A Surge in Pediatric Coronavirus Disease 2019 Cases: The Experience of Texas Children's Hospital from March to June 2020

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Key points: We describe the clinical characteristics and outcomes of children with SARS-CoV-2 infection in a health-care system in Texas. A high percentage of Hispanic children tested positive for SARS-CoV-2 and were hospitalized. Most children with SARS-CoV-2 infection had uncomplicated illness courses.

Abstract

Background:

An understanding of the clinical characteristics of children with coronavirus disease 2019 in diverse communities is needed to optimize the response of healthcare providers during this pandemic.

Methods:

We performed a retrospective review of all children presenting to the Texas Children's Hospital system with testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from March 10, 2020 through June 28, 2020.Demographics were recorded for all patients undergoing testing and clinical characteristics and outcomes were recorded for children with positive tests.

Results:

Of 16,554 unique patients ≤ 21 years of age who were tested for SARS-CoV-2, 1215 (7.3%) patients tested positive. Infants under 1 year of age and patients aged 18-21 years had the highest percent of positive tests at 9.9% (230/2329) and 10.7% (79/739), respectively. Hispanic children accounted for 66% (802/1215) of positive tests, though they only represented 42.1% (6972/16554) of all children tested for SARS-CoV-2. Of the 1215 children with a positive test, 55.7% had fever, 40.9% had cough, 39.8% had congestion or rhinorrhea, 21.9% had gastrointestinal complaints, and 15.9% were asymptomatic. Only 97 (8%) patients were hospitalized (of which 68% were Hispanic). Most hospitalized patients had underlying medical conditions (62/97, 63.9%), including obesity. Thirty-one hospitalized patients (31/97, 32%) required respiratory support and nine patients (9/97, 9.3%) received SARS-CoV-2 antiviral therapy. Two patients died.

Conclusions:

A relatively high percentage of Hispanic children tested positive for SARS-CoV-2 and were hospitalized. Most children with detection of SARS-CoV-2 had uncomplicated illness courses, some children were critically ill, and two patients died.

Keywords: coronavirus disease 2019; SARS-CoV-2; Children

Introduction

The novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19) was declared a pandemic by the World Health Organization on March 11, 2020 [1].There have been an astonishing 18.7 million cases globally and over 4.7 million cases with more than 156,000 deaths in the United States [2].

The epidemiology of COVID-19 is well described in various adult populations from different geographic locations throughout the United States. Racial and ethnic disparities among adults with COVID-19 infection is now well described, but there are fewer reports on the impact of this emerging pandemic on the lives of children and adolescents from ethnically diverse urban communities [3-5]. While aspects of COVID-19 epidemiology, including hospitalization rates, severity of illness and underlying conditions, have been studied among children in the United States infected with SARS-CoV-2, little is known about potential racial and ethnic disparity among children [6-9]. Otto and colleagues previously reported on a cohort of 424 children with SARS-CoV-2 infection across the Children's Hospital of Philadelphia Network [6]. Our report similarly contributes to the growing understanding of the epidemiology of SARS-CoV-2, while highlighting important demographic differences in a geographically distant part of the country. We additionally report on the presence of co-infections and radiographic and laboratory findings among children with SARS-CoV-2 infection.

The dynamics of the pandemic have varied between communities, as mitigating interventions and public health strategies across the nation have differed by state and within states. We previously reported on the clinical characteristics and outcomes of the first 57 consecutive cases of COVID-19 in children cared for through Texas Children's Hospital (TCH) [10]. As the pandemic has progressed, however, we experienced a surge of cases in Texas and a corresponding increase in the number of children infected with SARS-CoV-2 in the greater Houston area. This report serves to better characterize the epidemiology of

SARS-CoV-2 infection in children from infancy to young adulthood, who were seen throughout a large pediatric healthcare system at a time of increasing local transmission.

