International Journal of Infectious Diseases 122 (2022) 514–520

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Clinical and epidemiological characteristics of SARS-CoV-2 Infection in Los Angeles County youth during the first year of the pandemic

Tawny Saleh[a,*], Tara Kerin[a], Trevon Fuller[b], Sophia Paiola[a], Mary C. Cambou[c], Yash Motwani[c], Caitlin N. Newhouse[c], Shangxin Yang[d], Edwin Kamau[d], Omai B. Garner[d], Sukantha Chandrasekaran[d], Karin Nielsen-Saines[a]

[a] *Department of Pediatrics, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA*
[b] *Institute of the Environment & Sustainability, UCLA, Los Angeles, CA, USA*
[c] *Department of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA*
[d] *Department of Pathology and Laboratory Medicine, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA*

A R T I C L E I N F O

Article history:
Received 8 February 2022
Revised 3 June 2022
Accepted 23 June 2022

Keywords:
COVID-19
Children
Youth
Disease severity

A B S T R A C T

Objectives: The aim of this study was to characterize SARS-CoV-2 infection patterns in Los Angeles (LA) County youth followed at our institution during the first pandemic year.
Design: A prospective cohort of patients aged < 25 years who tested positive for SARS-CoV-2 using reverse-transcriptase polymerase chain reaction (RT-PCR) assays between March 13, 2020, and March 31, 2021, was evaluated at a large LA County health network. Demographics, age distribution, and disease severity were analyzed.
Results: There were 28,088 youth aged < 25 years tested for SARS-CoV-2 using RT-PCR, with 1849 positive results identified (7%). Among the positive results, 475 of 11,922 (4%) were identified at the pandemic onset (March-September 2020) (Cohort 1) and 1374 of 16,166 (9%) between October 2020 and March 2021 (Cohort 2), $P < 0.001$. When disease severity was compared across cohorts, Cohort 2 had a greater proportion of asymptomatic and mild/moderate disease categories than Cohort 1 (98% vs 80%, respectively); conversely, Cohort 1 had a near–10-fold higher proportion of severe disease than Cohort 2 (17% vs 1.8%). Cohort 2 comprised younger patients with a mean age of 13.7 years vs 17.3 years in Cohort 1. Older age was associated with a higher percentage of infection, with 63% of all confirmed cases found in participants aged 19 to 25 years in Cohort 1, compared with 38% of confirmed cases in Cohort 2. Age increase was also associated with greater disease severity by linear regression modeling ($P< 0.001$).
Conclusion: Coronavirus disease 2019 (COVID-19) disease severity in youth decreased over time in LA County during the first pandemic year, likely a reflection of changing demographics, with younger children infected. A higher infection rate in youth did not lead to higher disease severity over time.

Introduction

With increased testing availability, studies show that children aged 5 years or older have SARS-CoV-2 infection rates similar to those of adults (Grijalva *et al.*, 2020; Kim *et al.*, 2021; Lugon *et al.*, 2021; Smith *et al.*, 2021; Zimmermann and Curtis, 2020). Multiple studies suggest that individuals aged younger than 25 years are more likely to have asymptomatic SARS-CoV-2 infections or mild symptoms than older patients (Dawood *et al.*, 2022; Han *et al.*, 2021; Rosenberg *et al.*, 2020; Siebach *et al.*, 2021). Nevertheless, younger individuals still tend to shed SARS-CoV-2 with high viral loads in the upper respiratory tract that are comparable to or even higher than those reported in older adults (Somekh *et al.*, 2021). With the advent of new SARS-CoV-2 variants of concern (VOC), household transmission rates have increased with the introduction of more transmissible variants (Paul *et al.*, 2021). In one study, children aged 4 to 8 years and 9 to 13 years had increased odds of transmission, suggesting that children may play a larger role in SARS-CoV-2 transmission than older adolescents and adults (Stokes *et al.*, 2020).

* Corresponding author: Tawny Saleh, MD, Department of Pediatrics, Division of Infectious Diseases, David Geffen School of Medicine at UCLA, MDCC 22-340, 10833 LeConte Avenue, Los Angeles, CA 90095, USA.
E-mail address: tawnysaleh@mednet.ucla.edu (T. Saleh).

https://doi.org/10.1016/j.ijid.2022.06.040
1201-9712/

Los Angeles (LA) County is one of the largest and most socioeconomically diverse counties in the United States. It has more than 10 million residents, with youth (individuals aged < 25 years) comprising nearly one third of the population (US Census website). During the initial 6 months of the pandemic (March-September 2020), we conducted a prospective cohort study with case-control analyses in youth who received testing for SARS-CoV-2 at our academic institution in LA County (Newhouse *et al.*, 2021). In this study, patterns of COVID-19 symptoms varied significantly by age group, with number of symptoms correlating significantly with age. Younger youth, who were students, were less likely to have positive results when compared with older youth, who were employed. In addition, cases were more likely to be from non-English-speaking households, zip codes with a higher proportion of Hispanic individuals, and residents living below the poverty line (Newhouse *et al.*, 2021).

During the second half of the first year of the pandemic (October 2020-March 2021), LA County had a surge and reported the highest number of cases and deaths in all age groups in California, with 1,185,457 cases and 20,987 deaths (COVID19 Dashboard, 2022). In addition, novel SARS-CoV-2 variants became more predominant, including Alpha, Beta, and Gamma (Abdel Latif *et al.*, 2021). By the end of the first year of the pandemic, the Delta variant was detected and started to increase in LA County. The presence of novel variants raised concerns for increased infectivity and virulence.

