ARTICLE

A Systematic Review and Meta-analysis of the Initial Literature Regarding COVID-19 Symptoms in Children in the United States

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Introduction: COVID-19 symptom presentation among adults is mostly understood. However, understanding COVID-19 symptom presentation in children lags.

Method: A literature search was conducted in three electronic databases. Twenty-three initial publications addressing COVID-19 symptom presentation among hospitalized children in the United States met the criteria for review and meta-analysis.

Results: Fever, the most common symptom, was present in nearly all cases. Gastrointestinal, respiratory, oral symptoms, and rash occurred in over half of the cases. Disease severity assessment showed that comorbidities were present in one-third of patients; intensive care was needed for half of the patients, and supplemental oxygen and mechanical ventilation were needed by 13.3% and 7.1%, respectively.

Discussion: The magnitude and significance of COVID-19 symptoms in children compared with those in adults and three common childhood viral illnesses: influenza, respiratory syncytial virus, and gastroenteritis, are discussed. Important clinical differences were found that may help clinicians distinguish COVID-19 from other illnesses. J Pediatr Health Care. (2023) *XX*, 1−13

KEY WORDS

COVID-19, symptoms, children, United States

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INTRODUCTION

Much can still be learned from the COVID-19 pandemic. COVID-19 is a viral illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; Yuki et al., 2020). Although SARS-CoV-2 symptom presentation (COVID-19) in adults is fairly well understood, less remains known about symptom presentation in children. The objective of this manuscript is twofold: (1) to determine the most common COVID-19 symptoms in hospitalized children seen early in the pandemic and (2) to assess the frequency of COVID-related treatments and outcomes. Results from the meta-analysis are used to distinguish the magnitude and significance of COVID-19 symptom presentation in children compared with the symptoms seen in adults, as well as comparing COVID-19 to three other common childhood viral illnesses (influenza, respiratory syncytial virus [RSV], and gastroenteritis) in the United States. Such a distinction will aid in delivering appropriate care to children and result in more positive health outcomes.

COVID-19 is a contagious disease caused by SARS-CoV-2 (Yuki et al., 2020). The first known case was reported in December 2019 in Wuhan, China. The disease has since spread worldwide, leading to an ongoing pandemic (World Health Organization, 2021). Scientists believe COVID-19 is transmitted when people breathe in air contaminated by droplets and small airborne particles (Jayaweera et al., 2020). The risk of breathing these particles is highest when people are close (i.e., less than 3 ft apart). SARS-CoV-2 particles can also be inhaled over longer distances, particularly in confined spaces, such as indoors (Bazant & Bush, 2021). Transmission can further occur if particles are splashed or sprayed via contaminated fluids during coughing or (more rarely) by contacting contaminated surfaces (Jayaweera et al., 2020). People who are infected can transmit the virus to another person up to 2 days before they show symptoms, as can people who do not experience symptoms. People remain infectious for up to 10 days after the onset of symptoms in moderate cases and up to 20 days in severe cases (Centers for Disease Control and Prevention, 2021a).

Much of our knowledge regarding COVID-19 symptom presentation pertains to those seen in adults. Symptoms in adults may include fever, cough, headache, fatigue, breathing difficulties, and loss of smell and taste (Centers for Disease Control and Prevention, 2021b). At least one-third of people who are infected do not develop noticeable symptoms (Sah et al., 2021). Of those who develop symptoms noticeable enough to be considered ill, most (81%) develop mild to moderate symptoms, including mild pneumonia, whereas 14% develop severe symptoms (dyspnea, hypoxia, or > 50% lung involvement on imaging). Five percent suffer critical symptoms (respiratory failure, shock, or multiorgan dysfunction), with older individuals being at a higher risk (Yi et al., 2020). Others may continue to experience a range of effects for months after recovery, known as long COVID, and suffer damage to organs (Mayo, 2022).

Although COVID-19 outcomes in adults are fairly well understood, this knowledge may not be transferrable to children. For example, adults with comorbid conditions such as cardiovascular disease, diabetes, hypertension, and cancer are at increased risk for contracting and experiencing complications from COVID-19. However, these conditions are much less common in children. Moreover, adults from African American and Hispanic/Latinx populations are disproportionately impacted by COVID-19 (Alcendor, 2020). The effect of COVID-19 on children in these populations is unclear. To address this gap in knowledge, the purpose of this systematic review and meta-analysis is to summarize the initial literature regarding COVID-19 symptom presentation and outcomes among children in the United States.

