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SHORT COMMUNICATION

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Clinical presentations of adult and pediatric SARS-CoV-2-positive cases in a community cohort, Nashville, Tennessee

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Abstract

Compared to adults, the prevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) illness in children has been lower and less severe. However, reports comparing SARS-CoV-2 infection among children and adults are limited. As part of our longitudinal cohort study of adults and children with SARS-CoV-2 infection and their household contacts in Nashville, Tennessee, we compared the clinical characteristics and outcomes of SARS-CoV-2 infections between children and adults. Children were more likely to be asymptomatically infected and had a shorter illness duration compared to adults. The differences observed in clinical presentation across ages may inform symptom-specific testing, screening, and management algorithms.

KEYWORDS
COVID-19 in adults, pediatric COVID-19, SARS-CoV-2-positive adults, SARS-CoV-2-positive children

1 | INTRODUCTION

Symptoms of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19), range from asymptomatic detection to severe illness, with varying presentations by age.[1] Before the emergence of B.1.1.529 (Omicron) variant, more than 39 million children and adults had been diagnosed with COVID-19 in the United States.[2] Early studies suggested that children may have lower rates of symptomatic infection and hospitalization, as well as less effective transmission than adults.[3,4] Few studies feature direct comparisons between children and adults. Understanding the clinical spectrum across age groups may

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inform institutional and public health symptom-specific testing, screening, and management algorithms. We aimed to compare the clinical characteristics and outcomes between children and adults with SARS-CoV-2 infections in Nashville, Tennessee.

2 | METHODS

2.1 | Study design and population

We conducted a longitudinal community-cohort study, COPE (COVID-19, Outbreak, Pandemic, Exploration), among individuals who resided in Metropolitan Nashville, Tennessee, from March 20, 2020, to August 31, 2021. Individuals were eligible for enrollment if they or a household contact had test-positive or suspected SARS-CoV-2 infection. For this specific study, we limited to all individuals who had SARS-CoV-2 infection confirmed by detection of viral RNA in nasal specimens collected in an ambulatory or inpatient Vanderbilt University Medical Center (VUMC) affiliated testing location (i.e., emergency room, hospital, testing site, outpatient clinic) or another testing site (e.g., health department, local pharmacy, etc.). Informed consent and assent (children 7–17 years) were obtained by all individuals before enrollment. This study was approved by the Institutional Review Board at Vanderbilt University Medical Center (IRB #: 151683).

2.2 | Data collection

Trained research personnel conducted telephone interviews with enrolled individuals or parents/legal guardians to collect demographic information (age, sex, race, ethnicity, insurance), underlying medical conditions, illness history, testing location, and social histories using a standardized case report form.

Travel history was included if the person traveled outside of the Nashville area within 14 days before illness onset or enrollment date if the person was asymptomatic. Individuals were considered vaccinated for SARS-CoV-2 2 weeks after receiving two doses of BNT162b2 (Pfizer-BioNTech)[5] or mRNA-1273 (Moderna, Inc.),[6] or received one dose of Ad26.CoV2.S (Janssen/Johnson & Johnson)[7] when available to the respective age groups. Results from individual's SARS-CoV-2 clinical tests were reviewed and verified. A standardized medical chart review was conducted for hospitalized individuals to obtain information on clinical outcomes of interest (oxygen use, mechanical ventilation, length of hospital stay, length of intensive care unit stay, and death).

2.3 | Specimen collection and testing

Research respiratory (anterior nasal swabs) and blood specimens were obtained by research personnel or clinical staff at multiple time points throughout the study (e.g., within 3–6 weeks and 3 months after enrollment). Respiratory specimens were stored in viral transport medium. Respiratory and blood specimens were transported to a VUMC research laboratory for storage and testing. We conducted testing for SARS-CoV-2 by detecting viral RNA in nasal specimens using reverse-transcription quantitative polymerase chain reaction (RT-qPCR)[8] and by detection of serum IgG to the SARS-CoV-2 spike and nucleocapsid proteins using enzyme-linked immunosorbent assay (ELISA).[9] Those with negative RT-qPCR results, but a positive ELISA within 4–6 weeks of symptom onset and no history of vaccination, were classified as SARS-CoV-2 positive. All data and laboratory results were maintained in a secure REDCap™ (Research Electronic Data Capture, Vanderbilt University) database.[10]

2.4 | Statistical analysis

Analyses were restricted to individuals with SARS-CoV-2 infection. Descriptive statistics were summarized as absolute and relative frequency for categorical variables and mean (standard deviation) or median (interquartile range), where applicable. Demographic and clinical characteristics between children (<18 years) and adults (≥18 years) were evaluated using two-sample t-test with unequal variances for continuous variables and Pearson χ^2 test for categorical variables. Statistical significance determined to be achieved at a nominal level of $\alpha = 0.05$ (two-tailed, where appropriate). All analyses were conducted using statistical software StataIC 16.0 (StataCorp LLC).

