

SARS-CoV-2 viral load kinetics in symptomatic children, adolescents and adults

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Abstract

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, COVID19, children, viral shedding, virus transmission

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Brief report

The role of children in the COVID19 pandemic, in particular the risk of further transmission of Severe Acute Respiratory 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 Coronavirus Disease 2019 (COVID19) 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 load (VL) can serve as a surrogate for presence of infectious virus, as it was shown in several studies, with an estimated threshold for the presence of culturable virus of around $6.0 \log_{10}$ SARS-CoV-2 copies/mL [5-8]. Similar characteristics for virus isolation success in relation to VL have been shown by us earlier on 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, are in the meanwhile 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 even higher VL in children vs adults, with most analysis based on rather small number of children [10, 11].

To better understand VL kinetics over time for children and adolescents vs. 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 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). Presence and number of symptoms were systematically assessed at the time of diagnosis. VLs were calculated for the E gene target as described previously [12].

Using a regression model predicting VL with age groups (children as the reference category), we found slightly lower mean VL at the time of diagnosis for children (0-13 years, n=279) vs. adolescents (14-19 years, n=639, $p=.053$) and adults (≤ 20 years, n=7109, $p<.001$) of 6.16 ($SD\pm 1.93$), 6.41 ($SD\pm 1.87$) vs. 6.71 ($SD\pm 1.76$) SARS-CoV-2 \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 $r = .063$, $p<.001$) again with a similar, very small effect size ($R^2 = 0.4\%$) (**Supp. Fig. 1**). At the time of diagnosis, the majority of individuals of all age groups present with a VL above the accepted threshold for presence of infectious virus of $6.0 \log_{10}$ SARS-CoV-2 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) vs. children (58.4% , n=163) but no significant difference between children and adolescents (61.2% , n=391; $p=.433$). The percentage of individuals with VL in the range 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 < 16 years [9].

VL kinetics (per days post onset symptom, dpos, **Figure 1**) reveal lower VLs on the day of symptom onset across age groups compared to the following days, with an increase to peak VLs in the first 3 dpos and a further decline of VL towards the end of week 1. However, a steeper increase of 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 present with VL above $6.0 \log_{10}$ SARS-CoV-2 copies/mL up to 5 dpos, with a drop of mean VL below $6 \log_{10}$ SARS-CoV-2 copies/mL around 6 dpos. These findings are consistent to data showing successful virus isolation up to 7-8 dpos [5, 7, 8]. Of note, dynamics of viral shedding and clearance of children and adolescents resembles that of adults, with similar a shape of the shedding curves over time. Furthermore, we ran 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 ($p < .001$).

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 infectious virus presence were observed compared to adults. Of note, the effect size that was observed for the association with age and VL is 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 higher exposition to get infected as well as infect 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 to adhere to them. Individuals presenting with a higher number of symptoms upon diagnosis showed higher VLs in all age groups.

It has been much debated if 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 that VL, but not respiratory symptoms nor age, to be the leading driver of transmission in index cases > 18 years of age [13]. Furthermore, a large study conducted on clusters in Hunan during the first wave, concluded that susceptibility was dependent on age, but could not find significant difference for infectivity by age or clinical severity [14].

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

In our study, a peak of VL is seen between day 1 and 3 after symptom onset which would consider a higher transmission risk during that time than pre-symptom onset or on day 0. This is also in line with our findings of individuals with more symptoms presenting with 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 to 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 infectious virus presence were observed compared to 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 it 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 Centre, 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 the analysis of 53 specimens reported earlier on, thus our correlation of infectious virus presence is based on previous studies only.

Our data cannot inform about viral shedding kinetics of the newly emerged SARS-CoV-2 variants of concern (VOC), 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.

Acknowledgments

We thank Simon Regard, Delphine Courvoisier and Benjamin Meyer for help with data analysis.

Funding

This work was supported by the Private HUG Foundation.

Potential conflicts of interest

The authors report no potential conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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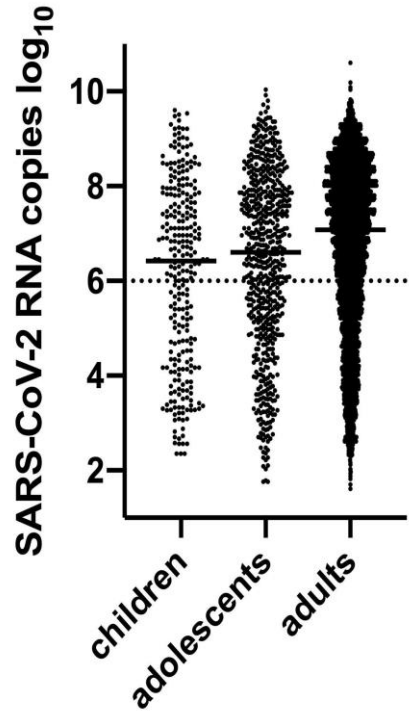
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Figure legend

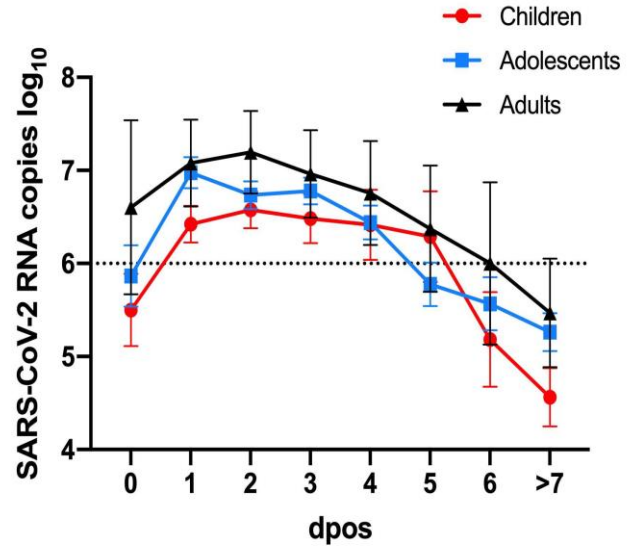
Figure 1. A. Mean \log_{10} SARS-CoV-2 RNA copy numbers/mL at time of diagnosis in nasopharyngeal swab specimens from symptomatic children (n= 279), adolescents (n= 639) and adults (n=7109). **B.** SARS-CoV-2 shedding kinetic over the first week of illness for children (n= 279), adolescents (n= 639) and adults (n=7109) per days post onset symptoms, dpos (dots/squares represent mean, bars SD). Dotted line – $6 \log_{10}$ SARS-CoV-2 RNA copy numbers/mL, threshold for presence of infectious virus.

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Figure 1



A



B