Methods

Study Design and Population

We performed a retrospective chart review of unique patients ≤ 21 years of age tested for SARS-CoV-2 by reverse transcription-polymerase chain reaction (RT-PCR) between the dates of 3/10/2020 - 6/28/2020 through the TCH system. TCH is in Houston, Texas and is one of the largest specialty pediatric health care organizations in the United States. The TCH system serves the greater Houston area and consists of a large quaternary care pediatric hospital with over 600 beds within the Texas Medical Center and 2 community based pediatric hospitals in Katy, Texas and The Woodlands, Texas. In addition, our healthcare network has over 50 primary care locations (Texas Children's Pediatrics practices), 11 urgent care centers in the community and 3 Emergency centers within the hospitals. Epic (Epic Systems, Verona, WI) is the common electronic health care record for the TCH system.

We excluded patients who were tested through Texas Children's Employee Health and obstetrical patients cared for through the TCH Pavilion for Women. For patients with a positive test during the study timeframe, only the first positive test was included. For patients without a positive test, only the first test performed was included. Testing indications and demographic information (age, gender, race and ethnicity) was abstracted from the electronic medical record for all patients with a valid test result for a SARS-CoV-2 PCR during the study timeframe (3/10/2020-6/28/2020). A manual chart review was performed by 5 investigators (C.F., L.M., A.D., E.T., and J.C.) for information on COVID-19 exposure history, underlying medical conditions, symptomatology, radiologic findings, additional viral testing results, and disease severity for all patients with a positive SARS-CoV-2 PCR result. Additional details were obtained for hospitalized children with positive tests, including length

of stay, need for intensive care, laboratory values, presence of co-bacterial or fungal pathogens, supportive treatments, and receipt of antiviral or immunomodulatory therapies. Hospitalized status required a length of stay of at least one night. Patients were considered to have an exposure to SARS-CoV-2 if they reported a household contact or non-household close contact with an individual with confirmed SARS-CoV-2 infection. Individuals residing in group homes or residential care facilities with confirmed SARS-CoV-2 cases were considered to have a household contact. Baylor College of Medicine Institutional Review Board approved this study.

Testing Algorithms and Guidelines

During the study timeframe, TCH system-wide COVID-19 exposure and symptom-based algorithms were utilized to guide clinical practice for SARS-CoV-2 testing, but testing was ultimately at provider discretion. Testing recommendations were revised based upon local epidemiology, updated CDC guidelines and increased testing capacity. Hospital-based testing for SARS-CoV-2 by PCR was initiated on March 10, 2020 and beginning March 22, 2020, surveillance testing for SARS-CoV-2 was implemented for all patients admitted to a pediatric intensive care unit or undergoing an aerosol generating procedure. A rapid PCR assay was available for patients undergoing emergent procedures. On May 14, 2020, surveillance testing was extended to include all patients needing admission to the pediatric hospitals at the medical center and community campuses. In general, outpatient testing algorithms prioritized testing of symptomatic patients with immunocompromising or chronic medical conditions or symptomatic patients with household contacts of a confirmed COVID-19 case or household contacts belonging to vulnerable populations. Testing of asymptomatic individuals, however, may have been performed due to exposure to a suspected or confirmed case of COVID-19 or due to requirements for childcare centers or camps. Drive-thru testing locations have been in operation since March 24, 2020 with additional sites added April 28, 2020. SARS-CoV-2 testing indication, defined as surveillance or patient

under investigation (PUI), is recorded for both drive-thru tests and hospital-based tests and was implemented April 10, 2020.

