RESEARCH LETTER

Age-Related Differences in Nasopharyngeal Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Levels in Patients With Mild to Moderate Coronavirus Disease 2019 (COVID-19)

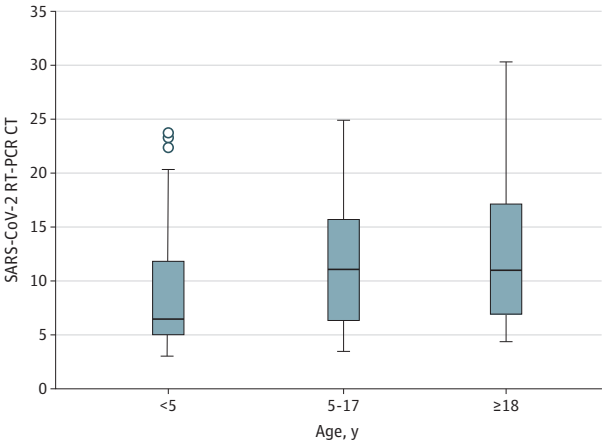
Children are susceptible to infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) but generally present with mild symptoms compared with adults.[1] Children drive spread of respiratory and gastrointestinal illnesses in the population,[2] but data on children as sources of SARS-CoV-2 spread are sparse.

Early reports did not find strong evidence of children as major contributors to SARS-CoV-2 spread,[3] but school closures early in pandemic responses thwarted larger-scale investigations of schools as a source of community transmission. As public health systems look to reopen schools and day cares, understanding transmission potential in children will be important to guide public health measures. Here, we report that replication of SARS-CoV-2 in older children leads to similar levels of viral nucleic acid as adults, but significantly greater amounts of viral nucleic acid are detected in children younger than 5 years.

Methods | Between March 23 and April 27, 2020, we performed SARS-CoV-2 reverse transcriptase–polymerase chain reaction (PCR) on nasopharyngeal swabs collected at various inpatient, outpatient, emergency department, and drive-through testing sites at a pediatric tertiary medical center in Chicago, Illinois. The Ann & Robert H. Lurie Children's Hospital of Chicago Institutional Review Board provided an exemption and full waiver of HIPAA authorization and informed consent. A Clinical Laboratory Improvement Amendments–certified laboratory analyzed samples using a US Food and Drug Administration Emergency Use Authorization PCR assay (Abbot RealTime SARS-CoV-2 Assay performed on the m2000 RealTime System [Abbott Laboratories]). PCR amplification cycle threshold (CT) values were recorded, with lower values indicating higher amounts of viral nucleic acid.

This cohort included all individuals aged younger than 1 month to 65 years who tested positive for SARS-CoV-2. Patients with symptoms suggestive of a COVID-19–compatible illness and/or high-risk exposures were tested. We included the first sample tested for patients with multiple samples. Because patients with severe infection have lower CT values,[4] we excluded 7 children who required supplemental oxygen support. We also excluded 7 asymptomatic patients, 29 patients with unknown duration of symptoms, and 19 patients whose symptoms started more than 1 week prior to testing. Swabs were collected using a standard bilateral nasopharyngeal sampling procedure. Several controls, including samples with known copy numbers, were included in each PCR run. Median and interquartile ranges for each group were measured and compared using the nonparametric Wilcoxon rank sum test. Two-sided *P* values less than .05 were considered statistically significant. Analyses were performed using Stata/IC statistical software version 16.0 (StataCorp).

Figure. Distribution of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Reverse Transcriptase–Polymerase Chain Reaction (RT-PCR) Amplification Cycle Threshold (CT) Values From Nasopharyngeal Swabs Collected From Patients With Coronavirus Disease 2019



Children younger than 5 years had significantly lower CT values compared with children aged 5 to 17 years (*P* = .02) and adults 18 years and older (*P* = .001). CT values were similar between children aged 5 to 17 years and adults 18 years and older (*P* = .34). Midlines indicate the median, boxes indicate interquartile ranges, whiskers indicate the upper and lower adjacent values (within 1.5-fold the interquartile range), and isolated data points indicate outliers.

Results | Our final cohort included 145 patients with mild to moderate illness within 1 week of symptom onset. We compared 3 groups: young children younger than 5 years (n = 46), older children aged 5 to 17 years (n = 51), and adults aged 18 to 65 years (n = 48). We found similar median (interquartile range) CT values for older children (11.1 [6.3-15.7]) and adults (11.0 [6.9-17.5]). However, young children had significantly lower median (interquartile range) CT values (6.5 [4.8-12.0]), indicating that young children have equivalent or more viral nucleic acid in their upper respiratory tract compared with older children and adults (**Figure**). The observed differences in median CT values between young children and adults approximate a 10-fold to 100-fold greater amount of SARS-CoV-2 in the upper respiratory tract of young children. We performed a sensitivity analysis and observed a similar statistical difference between groups when including those with unknown symptom duration. Additionally, we identified only a very weak correlation between symptom duration and CT in the overall cohort (Spearman ρ = 0.22) and in each subgroup (young children, Spearman ρ = 0.20; older children, Spearman ρ = 0.19; and adults, Spearman ρ = 0.10).

Discussion | Our analyses suggest children younger than 5 years with mild to moderate COVID-19 have high amounts of SARS-CoV-2 viral RNA in their nasopharynx compared with older children and adults. Our study is limited to detection of viral nucleic acid, rather than infectious virus, although SARS-CoV-2 pediatric studies reported a correlation between higher nucleic acid levels and the ability to culture infectious virus.[5] Thus, young children can potentially be important drivers of SARS-CoV-2 spread in the general population, as has been demonstrated with respiratory syncytial virus, where children with high viral loads are more likely to transmit.[6] Behavioral habits of young children and close quarters in school and day care settings raise concern for SARS-CoV-2 amplification in this population as public health restrictions are eased. In addition to public health implications, this population will be important for targeting immunization efforts as SARS-CoV-2 vaccines become available.

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