The purpose of this cohort study was to characterize the evolution of SARS-CoV-2 infection in LA County youth followed at our institution during the first year of the pandemic, comparing youth from the first 6 months and the second 6 months. There is an urgent need to collect more information on the immediate clinical repercussions of COVID-19 infection in youth and how the disease has evolved during the pandemic. A better understanding of how the disease presents over time in younger populations has important implications, given the development of VOC and the changing nature of the SARS-CoV-2 virus.

Methods

Population, Setting, and Data Collection

From March 13, 2020, until March 31, 2021, we conducted a cohort study of youth aged less than 25 years who tested positive for SARS-CoV-2 infection at our institution, which comprises a large academic medical center (Ronald Reagan Medical Center and Mattel Children's Hospital at UCLA), a community hospital (UCLA Santa Monica Hospital), and a widespread network of UCLA-affiliated clinics throughout LA County. Our primary outcomes of interest were disease severity and age distribution of illness in children and youth with a positive reverse-transcriptase polymerase chain reaction (RT-PCR) over time. All participants were tested for SARS-COV-2 through RT-PCR assays. Each participant was only counted once in the cohort, even if more than one PCR test was performed. If a participant had multiple positive and negative results, the first positive recorded result was used. Confirmed cases of COVID-19 were defined as any positive RT-PCR result. Cohort 1 youth who tested positive for COVID-19 through RT-PCR in the initial 6 months of the pandemic, from March to September 30, 2020 (Newhouse *et al.*, 2021), were compared with Cohort 2 youth of the same age who tested positive for COVID-19 in the second half of the initial year of the pandemic, from October 2020 to March 2021. This period coincided with a surge in SARS-CoV-2 cases in LA County in December 2020. Data abstracted from electronic medical records included demographics, zip code, clinical findings, and disease severity. All youth were classified as having asymptomatic, mild, moderate, severe, or critical COVID-19 according to the National Institutes of Health's Coronavirus Disease (COVID-19) Treatment Guidelines (COVID-19 Treatment Guidelines Panel, 2021). Study activities were approved by the UCLA Institutional Review Board (IRB).

Youth with a clinical diagnosis of multisystem inflammatory syndrome in children (MIS-C) were also evaluated and described separately (Centers for Disease Control and Prevention, 2021). Children with a MIS-C clinical diagnosis had either a positive RT-PCR or SARS-CoV-2 antibody test (without vaccination) or exposure to a person with suspected or confirmed COVID-19 within 4 weeks before the onset of symptoms (Centers for Disease Control and Prevention, 2021). All children with MIS-C had an RT-PCR and a serologic assay for SARS-CoV-2 performed.

Laboratory Testing

The UCLA Clinical Microbiology Laboratory performed all SARS-CoV-2 RT-PCR testing. Cycle threshold (Ct) values were analyzed for all positive RT-PCR tests; positive RT-PCR was defined as a Ct value < 40. For each patient with a positive result RT-PCR, the assay used and Ct values for each target were recorded. This method was previously described (Newhouse *et al.*, 2021). In children with MIS-C, serologic testing for anti-SARS-CoV-2 immunoglobulin G (IgG) and immunoglobulin M (IgM) was also performed. Sera were analyzed by enzyme-linked immunosorbent assay to detect the spike receptor-binding domain with IgG and IgM as previously described (Newhouse *et al.*, 2021).

Data Analysis

A descriptive analysis was performed of the demographics of all patients aged more than 25 years who had RT-PCR test results in our health system. To describe the total population of youth who received testing at UCLA, we conducted a chi-square test to compare basic demographic information among youth who tested positive for SARS-CoV-2 at our institution during the first and second waves of the pandemic. Disease severity was transformed into a numeric scale to examine severity as a continuous variable between cohorts, defined as Asymptomatic=1, Mild/Moderate=2, Severe/Critical=3, and Death=4. Individuals with no clinical data available in the medical records to generate a disease severity category or individuals tested outside of our institution were excluded from further analysis. Linear regression and correlation coefficients estimated the severity of symptoms by change in age, and βs between the regression lines for cases and controls were analyzed using a *t*-test.

For each zip code in LA County, we tabulated the proportion of residents of each race/ethnicity based on the most recent US census (Farris, 2020). Subsequently, we tallied the race/ethnicity of the highest proportion of the residents (hereafter "predominant ethnicity"). For each zip code, we calculated the total number of study participants tested for SARS-CoV-2 at UCLA during the first two periods of the pandemic, in addition to the number of tests that were positive. From these data, we calculated the mean positivity rate for all zip codes in each cohort. We subsequently classified each zip code as having above or below average positivity. The purpose of this analysis was that by leveraging these variables, we aimed to determine the number of zip codes with predominantly Hispanic or predominantly White residents with above average SARS-CoV-2 positivity rates in both cohorts during the pandemic.

Determination of VOC in LA County

Using genomic data on SARS-CoV-2 from the GISAID initiative, we calculated the frequency of SARS-CoV-2 VOC, Variants of Interest, and common lineages by month from March 2020 to March 2021 (Abdel Latif *et al.*, 2021).

Table 1
Demographics, comorbidities, and disease severity in LA County youth during two pandemic periods.