Nucleic Acid Amplification Assays

Qualitative detection of SARS-CoV-2 RNA was performed using four different assays by the TCH Molecular Microbiology Laboratory during the study period. Acceptable and validated specimen types for testing included nasopharyngeal swabs, nasal washes and bronchial specimens. Specimens were placed in transport tubes containing 3.0 mL of M4RT viral transport media (VTM) (ThermoFisher, Waltham, MA). For the RealStar SARS-CoV-2 RT-PCR kit (Altona Diagnostics, Hamburg, Germany), nucleic acid was first extracted from 200 uL of specimen in VTM using an easyMAG (bioMerieux, Durham, NC) or MagNApure 96 (Roche, Indianapolis, IN) instrument per the manufacturer's instructions. Amplification and detection were carried out on the ABI7500 instrument (ThermoFisher). This test targets the E and S genes of SARS-CoV-2 and has a limit of detection of 0.1 PFU/mL [11]. The Simplexa COVID-19 Direct test (Diasorin Molecular, Cypress, CA) was performed according to the manufacturer's instructions for use [12]. This test targets the ORF1ab and S genes of SARS-CoV-2 and has a limit of detection of 500 copies/mL. The Aptima SARS-CoV-2 assay (Hologic, San Diego, CA) was performed according to the manufacturer's instructions for use [13]. This assay targets two different regions of the ORF1ab gene and has a limit of detection of 0.01 TCID50/mL. The Xpert Xpress SARS-CoV-2 test (Cepheid, Sunnyvale, CA) was performed according to the manufacturer's instructions for use [14]. The test targets the E and N2 genes of SARS-CoV-2 and has a limit of detection of 0.01 PFU/mL. Clinicians in the ambulatory setting could also order SARS-CoV-2 testing through a national reference laboratory (Quest Diagnostics).

Statistical Analysis

Descriptive statistics were used for analysis of demographic and clinical data (STATA 11.0, College Station, TX).

Results

During the study period, 16,554 SARS-CoV-2 tests were performed on unique patients ≤ 21 years of age (see Supplemental Figure 1). Of these patients, 1215 (7.3%) patients tested positive for SARS-CoV-2 (Table 1). By age, infants under 1 year of age and patients aged 18-21 years had the highest percent of positive tests at 9.9% (230/2329) and 10.7% (79/739), respectively. Children aged 1-5 years had the lowest percent of positive tests (335/5842, 5.7%). Fifty-one percent of patients with positive tests were male. By race, 13% of Native Hawaiian or Other Pacific Islander tested positive. By ethnicity, 11.5% (802/6972) of Hispanic children tested positive vs 4.2% (365/8725) of non-Hispanic children. TCH Molecular Microbiology Laboratory performed 97.8% (16186/16554) of the tests. Of the rapid tests performed, 3.4% (32/938) were positive. By testing indication, PUIs had a higher percent of positive tests compared to patients undergoing surveillance testing, 16% (1002/6245) vs 1.8% (156/8690) respectively.

Clinical characteristics of all patients with detection of SARS-CoV-2 are shown (Table 2). Almost half of the patients (602/1215, 49.6%) reported a sick member in the household and one-third of patients (441/1215, 36.3%) had a laboratory-confirmed COVID-19 contact in the household. The most common symptoms included fever (55.7%), cough (40.9%), and congestion or rhinorrhea (39.8%). Gastrointestinal complaints were present in 21.9% (266/1215) of patients. Almost 16% of children were asymptomatic (193/1215). Most children (90.8%) had no chest imaging. Detection of a co-viral pathogen occurred infrequently (0.5%) and included: human metapneumovirus (3), rhinovirus (2), adenovirus (1), and parainfluenza virus (1) but was not tested for routinely.

Ninety-seven children (97/1215, 8%) with SARS-CoV-2 infection were hospitalized (Table 3). Of the hospitalized children, 66 (68%) were Hispanic, 28 (28.9%) were non-Hispanic, and ethnicity was unknown for 3 (3%) children. Most patients (89/97, 91.8%) were admitted within 1 day of the collection date of the SARS-CoV-2 positive test. Sixty-two children (63.9%) had underlying medical conditions, including 27 children with obesity. Forty (41.2%) patients were admitted for a non-COVID-19 diagnosis including 12 (12.4%) patients admitted with acute appendicitis (see Supplemental Table 1). The median age was 9.3 years (range 1 day – 21 years). Fourteen children (14.4%) were infants <60 days, only one of whom required intensive care for an arrhythmia. Infants were primarily evaluated to rule out serious bacterial infection in the setting of fever.