3 | RESULTS

From March 20, 2020, to August 31, 2021, 853 individuals (children: 256 [30%]; adults: 592 [70%]) from 396 households were enrolled, among whom 426 (children: 13%, adults: 87%) were SARS-CoV-2 positive (RT-qPCR = 398 [93%], serology = 28 [7%], Supplemental Information: Figure 1). The mean age was 12 and 42 years in children and adults, respectively. Participants were most frequently female, white, non-Hispanic, had private health insurance, and resided in Davidson County (Table 1). Overall, 35% of individuals reported having an underlying medical condition, with cardiovascular conditions most frequent among adults (17%) and respiratory among children (14%). Twenty individuals (4 children; 16 adults) were SARS-CoV-2-positive after vaccines were available to the public, and 10 of these (50% [3 children; 7 adults]) were fully vaccinated at the time of infection and detection via RT-qPCR.

3.1 | Clinical presentations in adults compared to children

Compared to adults, children were more likely to be asymptomatically infected with SARS-CoV-2 (children: 16% vs. adults: 5%; $p = 0.001$; Table 2). In symptomatic individuals, adults were more

TABLE 1 Sociodemographic characteristics of SARS-CoV-2 positive adults and pediatric patients

Characteristics	Entire cohort (*N* = 426) *n* (%)	Adults (*N* = 369) *n* (%)	Pediatrics (*N* = 57) *n* (%)	*p* Value
Age, years—mean (SD)	37.6 (16.5)	41.7 (13.8)	11.5 (4.9)	–
Age, years—median (IQR)	38.2 (25.5-48.5)	41.0 (31.1-50.0)	12.3 (8.0-15.2)	
Sex, female—*n* (%)	231 (54.2)	198 (53.7)	33 (57.9)	0.550
Race and ethnicity—*n* (%)				
White, non-Hispanic	338 (79.3)	302 (81.8)	36 (63.2)	**<0.001**
Other, non-Hispanic	42 (9.9)	28 (7.6)	14 (24.6)	
Hispanic	46 (10.8)	39 (10.6)	7 (12.3)	
Insurance type—*n* (%)				
Public	27 (6.3)	17 (4.6)	10 (17.5)	**0.003**
Private	351 (82.4)	309 (83.7)	42 (73.7)	
Both, public and private	15 (3.5)	13 (3.5)	2 (3.5)	
None/self-pay	33 (7.8)	30 (8.1)	3 (5.3)	
Travel history ≤ 14 days—*n* (%)				
None	367 (86.2)	320 (86.7)	47 (82.5)	0.257
International	7 (1.6)	7 (1.9)	0	
Domestic	52 (12.2)	42 (11.4)	10 (17.5)	
Smoke exposure—*n* (%)				
Self	30 (7.4)	30 (8.1)	–	–
Household member	33 (7.8)	28 (7.6)	5 (8.8)	0.756
Known close contact to COVID-positive case—*n* (%)	245 (57.7)	210 (57.1)	35 (61.4)	0.746
Underlying medical condition—*n* (%)				
≥1 underlying medical condition	148 (34.7)	132 (35.8)	16 (28.1)	0.256
Respiratory, including asthma	55 (12.9)	47 (12.7)	8 (14.0)	0.786
Cardiovascular	62 (14.6)	61 (16.5)	1 (1.8)	**0.003**
Neurological/neuromuscular	14 (3.3)	11 (3.0)	3 (5.3)	0.368
Hematological/oncological/immunosuppressive	15 (3.5)	12 (3.3)	3 (5.3)	0.443
Renal	2 (0.5)	2 (0.5)	0 (0.0)	0.577
Gastrointestinal/hepatic	15 (3.5)	12 (3.3)	3 (5.3)	0.443
Endocrine	28 (6.6)	25 (6.8)	3 (5.3)	0.668
Rheumatological/autoimmune	14 (3.3)	13 (3.5)	1 (1.8)	0.486
Other	11 (2.6)	11 (3.0)	0 (0.0)	0.187
Household size—mean (SD)	3.6 (1.5)	3.5 (1.5)	4.6 (1.2)	**<0.001**
Area of residence—*n* (%)				
Davidson county	282 (66.2)	252 (68.3)	30 (52.6)	**0.020**
Greater Nashville area	144 (33.8)	117 (31.7)	27 (47.4)	