METHODS

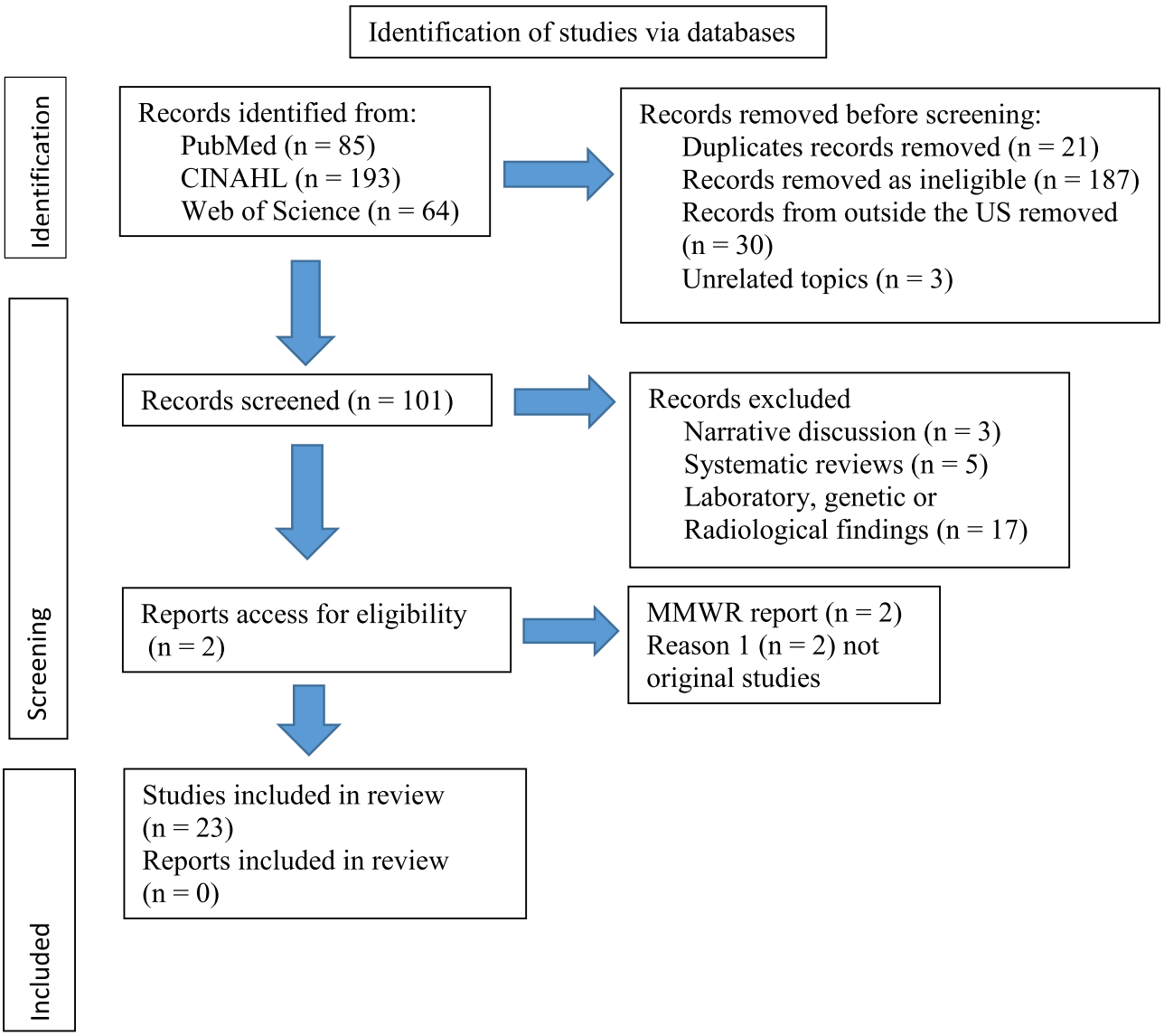
A literature search was conducted in consultation with a health science librarian in August 2020 in three electronic databases: PubMed, CINAHL, and Web of Science. Terms used in these searches included: "coronavirus" or "corona virus" or "nCoV" or "2019 nCoV" or "novel coronavirus" or "novel corona virus" or "COVID-19" or "SARS-CoV-2" or "severe acute respiratory syndrome coronavirus 2" or "coronavirus disease 2019" or "corona virus disease 2019" or "new coronavirus" or "new corona virus" or "new coronaviruses" or "novel coronaviruses" or "severe acute respiratory syndrome coronavirus 2" or "2019 nCoV" or "nCoV 2019" or "SARS coronavirus 2"; "English"; "USA"; "youth" or "child" or "adolescent"; "all years"; "English"; "United States"; "pediatrics." No filters or limitations were applied. Searches generated 342 publications: 85 articles from PubMed, 193 from CINAHL, and 64 from the Web of Science. Articles were included in the meta-analysis if they addressed COVID-19 cases among children in the United States, were published in peer-reviewed journals and were written in English. After the first and third authors simultaneously reviewed the publications, 241 were eliminated, including 21 duplicates, 187 ineligible, 30 outside the United States, and three unrelated topics (e.g., SARS, influenza, and bronchiolitis). One hundred and one publications were selected for further review. The same two authors reviewed the 101 publications and further excluded 25 publications (narrative discussions regarding COVID [n = 3]; systematic reviews [n = 5]; presented laboratory, genetic, or radiological findings [n = 17]); and two reports (Morbidity and Mortality Weekly reports; Figure). After an independent review of symptoms and disease severity by the second author, the final meta-analysis consisted of 23 publications.

