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BRIEF REPORT

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Viral Load Kinetics in Symptomatic Children, Adolescents, and Adults

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SARS-CoV-2 viral load (VL) can serve as a correlate for infectious virus presence and transmission. Viral shedding kinetics over the first week of illness for symptomatic children (n = 279), adolescents (n = 639), and adults (n = 7109) show VLs compatible with infectious virus presence, with slightly lower VL in children than adults.

Keywords. SARS-CoV2; COVID-19; children; viral shedding; virus transmission.

The role of children in the coronavirus disease 2019 (COVID-19) pandemic, in particular the risk of further transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by a pediatric or adolescent index case, is still unclear and under much debate. One year into the pandemic, a lack of data on both susceptibility to SARS-CoV-2 infection, as well as the risk posed by children to transmit to others, hinders targeted public health and infection-prevention strategies for educational institutions [1–3]. Unlike adults, children present without, or with less typical, symptoms for COVID-19 and are thus most likely underrecognized with most current testing algorithms, with a high risk of bias in currently available studies [3, 4].

SARS-CoV-2 RNA viral load (VL) can serve as a surrogate for the presence of infectious virus, as was shown in several studies, with an estimated threshold for the presence of culturable virus of approximately 6.0 $\log_{10}$ RNA copies/mL [5–8]. Similar characteristics for virus isolation success in relation to VL have been earlier shown by us for children as well [9]. As transmission is not only influenced by absolute VL but also by temporal dynamics of virus shedding, VLs over time, especially during the first week of acute illness, are crucial to understand periods of transmission risk. Viral shedding over time in adults, especially in the first week of symptoms when transmission is the highest, has been well investigated [5–8]. In contrast, few data exist on viral shedding kinetics over time by children, or they are solely based on the duration of viral shedding but not on quantitative VL, or limited to a very small number of children. For overall mean VL at the time of diagnosis between age groups, inconsistent results were reported, ranging from comparable to an even higher VL in children compared with adults, with most analyses based on rather small numbers of children [10, 11].

Methods To better understand VL kinetics over time for children and adolescents versus adults, we analyzed nasopharyngeal specimens from 8027 symptomatic SARS-CoV-2–positive individuals across all age groups in relation to number of symptoms and time since symptom onset, diagnosed in our institution by reverse transcriptase–polymerase chain reaction (RT-PCR) for SARS-CoV-2 (Cobas SARS-CoV-2 Test; Cobas 6800, Roche, Switzerland) (spanning the first pandemic wave in spring 2020 and a second pandemic wave in fall/winter 2020). The presence and number of symptoms were systematically assessed at the time of diagnosis. Viral loads were calculated for the E gene target, as described previously [12].

Results Using a regression model predicting VL with age groups (with children as the reference category), we found slightly lower mean (±SD) VLs at the time of diagnosis for children (0–13 years, n = 279) compared with adolescents (14–19 years, n = 639; $P = .053$) and adults (≤20 years, n = 7109; $P < .001$) of 6.16 ± 1.93 and 6.41 ± 1.87 versus 6.71 ± 1.76 $\log_{10}$ RNA copies/mL, respectively, albeit with a very small effect size ($R^2 = 0.5\%$) (Figure 1A). The same association between age and VL was observed when age was considered as a continuous variable (Pearson's $r = .063$, $P < .001$), again with a similar, very small effect size ($R^2 = 0.4\%$) (Supplementary Figure 1). At the time of diagnosis, the majority of individuals in all age groups presented with a VL above the accepted threshold for presence of infectious virus of 6.0 $\log_{10}$ RNA copies/mL, with a significantly higher ($P < .001$, tested with a logistic regression using children as the reference category) proportion of adults (68.6%, n = 4876) versus children (58.4%, n = 163) but no significant difference between children and adolescents (61.2%, n = 391; $P = .433$). The percentage of individuals with a VL in the range

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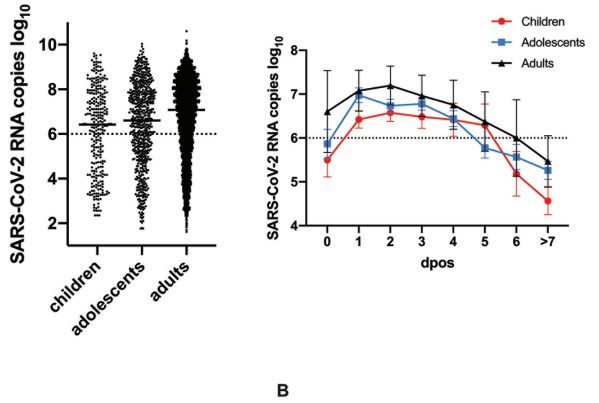

Figure 1. *A*, Mean $\log_{10}$ SARS-CoV-2 RNA copy numbers/mL at time of diagnosis in nasopharyngeal swab specimens from symptomatic children (n = 279), adolescents (n = 639), and adults (n = 7109). *B*, SARS-CoV-2 shedding kinetics over the first week of illness for children (n = 279), adolescents (n = 639), and adults (n = 7109) per days post-onset of symptoms (dpos). Dots/squares represent means; bars represent SDs. Dotted line: 6 $\log_{10}$ SARS-CoV-2 RNA copy numbers/mL, threshold for presence of infectious virus. Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

of culturable virus here is in the same range as our earlier results of successful virus isolation in cell culture in 52% of specimens in a small cohort of 53 children younger than 16 years [9].