Note: *p* Values were calculated using two-sample *t*-test with unequal variances for continuous and Pearson χ^2 test for categorical variables, with a level of $\alpha = 0.05$ (two-tailed, where appropriate).

TABLE 2 Illness characteristics of SARS-CoV-2 positive adults and pediatric patients

Illness characteristic	Total (*N* = 426) *n* (%)	Adults (*N* = 369) *n* (%)	Pediatrics (*N* = 57) *n* (%)	*p* Value
Asymptomatic	26 (6.1)	17 (4.6)	9 (15.8)	**0.001**
Symptoms	**Total (*n* = 400) *n* (%)**	**Adults (*n* = 352) *n* (%)**	**Pediatrics (*n* = 48) *n* (%)**	***p* Value**
Illness duration, days—mean (SD)	12.9 (11.7)	13.7 (12.0)	6.9 (6.4)	**<0.001**
Fever ≥ 100.4°F	166 (41.5)	143 (40.6)	23 (47.9)	0.408
Fever duration, days—mean (SD)	4.4 (4.1)	4.6 (4.3)	3.0 (3.0)	**0.044**
Feverish	245 (61.6)	215 (61.3)	30 (63.8)	0.868
Cough	277 (69.3)	250 (71.0)	27 (56.3)	**0.037**
Productive cough	101 (36.5)	92 (36.8)	9 (33.3)	0.722
Rhinorrhea	165 (41.3)	145 (41.2)	20 (41.7)	0.950
Nasal congestion	227 (56.8)	203 (57.7)	24 (50.0)	0.314
Sore throat	169 (42.3)	149 (42.3)	20 (41.7)	0.930
Chest tightness	169 (42.3)	155 (44.0)	14 (29.2)	0.050
Wheezing	79 (19.8)	75 (21.3)	4 (8.3)	**0.034**
Shortness of breath	168 (42.0)	159 (45.2)	9 (18.8)	**0.001**
Muscle aches	276 (69.0)	255 (72.4)	21 (43.8)	**<0.001**
Headache	295 (73.8)	266 (75.6)	29 (60.4)	**0.025**
Fatigue	349 (87.3)	306 (86.9)	43 (89.6)	0.605
Chills	226 (56.5)	205 (58.2)	21 (43.8)	0.058
Nausea	120 (30.0)	106 (30.1)	14 (29.2)	0.893
Abdominal pain	81 (20.3)	68 (19.3)	13 (27.1)	0.209
Diarrhea	169 (42.3)	158 (44.9)	11 (22.9)	**0.004**
Vomiting	33 (8.3)	28 (8.0)	5 (10.4)	0.569
Loss of appetite	233 (58.3)	211 (59.9)	22 (45.8)	0.063
Loss of taste	245 (61.3)	234 (66.5)	11 (22.9)	**<0.001**
Loss of smell	236 (59.2)	223 (63.5)	13 (27.1)	**<0.001**
Paresthesia	59 (14.8)	56 (16.0)	3 (6.3)	0.076
Eye pain/pressure	98 (24.5)	91 (25.9)	7 (14.6)	0.089
Skin sensitivity	52 (13.0)	48 (13.6)	4 (8.3)	0.305
Confusion	128 (32.1)	123 (35.0)	5 (10.4)	**0.001**
Conjunctivitis	17 (4.3)	13 (3.7)	4 (8.3)	0.135
Medical attention	**Total (*n* = 426) *n* (%)**	**Adults (*n* = 369) *n* (%)**	**Pediatrics (*n* = 57) *n* (%)**	***p* Value**
Testing facility	57 (12.4)	53 (13.3)	4 (7.0)	0.183
Telemedicine	15 (3.5)	14 (3.8)	1 (1.8)	0.437
Ambulatory care[a]	257 (60.3)	232 (62.9)	25 (43.9)	**0.006**
Emergency department	42 (9.9)	34 (9.2)	8 (14.0)	0.256
Inpatient	17 (4.0)	12 (3.3)	5 (8.8)	**0.048**
Prescribed/administered medications	**Total (*n* = 426) *n* (%)**	**Adults (*n* = 369) *n* (%)**	**Pediatrics (*n* = 57) *n* (%)**	***p* Value**
Antivirals	4 (0.9)	4 (1.0)	0 (0.0)	0.430
Antibiotics	49 (11.5)	44 (11.9)	5 (8.8)	0.488