CHARACTERISTICS	SARS-CoV-2 Positive (March-Sept 2020)		SARS-CoV-2 Positive (Oct 2020-March 2021)		P-value
	N=475		N=1149		
Sex	N	%	N	%	
Female	235	49.5%	559	48.7%	0.28
Male	239	50.3%	590	51.3%	
Not Specified	1	0.2%	0	0.0%	
Age group at testing					
<1	14	2.9%	43	3.7%	<0.001
1-5	49	10.3%	208	18.1%	
6-11	35	7.4%	177	15.4%	
12-18	78	16.4%	284	24.7%	
19-25	299	62.9%	437	38.0%	
Mean Age (SD)	17.3		13.7		<0.001
Race/ethnicity					
Asian	16	3.4%	42	3.7%	<0.001
Black/African American	29	6.1%	118	10.3%	
Hispanic/Latino	164	34.5%	600	52.2%	
White	133	28.0%	342	29.8%	
Other	35	7.4%	29	2.5%	
Unknown	98	20.6%	18	1.6%	
Type of Insurance					
None	30	6.3%	30	2.6%	<0.001
Medical/Safety Net	107	22.5%	308	26.8%	
HMO/Private	338	71.2%	811	70.6%	
Comorbidities					
Obesity (BMI> 98th percentile)	46	9.7%	149	13.0%	0.06
Pulmonary	61	12.8%	113	9.8%	0.07
Cardiac	17	3.6%	39	3.4%	0.85
Other	132	27.8%	330	28.7%	0.71
None	275	57.9%	813	70.8%	<0.001
Occupation (Patient)					
Working	89	18.7%	84	7.3%	<0.001
Student	250	52.6%	952	82.9%	
Disabled	1	0.2%	26	2.3%	
Other	20	4.2%	0	0.0%	
Unknown	115	24.2%	87	7.6%	
Severity					
Asymptomatic	89	18.7%	305	26.5%	<0.001
Mild/ Moderate	291	61.3%	821	71.5%	
Severe	79	16.6%	21	1.8%	
Death	1	0.2%	2	0.2%	
Unknown	15	3.2%	0	0.0%	

BMI: body mass index; HMO: health maintenance organization; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; SD: standard deviation.

Results

A total of 28,088 SARS-CoV-2 RT-PCR assays were performed in youth between March 13, 2020, to March 31, 2021 (Table 1 and Figure 1). A total of 1849 youth (7%) had positive PCR results during this period. This included 475 youth with positive results (4%) from 11,922 tested at the onset of the pandemic from March to September 2020 (Cohort 1) and 1374 youth with positive results (9%) from 16,166 tested from October 2020 to March 2021 (Cohort 2). Figure 1 depicts the overall number of youths tested and absolute cases over time. The number of youths who tested positive for SARS-CoV-2 was significantly higher (9% vs 4%, $p < 0.001$) in Cohort 2 than in Cohort 1, corresponding to the LA County's surveillance data (December 2020–February 2021 [COVID19Dashboard, 2022]). In Cohort 2, 225 youth had no clinical information available in the medical records and/or were tested at an outside facility, thus being excluded from further analysis. Data were analyzed for 1624 Cohort 2 youth.

Over time (Figure 2), there was a shift in the mean age of confirmed cases in the study population. In Cohort 1, the mean age was 17.3 years, whereas in Cohort 2, the mean age was 13.7 years (Table 1 $p<0.001$). In both periods, the older youth (19-25 years) represented the largest age group of all confirmed cases, with 63% in Cohort 1 and 38% in Cohort 2, respectively (Table 1). Nevertheless, during the second half of the first pandemic year, a higher proportion of younger youth tested positive than in the previous 6 months; this was especially notable in the group aged six to 11 years, in which positive results more than doubled, from 7.4% to 15.4% (Table 1 and Figure 2, $P<0.001$). In addition, a statistically significant higher proportion of Cohort 2 youth aged from 1-5 years, 10.3% vs 18.1%, and 12-18 years, 16.4% vs 24.7%, tested positive than did youth in Cohort 1 (Table 1 and Figure 2, $P<0.001$). A larger proportion of older youth (19-25 years) who tested positive in Cohort 1 were employed, especially as essential workers (older youth), than the youth in Cohort 2, in which most youth who tested positive were younger and students, with the proportion of working youth decreasing from 19% in the first cohort to 7% in the second cohort (Table 1, $p<0.001$).

Most of the children and youth who tested positive for SARS-CoV-2 had mild or asymptomatic illness, regardless of study period. When both time frames are compared, youth testing positive in Cohort 2 had a greater proportion (98.3%) of asymptomatic or mild/moderate illness than did those in Cohort 1 (80%) (Table 1, $p<0.001$). However, there was a 10-fold higher proportion of severe or critical illnesses in Cohort 1 than in Cohort 2, 16.6% vs 1.5% (Table 1, $p < 0.0001$). Using a linear regression model stratified for cohort, an increase in age was associated with the development of more severe disease. However, the first cohort saw a more drastic increase in disease severity with age ($B=0.03$, $p<0.001$, 95%CI 0.018, 0.035, $R=0.26$) than the second cohort ($B=0.004$,

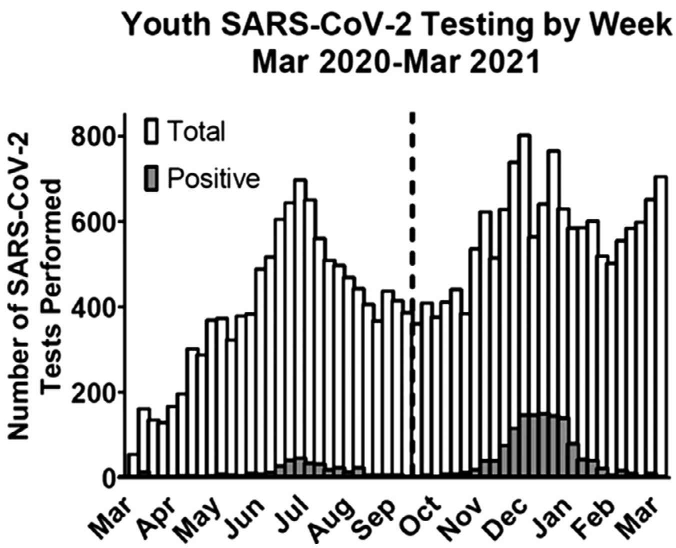

Figure 1. Increase in positivity over time during the first year of the pandemic, with the highest number of youth who tested positive identified during the pandemic surge in LA County (November 2020 to February 2021). From March 2020 to March 2021, 26,239 SARS-CoV-2 RT-PCR assays were performed in 28,088 patients aged less than 25 years, with 7% positive results. At the onset of the pandemic (March-September 2020), 4% of youth tested received a positive result (Cohort 1), and 9% of youth tested received a positive result between October 2020 and March 2021 (Cohort 2).