Analysis

Study characteristics, including sample size, description of the patient sample, research location, enrollment dates, age, and race of patients were assessed and summarized in Table 1. A dataset was created of the symptom characteristics and disease severity statistics of patients reported for each study (Tables 2 and 3). A wide range of symptoms was reported across studies, and the symptoms reported by each study differed. Fever, respiratory, or gastrointestinal symptoms could be determined for most studies. Other symptoms, such as cough, nausea, or fatigue, could only be determined in some studies. For disease severity measures, the number of patients with comorbid conditions could be determined for all studies. Other measures, such as supplemental oxygen use and intensive care, could only be determined for some of the studies. Symptom and disease severity measures were only included in the analysis if reported on by at least three studies. Summary statistics included the number of studies that reported on the symptom/measure and the total sample size for those studies. The proportion and percentages of patients with the symptom or other traits were also summarized across studies. Continuous outcomes were summarized by calculating the overall mean and standard deviation.

Random-effects meta-analyses of symptom and disease severity statistics across studies were conducted with Stata software (version 17; StataCorp LLC, 2021), and results are displayed in Table 4. The Metaprop Stata package was used to analyze proportional measures, and the meta-command

FIGURE. Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram of study selection.



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was used to analyze continuous outcomes. Case studies with no effect size variation were excluded from continuous outcome models. Overall pooled effect sizes and 95% confidence intervals (CIs) are reported for each outcome. Heterogeneity statistics are also reported for each outcome, including the χ^2 test of Q for whether study effects varied, Tau2 (the variance of true effect sizes), and I2 (percent of variance which reflects true differences in effect size *vs.* random error). Egger's tests of publication bias were run, though none were statistically significant. Metaregression analyses were conducted for each outcome to assess factors related to heterogeneity in the effect sizes of studies. Factors included study sample size, whether a study was a case report ($\leq$ 10 patients), the median age of study patients, whether the study reported race, the percentage of patients with comorbidities, and percent of male patients. Postestimation publication bias and metaregression analyses were conducted with maximum likelihood estimation. No sensitivity analyses were done.

RESULTS

Twenty-three studies with 484 patients were included in the final analysis (Table 1). Nine publications provided aggregate data (Bhumbra et al., 2020; Blumfield & Levin, 2020; Cheung et al., 2020; Feldstein et al., 2020; Kainth et al., 2020; Kaushik et al., 2020; Mithal et al., 2020; Shekerdemian et al., 2020; Zachariah et al., 2020); 14 studies were classified as case reports/case series because of having 10 or fewer patients (Craver et al., 2020; Danley & Kent, 2020; Del Greco et al., 2020; Feld et al., 2020; Gefen et al., 2020; Heinz

TABLE 1. Description of included studies

Study	*n*	Sample description	Hospital	Region	Enroll dates	Age range	Age median	Male sex	White	Black	Hispanic	Asian	Other	Unknown
Bhumbra et al.	19	Hospitalized children with COVID	Riley Hospital for Children at Indiana University Health	Indianapolis	February 26 to May 4, 2020	< 2–18 years	5	14	4	7	7	1	0	0
Blumfield & Levin	19	Case series, hospitalized children with COVID	Montefiore Medical Center	Bronx, NY	February 25 to May 1, 2020	2 months to 18 years	8	10						19
Cheung et al.	17	Children/adolescents with MIS	Columbia University Irving Medical Center	New York City	April 18 to May 5, 2020	1.8–16 years	8	8	2	4	4	1	6	0
Craver et al.	1	Case report/autopsy	Children's Hospital of New Orleans	New Orleans	March 2020		17	1	0	1	0	0	0	0
Danley & Kent	1	Case report: 4-month-old male with muscular ventricular septal defect and atopic dermatitis and COVID	Rush University Medical Center	Chicago	March 26, 2020		0.33	1						1
Del Greco et al.	4	Four cases of MIS	New York-Presbyterian Queens	Queens, NY	May 8, 2020	4–16 years	11.5	1						4
Feld et al.	3	Case series three infants < 2 months with COVID	Cohen Children's Medical Center	New Hyde Park, NY	March 2020	28-43 days	0.12	2						3
Feldstein et al.	186	Children and adolescents with MIS	53 Pediatric Health Centers	United States	March 15 to May 20, 2020	< 1–20 years	8.3	115	35	46	57	0	9	41
Gefen et al.	1	Case report: 16-year-old boy with autism	Cohen Children's Medical Center of New York	New Hyde Park, NY	Before May 2020		16	1						1
Heinz et al.	1	Case report: 6-month-old liver transplant patient	New York-Presbyterian Hospital	New York, NY	March 17, 2020		0.5	0						1
Kainth et al.	65	Hospitalized COVID patients < 22 years	Steven and Alexandra Cohen Children's Medical Center at Northwell Health	New Hyde Park, NY	January 23 to April 18, 2020	< 60 days to 22 years	10.3	33	14	17	15	8	24	2
Kaushik et al.	33	Children with MIS-C in intensive care units	Three tertiary care children's hospitals	New York City	April 23 to May 23, 2020	IQR: 6-13	10	20	3	13	15	1	1	0
Kest et al.	3	Three critically ill children with MIS-C	St. Joseph's Children's Hospital	New Jersey	April 4 to May 10, 2020	6–10 years	9	1	0	1	2	0	0	0
Lara et al.	1	Case study: Pediatric patient with COVID and acute fulminant myocarditis	Ochsner Hospital for Children	New Orleans, LA	April 2020	12 years	12	0	0	0	0	1	0	0
McLaren et al.	7	Case series: seven febrile infants aged ≤ 60 days with SARS-CoV-2	Vagelos College of Physicians and Surgeons, Columbia University	New York City	March 1 to April 15, 2020	≤ 60 days	0.11	6						7
Mithal et al.	18	Case Series: 18 infants aged < 90 days tested positive for SARS-CoV-2 in ED (*n* = 15) and outpatient (*n* = 3)	Ann and Robert H. Lurie Children's Hospital	Chicago, IL	April 11 to May 12, 2020	10-88 days	55.5	7	0	0	14	0	0	4
Needleman & Hanson	1	Case study: 3-week-old male with mild hypoxic-ischemic encephalopathy and COVID-19 hospitalized twice	Indiana University School of Medicine	Indianapolis, IN	Before June 2020	25 day	0.07	1						1