(Continues)

TABLE 2 (Continued)

Prescribed/administered medications	Total ($n = 426$) n (%)	Adults ($n = 369$) n (%)	Pediatrics ($n = 57$) n (%)	p Value
Bronchodilators	31 (7.3)	30 (8.1)	1 (1.8)	0.085
Steroids	12 (2.8)	11 (3.0)	1 (1.8)	0.602

Note: p Values were calculated using two-sample t-test with unequal variances for continuous and Pearson χ^2 test for categorical variables, with a level of $\alpha = 0.05$ (two-tailed, where appropriate).

[a]Includes primary care providers and urgent cares.

likely to report cough (71% vs. 56%), wheezing (21% vs. 8%), shortness of breath (45% vs. 19%), loss of taste (67% vs. 23%), and loss of smell (64% vs. 27%) than symptomatic children, respectively ($p < 0.05$). The most common symptoms reported among symptomatic children included fatigue (90%), feeling feverish (64%), and headache (60%). While there was no statistical difference in the frequency of fever, children had a shorter duration of fever compared to adults (3 vs. 5 days, Table 2). Adults had a statistically significant longer mean illness duration than children (14 vs. 7 days). Overall, 17/352 (5%) adults and 1/48 (2%) children reported persistence of at least one symptom for 4 weeks or longer, suggestive of "long COVID."[11]

3.2 | Clinical outcomes

Overall, 388 (91%) individuals with SARS-CoV-2 sought medical attention for their illness, with the majority receiving care in an ambulatory setting. Nine percent (42/426; children = 8 and adults = 34) reported an emergency room visit and 4% (17/426; children = 5/57 and adults = 12/369) reported being hospitalized for their illness (Table 2). All of these individuals except for one child were hospitalized for SARS-CoV-2 before vaccine availability. Among the 17 individuals hospitalized, 14 (82%) reported an underlying medical condition, with respiratory and cardiovascular conditions being the most common among children (60% [3/5]) and adults (58% [7/12]), respectively.

Of the five children hospitalized in our cohort with SARS-CoV-2 infection, the mean length of stay was 2 days and 20% (1/5) received oxygen supplementation. None of the children were admitted to the intensive care unit, required mechanical ventilation, or died. The child who was vaccinated for SARS-CoV-2 at the time of hospital admission had an underlying suppurative lung disease of unknown etiology and received intravenous antibiotics due to coinfection of SARS-CoV-2 and *Mycobacterium abscessus*. Of the 12 adults hospitalized in our cohort with SARS-CoV-2 infection, the mean length of hospital stay was 12 days and 58% (7/12) received supplemental oxygen for a mean of 9 days. Four adults were admitted to the intensive care unit (33% [4/12]), one required mechanical ventilation and vasopressors (8% [1/12]), and one died (8% [1/12]).

4 | DISCUSSION

In our longitudinal community cohort of both children and adults with SARS-CoV-2 infection from March 20, 2020, to August 31, 2021, we noted that children generally had milder symptoms and shorter illness duration than adults. Symptomatic children presented with nonspecific symptoms (e.g., fatigue, headache, subjective fever), whereas adults tended to have a clinical picture that may have been more distinguishable as COVID-19 (e.g., loss of taste and smell). Our study was unique in that we followed both adults and children over 3 months to fully characterize the duration and spectrum of their SARS-CoV-2-associated illness.