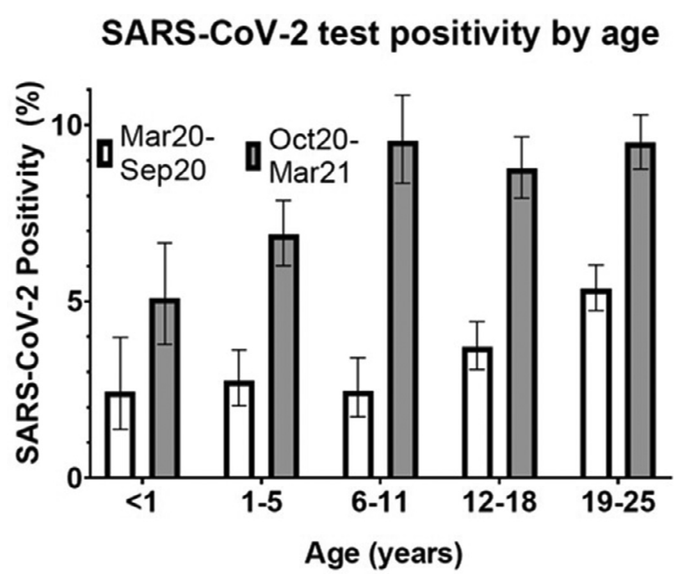

Figure 2. SARS-CoV-2 positivity by age among the two different waves. In the second period of the pandemic, there is more representation of younger-aged youth.

95% CI 0.002, p=0.01, R=0.08), R correlation comparison (p<0.004) (Figure 3 and Table 1). In total, three youth died because of COVID-19, with an overall case fatality of 0.18%. This included a boy aged 16 years with comorbidities and MIS-C in Cohort 1 (case fatality 0.21%) and two older youth (aged 19 and 23 years) with COVID-19 pneumonia (case fatality 0.17%). One youth was previously healthy, and the other had underlying comorbidities.

Race/ethnicity was available for 1508 youth with SARS-CoV-2 during the study period. Compared with other ethnic groups, Hispanic youth made up the largest group testing positive for SARS-CoV-2. There was a significant increase in the percentage of Hispanic youth who tested positive in Cohort 2 compared with Cohort 1, increasing from 34.5% to 52.2% (Table 1, p<0.001). The proportion of Black/African individuals with SARS-CoV-2 also increased in Cohort 2 compared with Cohort 1, from 6.1% to 10.3% (Table 1, p<0.0001). The proportion of patients with White and Asian ethnicity remained relatively the same throughout both periods (Table 1), although zip code-specific analysis showed an increase in White youth in areas with above average SARS-CoV-2 positivity (Figure 4C).

Zip codes with a higher proportion of Hispanic residents and/or residents living below the poverty line had a higher number of SARS-CoV-2 cases during both study periods (Figure 4, panels A and B). In Cohort 2, there were more areas of LA County impacted with a greater spread of SARS-CoV-2 infection in youth across the county, with the inclusion of more affluent neighborhoods (Figure 4, panels A and B). In Cohort 2, a greater number of White youth than Hispanic youth tested positive within their respective zip codes (Figure 4, panel C), which reflects a broader socioeconomic and ethnic distribution of infected youth in the second half of the first pandemic year. In addition, there was a higher proportion of patients with Medical/Safety net insurance in Cohort 2 than in Cohort 1, 26.8% vs 22.5%, respectively (Table 1, $P<0.001$). The proportion of insured and uninsured youth testing positive for SARS-CoV-2 during the two periods did not differ enough to achieve statistical significance.

From October 2020 to March 2021, several SARS-CoV-2 VOC emerged over time (Figure 5). In the first two months of the second half of the first year of the pandemic, the most common strain circulating in LA County was the Epsilon variant (B.1.247 and B.1.249). As the surge continued, other predominant variants, including the Alpha variant (B.1.1.7), started emerging. By the end of the study period, the Delta variant (B.1.617 and its derivative lineages) had begun to emerge (Abdel Latif *et al.*, 2021).

A total of 11 cases of MIS-C were identified over the study period in 1624 youth (0.68%). In Cohort 1, there were three patients with MIS-C with an average age of 12.5 years, with two boys affected. Two of the children were healthy, whereas the third youth had a chronic medical condition that required immune suppression. This patient died after a complicated hospital course. In Cohort 2, there were eight patients with MIS-C with an average age of 8.62 years, 62.5% male sex, and mainly Hispanic/Latinx ethnicity (75%). Two of the eight patients had underlying medical disorders with a predisposition to severe SARS-CoV-2 infection, but in Cohort 2, all children with MIS-C survived.

Discussion

During the first year of the COVID-19 pandemic in LA County, there was a change in age distribution, demographics, and clinical presentation of disease between the first and second six months of the initial year of the pandemic. In the first half of the year, most youth tested at our health system were older, aged between 19 and 25 years, with a higher positivity rate observed in this age range, consistent with trends in the distribution of COVID-19 at the time (Centers for Disease Control and Prevention [CDC], 2022). However, in the second 6 months, the proportion of children and youth aged younger than 15 years who tested positive for SARS-CoV-2 nearly doubled.