Twenty-four (30.7%) admitted patients had lymphopenia (absolute lymphocyte count (ALC) <1.0 x 10^9/L) and 18 (23%) had thrombocytopenia (<150 x 10^9/L). Hospitalized patients receiving respiratory support compared to those without respiratory support had a mean peak C-reactive protein of 11.7 mg/dL vs 5.5 mg/dL, respectively; additional laboratory values for hospitalized patients are summarized (see Supplemental Table 2). Three patients had bacteremia including one patient with a polymicrobial infection: *Escherichia coli* (2), methicillin-susceptible *Staphylococcus aureus* (1), and *Klebsiella pneumoniae* (1) and one patient had fungemia. Of the 14 infants <60 days, 4 had partial sepsis evaluations, while 5 had complete sepsis evaluations including cerebrospinal fluid studies (see Supplemental Table 3). All infants had negative cultures except for one patient with an *Escherichia coli* urinary tract infection.

The median length of stay for hospitalized patients was 2 days (range 1-22 days). Thirty-four children (34/97, 35%) required intensive care. Thirty-one patients (31/97, 32%) required respiratory support. Patients receiving immunomodulation and SARS-CoV-2 directed antiviral therapies included: remdesivir (n=9), steroids (n=9), intravenous immune globulin (n=5), anakinra (n=3), and convalescent plasma (n=2). Of the nine patients receiving remdesivir, the median age was 14 years (range 9.6-19.9 years), 8 children were

Hispanic, and 6 children were obese. Remdesivir was administered for a median of 4 days (range 3-5 days). Remdesivir was discontinued due to elevation of liver function tests in 2 patients and one patient expired before completion of a 5-day course. Four patients were treated for multisystem inflammatory syndrome in children (MIS-C). No patients required extracorporeal membrane oxygenation. Two patients died. One patient had underlying congenital heart disease and developed acute respiratory distress syndrome secondary to COVID-19. The other patient expired from complications related to a new oncologic diagnosis.

Discussion

We performed a retrospective chart review of all pediatric patients tested for SARS-CoV-2 through the TCH system from March 10, 2020 through June 28, 2020. Of 16,554 unique patients ≤ 21 years, 1215 (7.3%) tested positive. We previously reported on the first 57 children with positive tests for SARS-CoV-2 in the very early stage of the pandemic, during a time of escalating public health measures to increase social distancing [10]. Beginning in June, however, both the state of Texas and our local Houston area resumed activities in previously closed businesses, and we encountered a significant rise in the incidence of COVID-19 cases. An epidemic curve of our SARS-CoV-2 positive cases shows the increase in cases and the progression of the phased re-opening statutes which occurred in Texas in the preceding weeks (Figure 1). Unfortunately, Texas has emerged as one the epicenters for COVID-19 in the Southern United States with at the peak reporting more than 50 SARS-CoV-2 cases daily among patients in the TCH system.

The TCH system serves the greater Houston metropolitan area which contains nine Texas counties, including over 4.7 million people in Harris County. Harris County is racially and ethnically diverse with 54% Whites, 19% Blacks/African American, 15% some other race, 7% Asian, 3% multiracial, and <1% each American Indian/Alaskan Native and Native Hawaiian/Pacific Islander [15]. The Hispanic community comprises 43% of Harris County [15]. In our study, Hispanic children disproportionately tested positive for SARS-CoV-2.

Sixty-six percent (802/1215) of children with positive tests for SARS-CoV-2 were Hispanic, though they only represented 42.1% (6972/16554) of all children tested. We also found that most of the children hospitalized with SARS-CoV-2 were Hispanic (66/97, 68%). Otto *et al*. reported on a cohort of pediatric patients infected with SARS-CoV-2 across the Children's Hospital of Philadelphia Care Network and noted concerning racial and socioeconomic differences in SARS-CoV-2 positive patients where 10.6% of Black children and only 3.3% of White children tested for SARS-CoV-2 were positive [6]. We found that 11.5% (802/6972) of Hispanic children tested positive for SARS-CoV-2 versus 4.2% (365/8725) of non-Hispanic children. The role of social, economic, and health inequities and the relationship to increased risk of SARS-CoV-2 infection among different racial and ethnic groups needs further investigation [16].