(*continued on next page*)

TABLE 1. (*Continued*)

Study	*n*	Sample description	Hospital	Region	Enroll dates	Age range	Age median	Male sex	White	Black	Hispanic	Asian	Other	Unknown
Patel et al.	1	Case study: Severe pediatric COVID-19 patient presenting with respiratory failure and severe thrombocytopenia	Children's Healthcare of Atlanta and the School of Medicine	Atlanta, GA	Before April 2020		12	0						1
Perez et al.	2	Case series: two healthy adolescents with SARS-CoV-2 and cholestatic jaundice, and hepatitis	Cohen Children's Medical Center of New York	Bronx, NY	Before June 2020	16–17 years	16.5	1						2
Shekerdemian et al.	48	Children with COVID admitted to the ICU	14 U.S. hospitals	USA	March 14 to April 3, 2020	< 1 to 21 years	13	25						48
Spencer et al.	2	Case series: two children with COVID and clinical features suggestive of Kawasaki disease	New York-Presbyterian Morgan Stanley Children's Hospital	New York, NY	Before May 2020	7–11 years	9	1						2
Tsao et al.	1	Pediatric COVID patients with immune thrombocytopenia	Warren Alpert Medical School, Brown University	Providence, RI	Before May 2020	10 years	10	0						1
Zachariah et al.	50	Patients with COVID-19 hospitalized at a children's hospital	New York-Presbyterian Morgan Stanley Children's Hospital	New York, NY	March 1 to April 15, 2020	<1–21 years	9	27	27	0	25	0	0	0
Total	484					*n*/mean %/*SD*	10.5 11.1	275 56.8	85 17.6	89 18.4	139 28.7	12 2.5	40 8.3	138 29.7

Note. *ED, emergency department; ICU, intensive care unit; IQR, interquartile range; MIS, multisystem inflammatory syndrome; MIS-C, multisystem inflammatory syndrome in children; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2. Some participants are listed in multiple racial groups.*

TABLE 2. Symptoms reported by the study

Study	*n*	Symptom duration	Fever	Fever duration	Respiratory	Cough	Sore throat	Nasal mucus	Chest pain	Gastro-intestinal	Diarrhea	Vomit/ nausea	Anorexia	Abdominal pain	Neurologic	Headache	Mood/ mental	Rash	Smell/ taste	Conjunc-tivitis	Oral	Myalgia/ fatigue	Lymphad-enopathy
Bhumbra et al.	19	3	12		12	5	2		4	2		2							3				
Blumfield & Levin	19		17		13	13				9													
Cheung et al.	17	5	17	5	7					15					8			12		11	9	6	6
Craver et al.	1									1		1			1	1							
Danley & Kent	1	16	0		1	1		1		1	1		1										
Del Greco et al.	4		4		4		2	1		4	2	3	1	4	3	3		4		2	4		1
Feld et al.	3	1	3	1	1	0		1		3			3				2					2	
Feldstein et al.	186	25	186	6	131					171								110		103	78		18
Gefen et al.	1	5	1	1	1			0		0	0	0	0						0			1	
Heinz et al.	1		1		1	1	1	1		1	1												
Kainth et al.	65		57	1	39	32	5	17		40	7	22	26	11	21	11	7	5	3			22	
Kaushik et al.	33	4.5	31		11			7		23	16	23		21	4			14		12			
Kest et al.	3	4	3	4	2					3	3	2		2	1	1	1	2		2		1	
Lara et al.	1	3	1	2	1					1		1		1			1					1	
McLaren et al.	7		7		1	2		1		1	0	1	1									3	
Mithal et al.	18		14		1	8		5		4			5				1	1		2			
Needleman & Hanson	1	3	0		1			1		0													
Patel et al.	1	5	1	5	1	1				1		1											
Perez et al.	2	2.5	1	4	0					2	1	1	1	1							1		
Shekerdemian et al.	48				35					1					2								
Spencer et al.	2	5	1	5	0	1	2	1		2	1	2		1	2	1	2	2		2	2	1	
Tsao et al.	1	1	0		0	0			0	0			0	0				1			1		0
Zachariah et al.	50	2	40		17	23		6	9	7													
No. of studies	23	15	21	10	22	12	5	12	3	23	10	12	9	8	8	5	6	9	3	7	6	8	4
Total sample size	484	321	435	281	483	187	91	186	70	484	119	139	102	111	173	75	92	329	85	263	212	99	208
N/mean		5.7	397	3.4	280	87	12	42	13	292	32	59	38	41	42	17	14	151	6	134	95	37	25
%/SD		1.2	91.3	0.7	57.9	18.0	2.5	8.7	2.7	60.3	6.6	12.2	7.9	8.5	8.7	3.5	2.9	31.2	1.2	27.7	19.6	7.6	5.2