Many factors may have contributed to the higher number of children and younger youth testing positive in LA County in the second half of the pandemic, such as lockdown restrictions set in the first half of the pandemic being removed; children returning to school and other social activities; and possibly the emergence of SARS-CoV-2 VOC with greater infectivity leading to potentially higher infections in younger children. As may be surmised, differential infectivity of pediatric age groups has important implications for infection prevention within households and in schools/child care to minimize risk of household secondary transmission. In a

Correlation coefficient of disease severity by age in each cohort

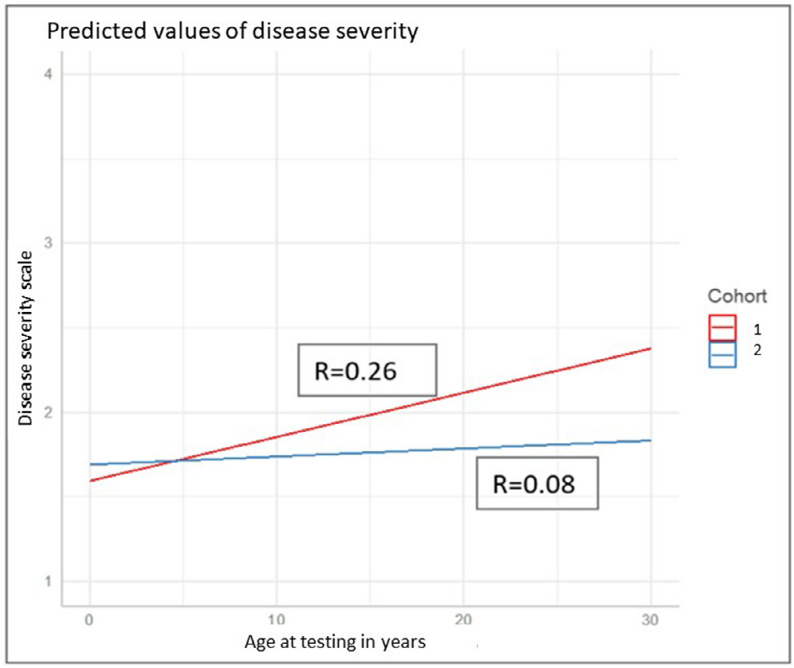

Figure 3. In an analysis of correlation coefficients of disease severity and age, increase in age was associated with development of more severe disease. Severity was transformed into a numeric scale to examine severity as a continuous variable between cohorts, defined as Asymptomatic=1, Mild/Moderate=2, Severe/Critical=3, Death=4. The first cohort saw a more drastic increase in severity with age (R=0.26, 95%CI 0.018, 0.035) than the second cohort (R=0.08, 95% CI 0.002, 0.008). R correlation comparison (p<=0.004).

study among children and adolescents from the Modena province of Italy, of those participants who underwent nasal SARS-CoV2 PCR testing, 84.2% reported close contact with a cohabiting relative with infection, and 45.3% were symptomatic (Paduano *et al.*, 2021). Furthermore, children and adults have been demonstrated to have similar incidence rates of SARS-CoV-2 infection (Dawood *et al.*, 2022), which underscores the need for a rapid evaluation of vaccine efficacy and safety in children to expand vaccine indications to younger age groups.

Although one would expect that more severe cases would be noted with a higher number of infections in Cohort 2, during the pandemic surge, cases of COVID-19 in youth tended to be milder and often asymptomatic. As such, the proportion of severe/critical cases in youth diminished significantly, likely owing to the age shift to younger age groups during the second period of the initial year of the pandemic. This finding was corroborated by our linear regression model, which demonstrated an increase in age was associated with development of more severe disease; this was particularly striking in Cohort 1 early in the pandemic. Our results likely reflect a larger representation of younger children in the second half of the first year of the pandemic, which is consistent with previous studies showing that youth tend to have milder symptoms or be asymptomatic (Bailey *et al.*, 2021; Choi *et al.*, 2020; Dawood *et al.*, 2022; Kim *et al.*, 2020; Lazzerini *et al.*, 2021). Even though a rare complication of COVID-19, cases of MIS-C typically peak several weeks after COVID-19 surges in the community. Not surprisingly, during the surge period in the second half of the year, we noted a higher number of MIS-C cases in Cohort 2. MIS-C cases were, nevertheless, exceedingly rare (0.68% cases in the entire cohort).

Although severe cases of COVID-19 can occur in children, adolescents, and young adults, most cases in younger age groups appear to be milder infections than those in adults aged 25 years or older (Liguoro *et al.*, 2020; Mehta *et al.*, 2020; Stokes *et al.*, 2020). In a systematic review of 18 studies evaluating symptoms and signs of COVID-19 in children and youth aged less than 20 years with documented infection, the proportion of asymptomatic infections ranged from 15 to 42% (Viner *et al.*, 2020). Consequently, symptoms in children may often go unrecognized before a laboratory diagnosis is made (Han *et al.*, 2021). With universal testing for SARS-CoV-2 upon admission to most hospitals, the rates of hospitalization for SARS-CoV-2 in children can be overestimated if hospitalizations for COVID-19-related illness are not differentiated from hospitalizations caused by situations in which incidental detection of SARS-CoV-2 occurs (Webb and Osburn, 2021; Woodruff *et al.*, 2021). In CDC surveillance studies of COVID-19 in the United States, the presence of underlying medical conditions has been associated with higher rates of hospitalization among youth with comorbidities (15 to 22%) than among youth without these findings (2 to 4%). Whether underlying conditions are associated with increased severity or only a lower threshold for admission owing to concerns for complications is not known (Centers for Disease Control and Prevention [CDC], 2022; Kim *et al.*, 2020; Webb and Osburn, 2021; Woodruff *et al.*, 2021).