Consistent with other international and domestic pediatric studies, we found that most children with COVID-19 had a mild clinical course [6, 17-22]. Fever and cough were the most common symptoms in our study and 15.9% of children were asymptomatic. Infants have previously been identified as a population at increased risk of hospitalization and potentially of severe disease with COVID-19 [22]. In a multinational study of children and adolescents in Europe, investigators found COVID-19 to cause a generally mild disease in children including infants, though age <1 month was associated with a need for intensive care unit admission [19]. In one report of SARS-CoV-2 positive infants <90 days of age, 50% (9/18) were hospitalized but none required intensive care [23]. In another pediatric study based in New York, investigators found that obesity was significantly associated with severe disease, but infants and immunocompromised patients were not at increased risk [7]. In our study, infants also had mild illness; one infant required intensive care and one infant was found to have a urinary tract infection.

Overall, we found that a relatively low percentage of patients with SARS-CoV-2 were hospitalized (97/1215, 8%) and furthermore over 40% of the admitted patients had a primary diagnosis other than COVID-19. Interestingly, 12 patients were hospitalized with acute

appendicitis. There are case reports detailing clinical presentations of COVID-19 mimicking appendicitis [24]. Appendicitis is the most common pediatric surgical diagnosis, however, and the relationship between SARS-CoV-2 and appendicitis remains unclear and warrants further investigation. Both pediatric and adult reports have found lymphopenia to be a common laboratory finding in patients with COVID-19, though this finding was only present in 30.7% of our admitted patients [7, 25].

Our study has several limitations that warrant acknowledgment, including those inherent in a retrospective chart review. Although TCH is the largest pediatric specialty care network in the area, we would not have captured patients presenting outside of our system or patients transferred into our system if a SARS-CoV-2 PCR was not performed at TCH. The evolution of testing recommendations and practices over the study period may have impacted our results including the rate of detection of infection in Hispanic vs non-Hispanic populations. Additionally, clinical data was limited to the content of the electronic medical record and documentation at times was incomplete. Furthermore, the requirement for a positive SARS-CoV-2 PCR assay for inclusion precludes any full discussion on MIS-C as we would not have captured patients who are SARS-CoV-2 PCR negative and antibody positive.

This study by examining all children tested for SARS-CoV-2 across a large pediatric healthcare system in a diverse population provides insight into disproportionate effects of COVID-19 among racial and ethnic minorities. Overall, most children with detection of SARS-CoV-2 had uncomplicated illness courses, children who were hospitalized often had underlying medical conditions, and fatal outcomes were rare.

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Tables

Table 1. Characteristics of pediatric patients tested for severe acute respiratory syndrome coronavirus 2 through the Texas Children's Hospital system, 3/10/20 – 6/28/20

Characteristic	**Total Tests**	**Positive Tests**	**Percent Positive (%)**
Number, n	16,554	1,215	7.3
Age, median (interquartile range)	6.1 (2-12.5)	7.1 (1.7-13.8)	-
Age group			
0-12 months, n (%)	2329 (14.1)	230 (18.9)	9.9
1-5 years, n (%)	5842 (35.3)	335 (27.6)	5.7
6-11 years, n (%)	3921 (23.7)	265 (21.8)	6.8
12-17 years, n (%)	3723 (22.5)	306 (25.2)	8.2
18-21 years, n (%)	739 (4.5)	79 (6.5)	10.7
Male sex, n (%)	9009 (54.4)	625 (51.4)	6.9
Female sex, n (%)	7543 (45.6)	590 (48.6)	7.8
Race			
American Indian and Native Alaskan, n (%)	44 (0.3)	3 (0.3)	6.8
Asian, n (%)	630 (3.8)	24 (2)	3.8
Black or African American, n (%)	2631 (15.9)	165 (13.6)	6.3
Multiracial, n (%)	187 (1.1)	10 (0.8)	5.4
Native Hawaiian and Other Pacific Islander, n (%)	23 (0.1)	3 (0.3)	13
White, n (%)	11833 (71.5)	919 (75.6)	7.8
Unable to Obtain, n (%)	1206 (7.3)	91 (7.5)	7.6
Ethnicity			
Hispanic, n (%)	6972 (42.1)	802 (66)	11.5
Not Hispanic, n (%)	8725 (52.7)	365 (30)	4.2
Unable to Obtain, n (%)	857 (5.2)	48 (4)	5.6
Test Lab Site			
TCH, n (%)	16186 (97.8)	1186 (97.6)	7.3
Quest, n (%)	368 (2.2)	29 (2.4)	7.9
Rapid Test, n (%)	938 (5.7)	32 (2.6)	3.4
Reason for Testing			
Patient Under Investigation (PUI), n (%)	6245 (37.7)	1002 (82.5)	16
Surveillance, n (%)	8690 (52.5)	156 (12.8)	1.8
Unknown, n (%)	1619 (9.8)	57 (4.7)	3.5