Note. *Symptom and fever duration were reported as the median number of days.*

TABLE 3. Disease severity by study

Study	n	Comorbid conditions	Hospital admission[a]	Hospital length of stay	Supplemental oxygen	Intubation/ mechanical ventilation	Intensive care	Intensive care length of stay	Death
Bhumbra et al.	19	8			3	4	7		1
Blumfield & Levin	19	12			4	8	14		2
Cheung et al.	17	0		7.1	9	0	15		0
Craver et al.	1	0							1
Danley & Kent	1	1		4.0	1	0	1		0
Del Greco et al.	4	1		5.0	0	0	2		0
Feld et al.	3	1		1.1	0	0	0		0
Feldstein et al.	186	51		7.0	8	37	148		4
Gefen et al.	1	1		12.0	0	0	0		0
Heinz et al.	1	1		22.0			1		0
Kainth et al.	65	21		3.2	17	5	23	5.4	1
Kaushik et al.	33	16		7.8		5	33	4.7	1
Kest et al.	3	0		6.0	1	1	1	6.0	0
Lara et al.	1	0		10.0		1	1		0
McLaren et al.	7	2	6	2.0		0	0		0
Mithal et al.	18	0	9		0	0	0		0
Needleman & Hanson	1	0		1.0	0	0	0		0
Patel et al.	1	0		24.0	1	1	1		0
Perez et al.	2	1	1		0	0	0		0
Shekerdemian et al.	48	40		7.0	21	18	48	5.0	2
Spencer et al.	2	1			1				0
Tsao et al.	1	0		1.0	0	0	0		0
Zachariah et al.	50	33		3.0	16	9	9		1
No. of studies	23	23	3	17	18	20	21	4	23
Total sample size	484	484	27	423	441	480	481	149	482
N/mean		190	16	7.2	82	89	304	5.3	13
%/SD		39.3	3.3	6.7	16.9	18.4	62.8	0.6	2.7

Note. *Hospital and intensive care length of stay was reported as the median number of days.*
[a]*Hospital admission was only assessed for studies that included nonhospitalized patients.*