Children from underrepresented racial and ethnic groups have been disproportionately affected by higher rates of SARS-CoV-2 infection (Newhouse *et al.*, 2021; Van Dyke *et al.*, 2021). In one study of LA County urban children and youth aged less than 18 years, from June to December 2020, children were found to play an important role as index cases. Secondary attack rates were disproportionately impacted by household income (Tanaka *et al.*, 2021). Furthermore, in a large US pediatric cohort study, children of Black, Hispanic, and/or Asian race/ethnicities had lower rates of testing than did White children but were significantly more likely to have positive test results (Bailey *et al.*, 2021). In our analysis, Hispanic youth made up the largest ethnic group to test positive during

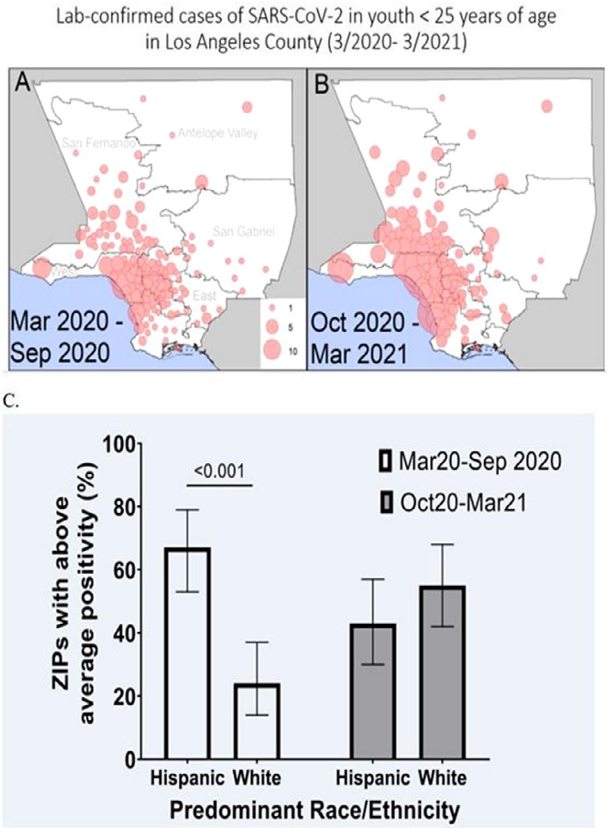

Figure 4. 4A and 4B: Comparison of Zip codes of youth infected by SARS-CoV-2 in two periods in the first year of the LA County pandemic. With the second wave, there is a greater spread and distribution to multiple neighborhoods in the county. 4C: When comparing the two periods of the pandemic, there is a greater percentage of positivity among Whites by zip code analysis in the second period.

the first year of the pandemic in LA County. However, with geographic epidemic modeling, when comparing both Cohorts 1 and 2, we noted an increase in the number of infections in youth from many ethnic groups and all socioeconomic classes, likely reflecting the impact of the pandemic surge during that period.

To the best of our knowledge, our cohort study is the first to characterize the evolution of SARS-CoV-2 infection in LA County youth followed at our institution during the pandemic. The study has several strengths, including a large sample size of ethnically and socioeconomically diverse youth with RT-PCR–confirmed SARS-CoV-2 infection. We were able to report on youth identified during different periods of the pandemic, with sufficient data to characterize COVID-19 outcomes in this studied population, demonstrating an association between age and risk of disease severity even among young individuals.

Although our patients came from socioeconomically diverse areas of LA County, having been recruited from a vast network of clinical centers and two hospitals, one study limitation is that our data come from a single institution. As a tertiary medical center, we have a pediatric patient population that tends to be more medically complex than the general population. Another study limitation is that 225 youth in Cohort 2 (14% of participants who tested positive during that period) were excluded from our analysis for lack of clinical data and/or because of testing performed at an outside institution, thus not meeting the eligibility criteria for study inclusion. During the study period, antigen testing for SARS-CoV-2 was not performed at our institution, and only RT-PCR results were evaluated. It is likely that these individuals were asymptomatic, given the lack of additional clinical information; however, we are unable to confirm this assumption. Our analysis predates the evaluation of the impact of vaccine administration to youth because patients in this age group began to be immunized in April 2021, which is after our study period ended. Therefore, we cannot extrapolate our study findings to populations exposed to COVID-19 vaccines.

In summary, we characterized the SARS-CoV-2 infection in youth during the first year of the pandemic, including a winter surge period in LA County. An increased proportion of younger children became infected with SARS-CoV2 virus as the pandemic unfolded. Interestingly, although the number of cases of COVID-19 in youth increased 2.4-fold during the 2020-2021 winter surge, and one would expect to see a higher number of sicker youths, a significant reduction in disease severity was noted during this period. This reflects higher infection rates in younger age groups. Future analysis of disease presentation in youth during subsequent COVID-19 pandemic periods should determine if this disease pattern continued to prevail with the availability of vaccines to this population.

Ethical approval

The study was reviewed and approved by the UCLA Institutional Review Board.

Declaration of Competing Interest

The authors have no competing interests to declare.

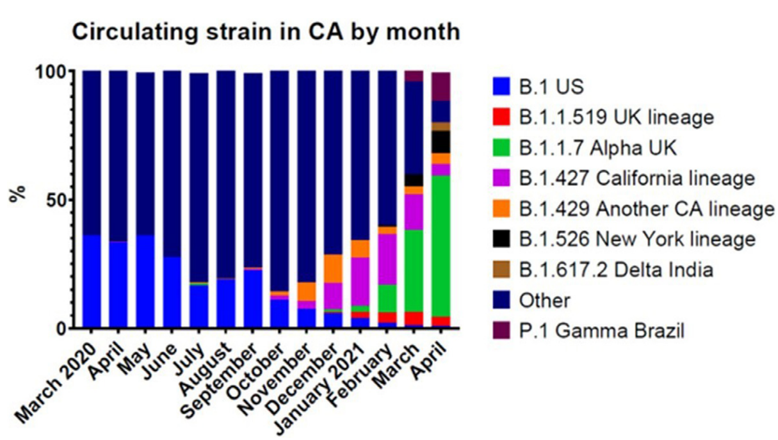

Figure 5. Different variants circulating by month in LA County from March 2020 to March 2021.