Table 2. Reported exposures, symptoms, additional viral testing, and radiographic findings in pediatric patients with detection of severe acute respiratory syndrome coronavirus 2

Characteristic	**Total patients No. (%)**
Patients	1215 (100)
Exposure	
COVID-19 confirmed household contact	441 (36.3)
COVID-19 confirmed non-household contact	277 (22.8)
Reported sick household contact	602 (49.6)
Symptom	
Fever[a] or cough or shortness of breath	791 (65.1)
Fever[a]	677 (55.7)
Cough	497 (40.9)
Shortness of breath	83 (6.8)
Congestion or rhinorrhea	483 (39.8)
Gastrointestinal complaint[b]	266 (21.9)
Headache	235 (19.3)
Sore throat	213 (17.5)
Loss of taste or smell	77 (6.34)
Asymptomatic	193 (15.9)
Imaging	
No chest radiograph	1,103 (90.8)
Chest radiograph abnormal	47 (3.9)
Viral Testing	
No additional viral testing	1,134 (93.3)
Detection of co-viral pathogen[c]	6 (0.5)

[a]Includes subjective fever

[b]Includes nausea, abdominal pain, emesis, and diarrhea

[c]Eighty-one patients underwent additional viral testing; a co-viral pathogen was identified in 6 of these patients (6/81, 7.4%)

Table 3. Characteristics, clinical course, and outcomes of hospitalized patients at Texas Children's Hospital with detection of severe acute respiratory syndrome coronavirus 2

Characteristic	**Hospitalized patients No. (%)**
Hospitalized patients	97 (100)
Male sex	52 (53.6)
Age, years, median (range)	9.3 (0.0-21.2)
Underlying medical condition	62 (63.9)
Length of stay, days, median (range)[a]	2 (1-22)
Need for intensive care	34 (35)
Abnormal chest radiograph	30 (31)
Respiratory support	
None	66 (68)
Nasal cannula	14 (14.4)
High-flow nasal cannula	6 (6.2)
Non-invasive mechanical ventilation	6 (6.2)
Mechanical ventilation	3 (3.1)
Other[b]	2 (2)
Abnormal echocardiogram[c]	5 (5.2)
Vasoactive requirement	4 (4.2)
Therapies received	
Steroids	9 (9.3)
Remdesivir	9 (9.3)
Intravenous immune globulin	5 (5.2)
Anakinra	3 (3.1)
Convalescent plasma	2 (2)
Death	2 (2)

[a]Three patients remain admitted

[b]Includes one patient with a pneumothorax on a non-rebreather mask and one patient on home ventilation settings but needing supplemental bleed in oxygen

[c]Includes four patients with multisystem inflammatory syndrome in children

Figure Legends

Figure 1. Hospitalized and non-hospitalized patients with a positive test for severe acute respiratory syndrome coronavirus 2 at Texas Children's Hospital from March 23, 2020 through June 28, 2020. Reopening phase 1 in the state of Texas included operation of retail stores, restaurants, movie theaters, malls, museums, and libraries at 25% capacity effective May 1, 2020. On May 5, 2020, barbershops, cosmetology businesses, hair salons and gyms were permitted to reopen. Phase 2 included reopening of restaurants at 50% capacity, bars at 25% capacity, and childcare facilities and bowling alleys on May 18, 2020. Phase 3 reopening allowed all businesses to operate at 50% capacity on June 3, 2020. On June 12, 2020 restaurants were permitted to operate at 75% capacity.

Figure 1