Our finding of milder COVID-19 illness supports earlier studies suggesting that SARS-CoV-2 tends to affect children less severely than adults.[1] Furthermore, published studies also note that children with SARS-CoV-2 infection have a higher proportion of asymptomatic detection than adults.[12] This is consistent with our higher frequency of asymptomatic infection in children (15.8%) compared to adults (4.6%). Corresponding estimates from another community-based, cross-sectional comparison of asymptomatic detection in children and adults were almost twice as high at 38.2% and 7.2%, respectively.[13] However, our frequency is lower than that reported in a meta-analysis of 77 studies, almost half of which were cross-sectional, where the pooled percentage of all age groups with confirmed SARS-CoV-2 who were asymptomatic was 40.5%.[12] However, estimates from cross-sectional studies may not accurately represent the proportion of individuals who remain asymptomatic for the duration of their SARS-CoV-2 infection, as they may include presymptomatic individuals.[14] In comparison, we systematically and longitudinally assessed signs and symptoms of COVID-19 in our cohort; thus, our estimates represent individuals who remained asymptomatic over 3 months from their first positive test result.

In our study, nearly half of the children presented with fever or cough, consistent with prior studies.[1] Loss of taste and smell and shortness of breath were less frequently reported among children than adults, and the duration of illness was shorter in children. We found that persistence of symptoms ≥1 month ("long COVID") was uncommonly reported among both children (2%) and adults (5%). The reported prevalence of long COVID prolonged persistence of symptoms following acute COVID-19 in children varies widely. This heterogeneity may be attributed to a lack of a standardized case

definition for long COVID with consistent use across studies, variable inclusion criteria and follow-up times, lack of distinction between infection- and pandemic-associated symptoms, and variable study settings. For example, Stephenson et al. showed that 66.5% of test-positive adolescents reported symptoms 3 months after testing, while 53.3% of test-negative adolescents reported symptoms after the same duration.[15] The estimate we report among children is based on objective clinical assessment and is representative of a community-based cohort, which may be lower than estimates from hospitalized cohorts.

Our study has some limitations. First, our study is a cohort derived from a single community based on convenience sampling and may not be generalizable to other populations outside of Metropolitan Nashville, Tennessee. Second, symptoms, such as loss of taste and smell, may be underreported by younger children. Selection bias may be present if individuals with a higher risk for severe COVID-19 sought clinical testing or health-conscious individuals were more likely to participate in our study. Finally, our study predates widespread vaccination and the emergence of the Omicron variant (B.1.1.529), which has been associated with a lower likelihood of ICU admission among adults hospitalized with COVID-19 in this period.[16] Thus, an analysis including infections when the Omicron variant (B.1.1.529) predominated may reveal differences in illness-related severity between children and adults. Further studies are needed to compare severity differences between children and adults relative to pandemic milestones, including widespread vaccine availability and the emergence of variants of concern.

Overall, there were several differences in the clinical features of SARS-CoV-2 infections between children and adults in our longitudinal community-based cohort surveillance study. Our findings may inform the development of symptom-specific clinical testing, management, and public health screening algorithms for pandemic mitigation.

AUTHOR CONTRIBUTIONS

Danielle A. Rankin conceptualized the study design and methodology, performed data curation, data analysis, project administration, drafted the initial manuscript, and reviewed and revised the manuscript. Ahmad Yanis conceptualized the study design and methodology, project administration, drafted the initial manuscript, and reviewed and revised the manuscript. Harrison L. Howe and Sean M. Bloos performed data curation and preliminary data analysis and reviewed and revised the manuscript. Rana Talj and Kailee N. Fernandez performed project administration, data collection and entry, and reviewed and revised the manuscript. Justin Z. Amarin assisted in writing the original manuscript draft and reviewed and revised the manuscript. Mercedes Bruce, Seifein Salib, and Samarian Hargrave performed data curation, data collection and entry, and reviewed and revised the manuscript. James D. Chappell and Andrew J. Spieker oversaw project administration, supervised, assisted with conceptualization, and reviewed and revised the manuscript. Natasha B. Halasa and Leigh M. Howard lead conceptualization, study design, project administration, supervision, writing the original manuscript draft and reviewed and revised the manuscript. All authors have read and approved the final version of the manuscript, Danielle Rankin had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

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CONFLICT OF INTEREST

Natasha Halasa, MD, MPH, receives grant support from Sanofi And Quidel and Speaker Compensation from an education grant supported by Genentech. Sanofi also donated vaccines and influenza antibody testing for the influenza vaccine trials. The remaining authors declare that there are no conflict of interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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