TABLE 4. Symptom and disease severity meta-analyses

Variables	No. of studies	Total sample size	% (95% Confidence interval)[a]	Heterogeneity statistics χ^2 (df)	Heterogeneity statistics I^2	Heterogeneity statistics T^2	Metaregression Predictor: b (*SE*)
Symptoms							
Symptom duration	7	310	6.1 (−0.1 to 12.4)	740.6 (6)[b]	99.5	70.8	Sample size: 0.1 (0.01)
Fever	21	435	95.0 (82–100)[b]	89.5 (20)[b]	77.6	0.2	
Fever duration	4	271	2.9 (−0.03 to 5.8)	369.5 (3)[b]	98.9	7.2	Sample size: 0.03 (0.006)
Respiratory distress/dyspnea	22	483	52.0 (36.0–67.8)[b]	86 (21)[b]	75.6	0.2	
Cough	12	187	44.4 (31.4–57.7)[b]	15.1 (11)	26.9	0.2	
Sore throat	5	91	28.8 (1.1–67.6)[b]	16.6 (4)[b]	75.9	0.3	
Rhinorrhea/congestion	12	186	16.1 (6.7–27.5)[b]	14.2 (11)	22.3	0	
Chest pain	3	70	11 (2.2–23.3)[b]	0.2 (2)	0	0	
Gastrointestinal	23	484	61.5 (33.4–86.9)[b]	327.8 (22)[b]	93.3	0.8	% Comorbidities: −0.6 (0.3)
Diarrhea	10	119	39.0 (9.6–72.2)[b]	36.6 (9)[b]	75.4	0.3	
Vomiting/nausea	12	139	49.6 (24.1–75.2)[b]	33.3 (11)[b]	67	0.2	
Poor feeding/anorexia	9	102	33.3 (15.1–53.5)[b]	10.9 (8)	26.4	0	
Abdominal pain	8	111	56.1 (18.9–90.6)[b]	34.3 (7)[b]	79.6	0.4	Sample size: −0.01 (0.004)
Neurological	8	173	32.3 (10.3–58.0)[b]	37.7 (7)[b]	81.4	0.2	% Comorbidities: −0.6 (0.3)
Headache	5	75	41.1 (5.8–81.1)[b]	9.6 (4)[b]	58.4	0.3	
Emotional/mental change	6	92	30.1 (2.7–66.0)[b]	17.6 (5)[b]	71.6	0.3	
Rash	9	329	52.0 (23.2–80.3)[b]	97 (8)[b]	91.7	0.4	
Dysgeusia/anosmia	3	85	0.4 (0.0–8.8)	2.5 (2)	18.6	0	
Conjunctivitis	7	263	47.1 (28.1–66.5)[b]	21.2 (6)[b]	71.7	0.1	
Oral/saliva changes	6	212	66.0 (37.6–90.4)[b]	11.7 (5)[b]	57.1	0.1	
Myalgia/fatigue	8	99	33.9 (21.8–46.8)[b]	4.8 (7)	0	0	
Lymphadenopathy	4	208	12.5 (0.0–38.0)[b]	7.7 (3)	60.8	0.1	
Disease severity							
Comorbid conditions	23	484	31.8 (14.9–50.7)[b]	129.6 (22)[b]	83.0	0.3	No race reported: 0.3 (0.1)
Hospital admission	3	27	62.8 (35.4–87.1)[b]	2.6 (2)	23.1	0	
Hospital length of stay	10	416	4.8 (3.0–6.6)[b]	309.5 (9)[b]	96.2	6.4	Case report: −3.9 (1.2) Age: 0.4 (0.1)
Supplemental oxygen	18	441	13.3 (2.3–28.7)[b]	90.0 (18)[b]	80.0	0.2	Study size: −0.001 (0.001)
Intubation/mechanical ventilation	20	480	7.1 (1.1–16.1)[b]	47.3 (19)[b]	59.8	0.1	
Intensive care	21	481	49.9 (23.2–76.6)[b]	289.7 (20)[b]	93.1	0.7	
Intensive care length of stay	4	149	4.9 (4.3–5.6)[b]	0.8 (3)	0.0	0.0	
Death	23	482	0.0 (0.0–0.0)	13.3 (22)	0	0	

Notes. *Hospital admission was only assessed for studies that included nonhospitalized patients. Case studies with no effect size variation were excluded from continuous outcome models.*
[a] *Different from zero.*
[b] *Effect is different from zero or heterogeneity χ^2 test is significant. Only significant predictors for metaregression are shown.*

et al., 2020; Kest et al., 2020; Lara et al., 2020; McLaren et al., 2020; Needleman & Hanson, 2020; Patel et al., 2020; Perez et al., 2020; Spencer et al., 2020; Tsao et al., 2020). Patient enrollment in all studies occurred in the early stages of the pandemic between February and June 2020. Studies primarily included hospitalized children and adolescents with COVID-19, though three included patients not admitted for hospitalization but seeking care at hospital facilities. Studies were conducted in Georgia (n = 1), Illinois (n = 2), Indiana (n = 2), Louisiana (n = 2), New Jersey (n = 1), New York (n = 12), Rhode Island (n = 1), and at multiple sites (n = 2). The age range was from < 1 to 21 years, and the average median age across studies was 10.5 years old. Over half of the patients (56.8%; n = 275) were male children. Race of patients was reported in 10 studies (Bhumbra et al., 2020; Cheung et al., 2020; Craver et al., 2020; Feldstein et al., 2020; Kainth et al., 2020; Kaushik et al., 2020; Kest et al., 2020; Lara et al., 2020; Mithal et al., 2020; Zachariah et al., 2020). The race of children across studies was 17.6% White, 18.4% Black, 28.7% Hispanic, 2.5% Asian, 8.3% other, and 29.7% unknown. Some participants were listed in multiple racial groups.

Meta-analysis revealed fever to be the most common symptom, estimated to occur in 95% of children seeking medical care (Table 4). Fever was also the symptom that could be the most reliably estimated, as evidenced by the comparatively small CIs. Respiratory and gastrointestinal symptoms were also relatively common, occurring in 52.0% and 61.5% of children. Other symptoms estimated to occur in 50% or more of children were oral/mucosal changes (66.0%), abdominal pain (56.1%), rash (52.0%), and nausea/vomiting (49.6%). Dysgeusia and anosmia (loss of taste and smell), commonly reported in adults, were reported in only three studies in this meta-analysis. Almost no children experienced these symptoms. The symptom duration was about six days, and the fever was three days.

Comorbid conditions were estimated to be present in 33% of children seeking medical care. Of patients presenting to a hospital seeking medical care, 62.8% were admitted (assessed in three studies). The average length of hospital stay was about 5 days. Intensive care was needed in about half of the cases, and the average length was about 5 days. In 13.3% of cases, supplemental oxygen was needed, and intubation or mechanical ventilation was needed in 7.1%. Thirteen deaths (2.68%) in total were reported across studies.

