	14
Hospitalization status		
Hospitalized	69	62
Not hospitalized	43	38
Admitted to ICU[c]		
Yes	55	49
Unknown	14	10
Not applicable	47	42
Outpatient medical visits before death[d]		
Emergency department visit only	16	13
Clinic or urgent care visit only	25	22
Both emergency department and clinic or urgent care visit	4	4
None	35	31
Unknown	32	29
Location of death		
Hospital	69	62
Emergency department	23	21
Home	18	16
Hospice care	1	1
Unknown	1	1
COVID-19 contribution to death		
Underlying	48	43
Contributing factor	21	19
Unknown, death certificate not available	5	4
Death certificate not available	38	34

[a] The interim COVID-19 case definition published by the Council of State and Territorial Epidemiologists on August 5, 2020, was used to classify cases as confirmed or probable.[16]

[b] Cases met MIS-C criteria if they fulfilled the case definition published in the CDC Health Alert Network Health Advisory on May 14, 2020.[17]

[c] Restricted to those patients who were admitted to the hospital.

[d] Defined as seeking care in an emergency department, urgent care center, or outpatient clinic ≥1 d before death or hospitalization, whichever came first.

decedents (Table 5). A high proportion of decedents admitted to the hospital required mechanical ventilation. Immunomodulatory therapy was relatively common, even for decedents who did not have MIS-C, and remdesivir was administered to nearly one-third of hospitalized children. The use of immunomodulatory therapy in pediatric patients without MIS-C is not recommended in current guidelines.[53] These results provide insight into treatment practices in severely ill children and adolescents in the early phase of the pandemic, before updated recommendations were established and should not be taken as treatment recommendations.

This study has at least 6 limitations. First, there was no comparison group of children and adolescents who survived COVID-19 in this study, so we are unable to describe risk factors for death. Second, in some cases, death might have been incidentally associated with SARS-CoV-2 infection. Causal inference is difficult in descriptive studies and it is not always possible to determine if decedents died of COVID-19 or died of other causes with active SARS-CoV-2 infection. However, a recent report found that death certificates provide accurate data for COVID-19 mortality surveillance.[54] Third, complete medical records, including laboratory data, were not available for all decedents. Fourth, data were entered by multiple abstractors, which might have introduced data entry inconsistencies. Fifth, we do not have data on the number of COVID-19 cases in each age group during this period and cannot calculate case fatality rates or perform age adjustment. Finally, this case series was assembled during the first 6 months of the pandemic, before the emergence of multiple novel variants of concern and rapid expansion of vaccination. The combination of new variants of concern and increased rates of vaccination is likely to result in different symptomatology, illness severity, and case fatality from what is described here.

CONCLUSIONS

In this case series of individuals <21 years of age with SARS-CoV-2-associated deaths, most decedents were older adolescents or young adults and members of racial and/or ethnic minority groups. Obesity, developmental disorders, and asthma were the most commonly reported underlying conditions. Persons <21 years of age with COVID-19 resulting in death frequently had underlying medical conditions, whereas decedents with MIS-C were more likely to have no underlying medical conditions than decedents who did not meet MIS-C criteria. Acute respiratory failure requiring mechanical ventilation, shock, and cardiac arrythmias were common complications during hospitalization. Pediatric providers who care for children with complex medical needs should continue to counsel families about the importance of preventive behaviors and the risk for severe COVID-19 as well as counsel families to seek medical attention early if they develop COVID-19-like symptoms. These children may be at increased risk of decompensation during hospitalization

TABLE 4 Underlying Medical Conditions for All Decedents, Decedents Who Met MIS-C Criteria, and Decedents Who Did Not Meet MIS-C Criteria ($N = 112$)