Viral load kinetics (per days post-onset of symptoms [dpos]) (Figure 1B) reveal lower VLs on the day of symptom onset across age groups compared with the following days, with an increase in peak VLs in the first 3 dpos and a further decline in VL towards the end of week 1. However, a steeper increase in the VL from 0 to 1 dpos is seen for children and adolescents versus adults, where SD intervals overlap between day 0 and the consecutive days. All groups presented with VLs above 6.0 $\log_{10}$ RNA copies/mL up to 5 dpos, with a decrease in mean VLs below 6 $\log_{10}$ RNA copies/mL at approximately 6 dpos. These findings are consistent with data showing successful virus isolation up to 7–8 dpos [5, 7, 8]. Of note, dynamics of viral shedding and clearance in children and adolescents resemble that in adults, with a similar pattern of shedding curves over time. Furthermore, we conducted a simple linear regression to predict $\log_{10}$ VL with the total number of symptoms. We also tested whether the association was the same for each age group. We found that the VL increased when number of symptoms increased ($P < .001$).

Discussion Our data indicate that pediatric and adolescent index cases, similar to adults, could transmit SARS-CoV-2 for the majority of time during the first week of illness, although slightly lower VLs and a slightly shorter time above the threshold for the presence of infectious virus were observed compared with adults. Of note, the effect size that was observed for the association with age and VL was very small, and any potential relevance of such a small effect size under real-life conditions remains to be investigated, as children have a higher number of contacts and thus a higher possibility of becoming infected as well as infecting others [2]. In addition, even if institutional infection-prevention measures are taken, such as distancing, hand hygiene, and mask wearing, younger children are less capable of adhering to them. Individuals presenting with a higher number of symptoms upon diagnosis showed higher VLs in all age groups.

It has been much debated whether VL alone can serve as a valid surrogate for transmission or if other factors, such as age, presence of symptoms, or behavioral factors, are more relevant. Recently, a study on 282 clusters from Spain showed VL, but not respiratory symptoms or age, to be the leading driver of transmission in index cases older than 18 years of age [13]. Furthermore, a large study conducted on clusters in Hunan Province, China, during the first wave, concluded that susceptibility was dependent on age but did not find a significant difference for infectivity by age or clinical severity [14].

Interestingly, in our study, we found lower mean VLs across all age groups on the same day of symptom onset (0 dpos), which is in contrast to earlier studies, which report VLs to peak shortly before or at the time of first symptoms. Reasons for this might be increased disease awareness and broader testing algorithms that also include nonspecific symptoms that may be present earlier than typical COVID-19 symptoms.

In our study, a peak in VL was seen between days 1 and 3 after symptom onset, which would indicate a higher transmission risk during that time compared with before symptom onset or on day 0. This is also in line with our findings in individuals with more symptoms presenting with a higher VL.

To the best of our knowledge, our study is the first to describe viral shedding kinetics over time and their association with number of symptoms during the early acute period known for children and adolescents compared with adults. Assuming that VL is the main driver of SARS-CoV-2 transmission, our data indicate that symptomatic pediatric and adolescent index cases could transmit SARS-CoV-2 for the majority of time during the first week of illness, although slightly lower VLs and a shorter time above the threshold for the presence of infectious virus were observed compared with adults.

Our study has several limitations. The analysis relied on pooled data across time from multiple individuals but not on consecutive swabs from the same individuals over the course of disease, as was done for most of the studies on viral shedding in adults. Furthermore, we assessed only symptomatic children, although a large proportion of children are asymptomatic. In our testing center, we rarely test asymptomatic children, and usually the time of infection is not known in those cases. No virus culture was performed on the samples analyzed in this study, except for the analysis of 53 specimens reported earlier; thus, our correlation of the presence of infectious virus is based on previous studies only.

Our data cannot inform on the viral shedding kinetics of the newly emerged SARS-CoV-2 variants of concern (VOCs), as all data used in our analysis originate from 2020, when no circulation of VOCs in Switzerland was yet observed. Thus, it would be important to repeat our analysis for VOCs such as B.1.1.7, which are currently spreading in Europe and more frequently reported as the cause for outbreaks among minors. More data on transmission risk by children are needed to better understand conditions under which educational institutions can remain open while safe. Early testing of symptomatic individuals could identify those presenting with the highest VL, and limit transmission.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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Potential conflicts of interest. The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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