Symptom and disease severity estimates were generally heterogeneous across studies; therefore, factors related to differences in the estimates were assessed with metaregression. A larger sample size was associated with longer symptom and fever duration and a lower frequency of reporting abdominal pain or supplemental oxygen use. Case studies were associated with a greater length of hospital stay, and patients had a higher median age. A higher percentage of patients with comorbidities were associated with less gastrointestinal or neurological symptoms reporting. Studies that did not report race had a higher percentage of patients with comorbid conditions. No publication bias was found.

DISCUSSION

This meta-analysis aimed to summarize the initial literature regarding COVID-19 symptom presentation and outcomes among children receiving hospital care in the United States. As reported by pediatric health care providers, common symptoms included fever and gastrointestinal and respiratory distress. Less than 3% of the 484 children included in the review and meta-analysis died of COVID-19.

Comparison to Adult Cases

Symptomatology associated with COVID-19 is reported to increase with age (Mayo, 2022). Loss of smell and taste are often highlighted as important symptoms indicating that an individual has contracted SARS-CoV-2 (Centers for Disease Control and Prevention, 2021b). However, our results do not support this notion. The lack of support may be due to the frequency with which children report these symptoms or the lack of documentation in the medical record (Kumar et al., 2021; Ranabothu et al., 2020). More specifically, because children may lack the vocabulary to express sensory experiences, we speculate that the loss of smell and taste may be exhibited in behavior and not verbalized to clinicians. As such, the loss of smell and taste may contribute to poor feeding and/or anorexia.

Age has also been shown to be the strongest indicator for severe COVID-19 outcomes (Mayo, 2022). Individuals aged > 65 years accounted for 81% of the deaths related to COVID-19 (Mayo, 2022). However, younger children are clinically more likely to be affected by fluid loss and seem to be those who would be at the most risk for morbidity and mortality. Our study found that children who died were aged > 5 years. Studies also showed that risk severity increases as preconditions increase (Centers for Disease Control and Prevention, 2021b). Comorbidities in children, such as HIV, disabilities, neurological disorders, sickle cell disease, and being overweight and obese, are shown to be linked to more severe symptoms and slower recovery, specifically from COVID-19 (Tsankov et al., 2021). The associations between comorbid states and specific outcomes (e.g., death) were not described in detail within the 23 articles. However, our study did find that children with comorbidities presented with neurological symptoms.

Studies have also shown that populations are not affected equally by COVID-19. Based on the Centers for Disease Control and Prevention's National Vital Statistics System mortality data, an estimated 700,000 excess deaths occurred in the United States from February 1, 2020 to September 30, 2021 (Centers for Disease Control and Prevention, 2022). The largest percentage increases in mortality occurred among adults aged 25−44 years and among Hispanic or Latinx people (Blanton et al., 2019). The mortality rate among children in our analysis was < 3% (n = 13; N = 484). The race and ethnicity of these children could not be determined because of variations in the reporting of that data among the 23 publications.

Compared with Three Common Childhood Viral Illnesses

Compared with three other common childhood viral illnesses seen in the United States, COVID-19 symptom presentation appears like those seen with influenza, RSV, and gastroenteritis, as well as other viral illnesses caused by adenovirus and rhinovirus.

Symptoms associated with influenza are cough and fever lasting 5 days. In the 2018−2019 season, between 54,381 (10%; Centers for Disease Control and Prevention, 2022) and 177,039 (15%; Xu et al., 2019) specimens tested positive for influenza. Moreover, 88.2% of the data (n = 10,766) included age information, further showing that the prevalence of influenza among children aged 0−4 years was (1,627 [15.7%] to 4,844 [12.6%]) as compared with children aged 5−24 years (3,493 [32.4%] to 12,508 [32.4%]). The cumulative hospitalization rate per 100,000 was 72 for children aged 0−4 years and 20.4 for children and adolescents aged 5−15 years (Xu et al., 2019). Twenty-eight (Blanton et al., 2019) to 116 (Xu et al., 2019) children died of influenza during the 2018−19 season. The average age of children who died was 6.1−6.5 years (range = 2 months to 17 years; Blanton et al., 2019; Xu et al., 2019). Results from a retrospective cohort study from the Programme de Médicalisation des Systèmes d'Information database found that influenza affected more children (n = 8,942; 19.2%) than did COVID-19 (n = 1,227; 1.4%); however, significantly more children aged < 5 years with COVID-19 (2.3%) required treatment in the intensive care unit than those with influenza (0.9%; Piroth et al., 2021). No significant difference was found in children with COVID-19 and influenza mortality rates. Children aged 11−17 years with COVID-19 were 10 times more likely to die in the hospital than those with influenza (Piroth et al., 2021).