	All Decedents ($N = 112$)		Met MIS-C Criteria ($n = 16$)		Did Not Meet MIS-C Criteria ($n = 80$)	
	n	%	*n*	%	*n*	%
No. underlying medical conditions						
None	16	14	5	31	10	13
1	24	21	1	6	17	21
2	22	20	4	25	15	19
3	15	13	2	13	13	16
4	10	9	1	6	8	10
≥5	25	22	3	19	17	21
Metabolic and endocrine	51	46	7	44	39	49
Obesity	47	42	5	31	37	46
Diabetes mellitus[a]	11	10	1	6	9	11
Other[b]	12	11	2	135	9	11
Neurologic and developmental	37	33	5	31	24	30
Developmental disorder	25	22	3	19	15	19
Seizure disorder	17	15	3	19	11	14
Other[c]	20	18	2	13	15	19
Respiratory	35	31	6	38	24	30
Asthma or reactive airway disease	33	29	5	31	23	29
Other[d]	6	5	1	6	2	3
Cardiovascular	20	18	3	19	14	18
Hypertension	10	9	0	0	9	11
Congenital heart disease	6	5	1	6	4	5
Cardiomyopathy	3	35	1	6	2	3
Other[e]	8	7	1	6	5	6
Gastrointestinal or hepatic	21	19	4	25	12	15
Dependent on gastric tube feedings	18	16	4	25	11	14
Gastroesophageal reflux	5	4	0	0	2	3
Other[f]	5	4	3	19	2	3
Malignancy	13	12	1	6	8	10
Hematologic malignancy	8	7	0	0	4	5
Nonhematologic malignancy	5	4	1	6	4	5
Immunologic	12	11	0	0	10	13
Immunosuppressive therapy	6	5	0	0	6	8
Solid organ or stem cell transplant recipient	3	3	0	0	3	4
Other[g]	7	6	0	0	5	6
Genetic	12	11	2	13	7	9
Chromosomal abnormality[h]	5	4	2	13	2	3
Other[i]	7	6	0	0	5	6
Hematologic[j]	8	7	0	0	6	8
Psychiatric[k]	8	7	1	6	6	8
Substance use[l]	6	5	0	0	6	8
Renal[m]	6	5	0	0	5	6
Dermatologic[n]	5	4	1	6	3	4
Rheumatologic[o]	3	3	0	0	3	4
Other	13	12	2	13	9	11
Sleep apnea	8	7	1	6	6	8
Other[p]	6	5	2	13	3	4

[a] Includes both type 1 and type 2.

[b] Includes hypothyroidism (4), panhypopituitarism (1), diabetes insipidus (1), hypothalamic-pituitary axis dysfunction (1), adrenal insufficiency (1), osteoporosis (1), and other or unknown (4).

[c] Includes autism (5), blindness (3), microcephaly (2), Charcot-Marie-Tooth disorder (2), chronic inflammatory demyelinating polyradiculoneuropathy (1), hearing loss (1), septo-optic dysplasia (1), migraine (1), ataxia telangiectasia (1), hydrocephalus (1), and other or unknown (2).

[d] Includes bronchopulmonary dysplasia (1), interstitial lung disease (1), and other or unknown (2).

[e] Includes lipid disorder (5), Wolff-Parkinson-White syndrome (1), and other or unknown (9).

[f] Includes history of necrotizing enterocolitis (2), history of malrotation (1), celiac disease (1), dysphagia (1), and history of liver transplant (1).

[g] Includes graft-versus-host disease (1) and other or unknown (6).

[h] Includes trisomy 13 (2), trisomy 21 (1), and unspecified chromosomal deletion (2).

[i] Includes congenital muscular dystrophy (2), cobalamin C deficiency (1), metachromatic leukodystrophy (1), neurofibromatosis (1), Rett syndrome (1), and overgrowth syndrome (1).

[j] Includes anemia (4), deep vein thrombosis (2), sickle cell anemia (1), recurrent thrombosis (1), clotting disorder not otherwise specified (1), and other or unknown (1).

[k] Includes anxiety (1), major depressive disorder (1), history of suicide attempt (1), and other or unknown (6).

[l] Includes cigarette smoking (1), vaping (1), and unspecified substance abuse or misuse (5).

[m] Includes end-stage renal disease (2), neurogenic bladder (1), renal cyst (1), renal hyperplasia (1), history of continuous renal replacement therapy during a previous hospitalization (1), and other or unknown (1).

[n] Includes eczema (5).

[o] Includes juvenile rheumatoid arthritis (1), limited scleroderma (1), and systemic lupus erythematosus (1).

[p] Includes glaucoma (1), cleft palate (1), herpes simplex 1 infection (1), congenital cytomegalovirus (1), malnutrition (1), and other or unknown (1).