Funding

MC received funding from the T32 Post-Doctoral Training Program Grant (T32MH080634, PIs Currier and Gorbach). TF, TK, and KN-S received support from the National Institutes of Health/National Institute of Allergy and Infectious Diseases (AI140718, PI Nielsen). KN-S received support from the UCLA W. M. Keck Foundation COVID 19 Research Award Program (PI Nielsen) and the Simons Foundation Autism Research Initiative (SFARI) 866410 (PI Nielsen).

References

Abdel Latif A, Mullen JL, Alkuzweny M, Tsueng G, Cano M, Haag E, Zhou J, Zeller M, Hufbauer E, Matteson N, Wu C, Andersen KG, Su AI, Gangavarapu K, Hughes LD, California, United States Mutation Report. https://outbreak.info/location-reports?loc=USA_US-CA, 2021 (accessed June 29 2021).

Bailey LC, Razzaghi H, Burrows EK, Bunnell HT, Camacho PEF, Christakis DA, Eckrich D, Kitzmiller M, Lin SM, Magnusen BC, Newland J, Pajor NM, Ranade D, Rao S, Sofela O, Zahner J, Bruno C, Forrest CB. Assessment of 135 794 pediatric patients tested for severe acute respiratory syndrome coronavirus 2 across the United States. JAMA Pediatr 2021;175:176–84.

Centers for Disease Control and Prevention (U.S.). COVID data tracker. Demographic trends of COVID-19 cases and deaths in the US reported to the CDC, www.cdc.gov/covid-data-tracker/index.html#demographics, (accessed 5 January 2022).

Centers for Disease Control and Prevention, Partner updates: case definition for MISC. https://www.cdc.gov/mis-c/hcp/, 2021 (accessed 20 December 2021).

Choi SH, Kim HW, Kang JM, Kim DH, Cho EY. Epidemiology and clinical features of coronavirus disease 2019 in children. Clin Exp Pediatr 2020;63:125–32.

Dawood FS, Porucznik CA, Veguilla V, Stanford JB, Duque J, Rolfes MA, Dixon A, Thind P, Hacker E, Castro MJE, Jeddy Z, Daugherty M, Altunkaynak K, Hunt DR, Kattel U, Meece J, Stockwell MS. Incidence rates, household infection risk, and clinical characteristics of SARS-CoV-2 infection among children and adults in Utah and New York City, New York. JAMA Pediatr 2022;176:59–67.

Grijalva CG, Rolfes MA, Zhu Y, McLean HQ, Hanson KE, Belongia EA, Halasa NB, Kim A, Reed C, Fry AM, Talbot HK. Transmission of SARS-COV-2 infections in households - Tennessee and Wisconsin, April–September 2020. MMWR Morb Mortal Wkly Rep 2020;69:1631–4.

Han MS, Choi EH, Chang SH, Jin BL, Lee EJ, Kim BN, Kim MK, Doo K, Seo JH, Kim YJ, Kim YJ, Park JY, Suh SB, Lee H, Cho EY, Kim DH, Kim JM, Kim HY, Park SE, Lee JK, Jo DS, Cho SM, Choi JH, Jo KJ, Choe YJ, Kim KH, Kim JH. Clinical characteristics and viral RNA detection in children with coronavirus disease 2019 in the Republic of Korea. JAMA Pediatr 2021;175:73–80.

Kim J, Choe YJ, Lee J, Park YJ, Park O, Han MS, Kim JH, Choi EH. Role of children in household transmission of COVID-19. Arch Dis Child 2021;106:709–11.

Kim L, Whitaker M, O'Halloran A, Kambhampati A, Chai SJ, Reingold A, Armistead I, Kawasaki B, Meek J, Yousey-Hindes K, Anderson EJ, Openo KP, Weigel A, Ryan P, Monroe ML, Fox K, Kim S, Lynfield R, Bye E, Shrum Davis S, Smelser C, Barney G, Spina NL, Bennett NM, Felsen CB, Billing LM, Shiltz J, Sutton M, West N, Talbot HK, Schaffner W, Risk I, Price A, Brammer L, Fry AM, Hall AJ, Langley GE, Garg S. COVID-NET Surveillance Team. Hospitalization rates and characteristics of children aged <18 years hospitalized with laboratory-confirmed COVID-19 - COVID-NET, 14 states, March 1–July 25, 2020. MMWR Morb Mortal Wkly Rep 2020;69:1081–8. COVID19 Dashboard http://dashboard.publichealth.lacounty.gov/. accessed 31 January 2022.

Lazzerini M, Sforzi I, Trapani S, Biban P, Silvagni D, Villa G, Tibaldi J, Bertacca L, Felici E, Perricone G, Parrino R, Gioè C, Lega S, Conte M, Marchetti F, Magista A, Berlese P, Martelossi S, Vaienti F, Valletta E, Mauro M, Dall'Amico R, Fasoli S, Gatto A, Chiaretti A, Dragovic D, Pascolo P, Pilotto C, Liguoro I, Miorin E, Saretta F, Trobia GL, Di Stefano A, Orlandi A, Cardinale F, Lubrano R, Testa A, Binotti M, Moressa V, Barbi E, Armocida B, Mariani I. COVID-19 Italian Pediatric Study Network. Characteristics and risk factors for SARS-CoV-2 in children tested in the early phase of the pandemic: a cross-sectional study, Italy, 23 February to 24 May 2020. Euro Surveill 2021;26.