In contrast, RSV primarily affects children aged < 5 years; however, adults may also contract the virus. The most common symptoms include cough (98%), fever (75%), and labored respirations (73%). RSV accounts for > 58,000 hospitalizations in children aged < 5 years (https://www.cdc.gov/surveillance/nrevss/rsv/index.html). In a prospective, population-based surveillance study between 2000 and 2004, 18% of 5,067 specimens from children tested positive and were associated with 20% of annual hospitalizations. RSV-associated hospitalization was three per 1,000 children aged < 5 years and 17 per 1,000 children aged < 6 months. Significantly more inpatients were non-Hispanic white children under the age of 6 months and had private insurance (Hall et al., 2009). In another prospective population-based surveillance conducted in seven U.S. pediatric hospitals from November 2015 to June 2016, 35% of hospitalized children (n = 1,043) tested positive, 87% were aged < 2 years, and 50% were aged < 6 months. The hospitalization rate was higher among males (3.3 [95% CI, 3.0−3.6]) than females (2.6 [95% CI, 2.3−2.9]; Rha et al., 2020). Of the approximately 58,000 children hospitalized (Hall et al., 2009), between 100 and 500 (0.86%) died of RSV (Thompson et al., 2003). Reporting death from RSV is not required, which creates uncertainty regarding fatal outcomes associated with the disease (Byington et al., 2015).

Comparing gastrointestinal symptoms associated with SARS-CoV-2 to gastroenteritis (vomiting, diarrhea) in children in the United States, gastroenteritis in the United States accounts for 200,000 hospitalizations and 300 deaths each year (Hartman et al., 2019). More specifically, 6.1% to 29.4% of children with gastroenteritis test positive for rotavirus, whereas *Norovirus* accounts for 11.9% of positive tests (Muhsen et al., 2019). Together, rotavirus and *Norovirus* account for more than 58% of all cases of gastroenteritis and 10% of pediatric deaths (Rivera-Dominguez & Ward, 2018).

Comparing these three illnesses, COVID-19 symptom presentation may begin 1−14 days after exposure. The frequency of positive laboratory tests is 3.9% in children aged 0−4 years and 6.3% in children aged 5−17 years. These rates are compared with an overall positivity rate of 14.4% (Dhochak et al., 2020). As such, the incidence of COVID-19 in children is less than the rate of COVID-19 in adults (Lu et al., 2020) and less than the rate of influenza and RSV in children. The rate of hospitalization among children with COVID-19 has been calculated at 5.4% (Kim et al., 2021). Only two studies in this meta-analysis reported admission rates ranging from 4.7% (Bhumbra et al., 2020) to 74% (Zachariah et al., 2020). Higher hospitalization rates among children with COVID-19 may be attributed to an overabundance of caution when caring for patients with a novel illness. Furthermore, a comparison of mortality among children with COVID-19, influenza, RSV, and gastroenteritis shows that children with gastroenteritis are more likely to die than those with other viral illnesses. More specifically, of the 73 million children diagnosed with COVID-19, < 700 (0.001%) have died of the virus (American Academy of Pediatrics, 2022).

In light of the current uptick in RSV and influenza, the presentation of COVID-19 symptoms is not to be taken lightly but put into perspective in relation to these common childhood viral illnesses. Because of the similarity among symptoms of SARS-CoV-2 and other common childhood viral illnesses, diagnosing COVID-19 empirically is challenging. Therefore, testing is warranted to identify the causative agent of the illness. Regardless of test results, treatment for most viral illnesses is supportive unless a bacterial origin is identified.

Strengths

Our article provides a systematic review and meta-analysis of initial publications identifying key clinical symptom presentations that help clinicians recognize this disease process and intervene early to reduce poor outcomes rather than relying solely on laboratory results. Strengths of our work include the assessment of factors related to heterogeneity in reporting COVID-19 symptoms and disease severity for hospitalized children, as well as the lack of publication bias. Our meta-analysis also identifies inconsistencies in demographics reporting, disease prevalence, symptoms,

hospitalizations, morbidity, and mortality. These inconsistencies create challenges for the clinician when making clinical decisions about significant symptoms that distinguish one disease from another. Therefore, reporting demographic information along with symptomology, hospitalization, morbidity, and mortality is warranted to advance health equity.

Limitations

Comparison of COVID-19 symptom presentation from evidence in the literature was challenging. Symptom presentation, ethnicity, race, and age group were inconsistently reported across publications, limiting the depth of detailed analysis. Comparison of the incidence of COVID-19 and the three common childhood illnesses was also challenging because COVID-19 data are reported cumulatively, whereas symptoms of common viral illnesses are reported seasonally. Comparison of the outcomes from these diseases was also challenging because reporting the incidence of RSV and death resulting from RSV is not required. Finally, all publications did not include ethnicity and/or race data. As a result, we could not determine whether symptom presentation in children differed between ethnic and/or racial groups.

Conclusions

SARS-CoV-2 is a viral vector with variable symptom presentation. As we continue to study COVID-19 symptom presentation in children and compare it to other viral illnesses and their outcomes, we hope to better understand the clustering of symptoms and the relationship between symptom clusters and health outcomes. This knowledge will allow for the early identification of those at greatest risk for rapid clinical decline and possible death.

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