TABLE 5 Selected Medical Interventions and Complications for All Decedents Admitted to the Hospital, Those Admitted to the Hospital Who Met MIS-C Criteria, and Those Admitted to the Hospital Who Did Not Meet MIS-C Criteria

	All Decedents[a]		MIS-C (n = 14)		Not MIS-C[b]	
	n	%	*n*	%	*n*	%
Respiratory support						
Noninvasive positive pressure ventilation	16	27	3	21	11	27
Endotracheal intubation and mechanical ventilation	45	75	11	79	29	71
Extracorporeal membrane oxygenation therapy	8	13	4	29	4	10
Medical interventions and therapeutics						
Anticoagulation	37	62	9	64	25	61
Vasopressor and/or inotrope support	36	60	8	57	25	61
Corticosteroids	28	45	7	50	22	54
Remdesivir	21	35	5	36	12	29
Azithromycin	22	37	4	29	17	41
Cardiopulmonary resuscitation	19	32	4	29	14	34
Convalescent plasma therapy	16	27	6	43	8	20
Hydroxychloroquine	16	27	4	29	12	29
Immune modulators (anakinra, canakinumab, tocilizumab)	15	25	6	43	6	15
Complications during hospital course						
Acute respiratory failure	51	82	8	57	37	88
Shock	35	56	9	64	22	52
Acute respiratory distress syndrome	31	50	6	43	22	52
Sepsis	25	40	5	36	17	40
Acute renal failure	21	34	4	29	15	36
Cardiac arrhythmia	16	26	5	36	11	26
Cerebrovascular unintentional injury	4	6	3	21	1	2
Deep vein thrombosis or pulmonary embolism	4	6	1	7	3	7
Acute liver failure	3	5	1	7	2	5
Myocarditis	3	5	2	14	1	2

[a] Sample size varied by category, with n = 60 for both respiratory support and medical interventions and therapeutics and n = 62 for complications during hospital course.
[b] Sample size varied by category, with n = 41 for both respiratory support and medical interventions and therapeutics and n = 42 for complications during hospital course.

and should be monitored closely if admitted to the hospital. Vaccination is available for persons >11 years of age, and vaccine uptake will be a critical intervention to prevent COVID-19 mortality in this age group.[55] Continued assessment of pediatric and adolescent deaths as the pandemic continues is critical to understanding disease and mortality in this population.

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APPENDIX

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ABBREVIATIONS

CDC: US Centers for Disease Control and Prevention
COVID-19: coronavirus disease 2019
IQR: interquartile range
MIS-C: multisystem inflammatory syndrome in children
SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

Dr McCormick coordinated and supervised data collection, collected data, drafted the initial manuscript, and reviewed and revised the manuscript; Dr Richardson performed all statistical analyses, assisted with drafting the initial manuscript, and reviewed and revised the manuscript; Dr Young coordinated and supervised data collection, collected data, and reviewed and revised the manuscript; Dr Viens designed data collection instruments, coordinated and supervised data collection, collected data, assisted with drafting the initial manuscript, and reviewed and revised the manuscript; Drs Gould, Reagan-Steiner, and Koumans coordinated and supervised data collection, reviewed and revised the manuscript, and critically reviewed the manuscript for important intellectual content; Drs Kimball and Rosenblum collected data, assisted with drafting the initial manuscript, and reviewed and revised the manuscript; Dr Pindyck coordinated and supervised data collection, assisted with drafting the initial manuscript, and critically reviewed the manuscript for important intellectual content; Dr Siegel assisted with drafting the initial manuscript and critically reviewed the manuscript for important intellectual content; Dr Vu collected data, conducted the initial analyses, and critically reviewed the manuscript for important intellectual content; Drs Burch, Byers, and Harduar-Morano, Ms Kawasaki, Drs Kirkey, Lee, Lewis, Openshaw, Pont, Reilly, Tobin-D'Angelo, and Venkat, Ms White, Drs Wilson and Zamcheck, Ms Barbeau, Ms de Fijter, Mr Garcia, Ms Gumke, Ms Hand, Ms Kauerauf, Mr Kolsin, Mr Komatsu, Ms Larson, Ms Lash, Ms Leapley, Mr Naqvi, Ms Ojo, Ms Reid, Ms Richardson, and Mr Siniscalchi collected data and critically reviewed the manuscript for important intellectual content; Dr Bixler reviewed and revised the manuscript and critically reviewed the manuscript for important intellectual content; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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