Liguoro I, Pilotto C, Bonanni M, Ferrari ME, Pusiol A, Nocerino A, Vidal E, Cogo P. SARS-COV-2 infection in children and newborns: a systematic review. Eur J Pediatr 2020;179:1029–46.

Lugon P, Fuller T, Damasceno L, Calvet G, Resende PC, Matos AR, Machado Fumian T, Malta FC, Salgado AD, Fernandes FCM, Abreu de Carvalho LM, Guaraldo L, Bastos L, Cruz OG, Whitworth J, Smith C, Nielsen-Saines K, Siqueira M, Carvalho MS, Brasil P. SARS-CoV-2 infection dynamics in children and household contacts in a slum in Rio de Janeiro. Pediatrics 2021;148.

Mehta NS, Mytton OT, Mullins EWS, Fowler TA, Falconer CL, Murphy OB, Langenberg C, Jayatunga WJP, Eddy DH, Nguyen-Van-Tam JS. SARS-CoV-2 (COVID-19): what do we know about children? A systematic review. Clin Infect Dis 2020;71:2469–79.

Newhouse CN, Saleh T, Fuller T, Kerin T, Cambou MC, Swayze EJ, Le C, Seo W, Trejo M, Garner OB, Chandrasekaran S, Nielsen-Saines K. Predictors of SARS–CoV-2 infection in youth at a Large, Urban Healthcare Center in California, March-September 2020. Front Pediatr 2021;9.

Paduano S, Facchini MC, Greco A, Borsari L, Mingrone VM, Tancredi S, Fioretti E, Creola G, Iacuzio L, Casaletti G, Vinceti M, Bargellini A, Filippini T. Characteristics and risk factors of isolated and quarantined children and adolescents during the first wave of SARS-CoV-2 pandemic: A cross-sectional study in Modena, Northern Italy. Acta Biomed 2021;92.

Paul LA, Daneman N, Schwartz KL, Science M, Brown KA, Whelan M, Chan E, Buchan SA. Association of Age and Pediatric Household Transmission of SARS–CoV-2 Infection. JAMA Pediatrics 2021;175:1151–8.

Rosenberg ES, Dufort EM, Blog DS, Hall EW, Hoefer D, Backenson BP, Muse AT, Kirkwood JN, St George K, Holtgrave DR, Hutton BJ, Zucker HA. COVID-19 Testing, Epidemic Features, Hospital Outcomes, and Household Prevalence, New York State-March 2020. Clinical Infectious Diseases 2020;71:1953–9.

Farris D. PolicyMap. J Med Libr Assoc 2020;108:158–60.

Siebach MK, Piedimonte G, Ley SH. COVID-19 in childhood: transmission, clinical presentation, complications and risk factors. Pediatr Pulmonol 2021;56:1342–56.

Smith BK, Janowski AB, Danis JE, Harvey IB, Zhao H, Dai YN, Farnsworth CW, Gronowski AM, Roper S, Fremont DH, Wang D. Seroprevalence of SARS–CoV-2 antibodies in children and adults in St. Louis, Missouri, USA. mSphere 2021;6:e01207–20.

Somekh I, Sharabi A, Dory Y, Simões EAF, Somekh E. Intrafamilial spread and altered symptomatology of SARS-CoV-2, during predominant circulation of lineage B.1.1.7 variant in Israel. Pediatr Infect Dis J 2021;40:e310–11.

Stokes EK, Zambrano LD, Anderson KN, Marder EP, Raz KM, El Burai Felix S, Tie Y, Fullerton KE. Coronavirus disease 2019 case surveillance - United States, January 22–May 30, 2020. MMWR Morb Mortal Wkly Rep 2020;69:759–765.

Tanaka ML, Marentes Ruiz CJ, Malhotra S, Turner L, Peralta A, Lee Y, Jumarang J, Perez SE, Navarro J, Dien Bard J, Gordon A, Allen EK, Thomas PG, Pannaraj PS. SARS-CoV-2 transmission dynamics in households with children, Los Angeles, California. Front Pediatr 2021;9.

Van Dyke ME, Mendoza MCB, Li W, Parker EM, Belay B, Davis EM, Quint JJ, Penman-Aguilar A, Clarke KEN. Racial and ethnic disparities in COVID-19 incidence by age, sex, and period among persons aged <25 years - 16 U.S. Jurisdictions, January 1–December 31, 2020. MMWR Morb Mortal Wkly Rep 2021;70:382–388.

Viner RM, Ward JL, Hudson LD, Ashe M, Patel SV, Hargreaves D, Whittaker E. Systematic review of reviews of symptoms and signs of COVID-19 in children and adolescents. Arch Dis Child 2020;0:1–6.

Webb NE, Osburn TS. Characteristics of hospitalized children positive for SARS–CoV-2: experience of a large center. Hosp Pediatr 2021;11:e133–41.

Woodruff RC, Campbell AP, Taylor CA, Chai SJ, Kawasaki B, Meek J, Anderson EJ, Weigel A, Monroe ML, Reeg L, Bye E, Sosin DM, Muse A, Bennett NM, Billing LM, Sutton M, Talbot HK, McCaffrey K, Pham H, Patel K, Whitaker M, McMorrow M, Havers F. COVID-NET surveillance team. Risk factors for severe COVID-19 in children. Pediatrics 2021;149.

Zimmermann P, Curtis N. Coronavirus infections in children including COVID-19: an overview of the epidemiology, clinical features, diagnosis, treatment and prevention options in children. Pediatr Infect Dis J 2020;39:355–68.