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Letter to the Editor

## Are SARS-CoV-2 viral loads in children lower than in adults?

We read with interest the article by Jiménez et al. on the activity of ACE2 in saliva in different population groups.[1] The authors reported that ACE2 activity in saliva correlates with the susceptibility to SARS-Cov-2 infection and disease severity. The saliva ACE2 activity of children is lower than adults. This suggests that children may have low susceptibility to SARS Cov-2 because of lower ACE2 activity. One of the hypotheses about the milder course and less contagiousness of COVID-19 in children is that the viral load is lower in children. There are conflicting results in studies comparing the cycle threshold (Ct) values and viral loads between children and adults. While the viral loads were similar in some studies, it was lower in children in others, while another study found younger children (<5 years) to have a higher viral load.[2–7] With the available data so far, it is not possible to reach a definite conclusion on the viral load in children compared to adults.

The Ct value refers to the number of cycles in an RT-PCR assay needed to amplify viral RNA to reach a detectable level. Ct can indirectly reflect the level of viral load in a specimen. We conducted this study to evaluate viral loads by comparing Ct values of children and adults in a large cohort, in a single large laboratory where SARS-CoV-2 PCR testing is routinely performed. This study was conducted between 23 August 2021 and 11 October 2021 at the General Hospital and Children's Hospital of the Ankara City Hospital. All hospitals within the Ankara City Hospital use the same PCR laboratory. Adult patients aged >18 years and pediatric patients aged ≤18 years with a positive SARS-CoV-2 PCR test were included in this study. The baseline characteristics of the participants are described in Table 1. The Ct values of the pediatric and adult patients were compared.

A total of 1754 children and 2996 adult patients were included in the study. The Ct value was 23.3 ± 4.2 in the ≤18 years group and 24.2 ± 4.5 in the>18 years group ($p < 0.001$). The number of patients and the mean Ct value according to each age group are shown in Table 2. A difference was found between age groups in terms of Ct values ($p < 0.001$).

Ct values and corresponding viral load value ranges have been previously reported. We classified the Ct values with a Ct value of < 24 referred to as high, 25–29 as moderate, and >30 as low viral load.[8,9] In terms of having a Ct value corresponding to low, medium, high viral load; 1122 (64%) of the children had a low Ct (Ct ≤ 24), 509 (29%) had a medium value (Ct = 25–29), and 123 (7%) had a high value (Ct > 30); 1734 (57.9%) of the adults had a low Ct (Ct ≤ 24), 905 (30.2%) had a medium value (Ct = 25–29), and 357 (11.9%) had a high value (CT > 30) ($p < 0.001$).

Linear regression using Ct ≤ 24 as a predictor variable and age (being a child or adult), immune suppression, diabetes, the severity of the clinical condition, and symptom duration/ time after exposure as independent variables was performed. Being a child and symptom duration/ time after exposure was found to be significant (OR 0.63 95% CI 0.138–1.189, $p = 0.013$, OR 0.29 95% CI 0.231–0.353, $p < 0.001$). Being an adult led to a 0.6% increase in Ct value. Every one-day increase in symptom duration/ time after exposure led to a 0.2% increase in Ct value. The other variables were not found to be related.

**Table 1**
The dermographic characteristics of pediatric and adult patients.

| | Children | Adults |
|---|---|---|
| Age (median, min-max) | 12 (0–18) | 39 (19–99) |
| Clinical severity n (%) | | |
| -Outpatient | 1706 (97.3) | 2660 (88.8) |
| -Hospitalization | 34 (1.9) | 231 (7.7) |
| -Need for intensive care | 14 (0.8) | 105 (3.5) |
| Diabetes n (%) | 8 (0.5) | 287 (9.6) |
| Immunosuppression | 2 (0.1) | 94 (3.1) |
| Symptom duration/ time after exposure on the test day median (%25–75) | 2 days (1–5days) | 4 day (2–6 days) |

When the effect of the testing day (total symptom duration or time after exposure on the test day) was kept constant, the difference between the CT values of the adult and pediatric groups was significant, and the Ct value was lower in children (Table S1).

In this study, and the Ct value was found to be lower in children than in adults. This indicates that the viral load of SARS-CoV-2 was higher in children. There was no difference in viral load among the child age groups. This finding was in contrast to the literature and partially supported Heald-Sargent et al.'s study that showed a higher viral load under 5 years of age,[4] Considering that the mean Ct value in children and in adults, the difference was about 1 unit. Every one unit increase in Ct has been reported to result in a decrease in positive culture by 32% with the probability of reproduction in viral culture decreasing significantly when the Ct value rises above 24.[8] A low Ct value (≤24) was more common in children than in adults, supporting the fact that the viral load is higher in children than in adults.

It has been reported that culture positivity is usually detected between the 1st and 5th day of symptoms. Increased duration of symptoms is associated with a negative culture result.[8] In this study, the symptom duration/time after exposure on the test day was lower in children than in adults. Therefore, we statistically assessed whether this difference could result in a lower Ct value in children. However, the Ct value was still found to be lower in children than in adults.

Ct values vary between laboratories. It has been shown that the same Ct value corresponds to different viral loads between different laboratories. One study compared distributions of Ct values and quantitative measures (copies/mL) for the SARS-CoV-2 RNA load of COVID-19–positive patients in three different laboratories. The

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**Table 2**
Ct value according to age groups.

| Age group (years) | N | Ct (mean±SD) | CT <24 N (%) | CT=25–29 N (%) | CT>30 N (%) |
|---|---|---|---|---|---|
| 0–6 | 300 | 23.3 ± 4.5 | 179 (59.7) | 99 (33) | 22 (7.3) |
| 7–12 | 721 | 23.4 ± 4.2 | 457 (63.4) | 209 (29) | 55 (7.6) |
| 13–18 | 733 | 23.1 ± 4.2 | 486 (66.3) | 201 (27.4) | 46 (6.3) |
| 19–30 | 790 | 23.9 ± 4.5 | 482 (61) | 222 (28.1) | 86 (10.9) |
| 31–42 | 948 | 24.1 ± 4.3 | 557 (58.8) | 289 (30.5) | 102 (10.8) |
| 43–54 | 657 | 24.5 ± 4.3 | 376 (57.2) | 199 (30.3) | 82 (12.5) |
| 55–66 | 339 | 24.4 ± 4.6 | 187 (55.2) | 107 (31.6) | 45 (13.3) |
| ≥67 | 262 | 24.7 ± 4.9 | 132 (50.4) | 88 (33.6) | 42 (16) |
| Total | 4750 | | | | |

measured equivalent concentrations (copies/mL) corresponding to the Ct values were different in all three laboratories. The difference in the number of copies between laboratories for the same Ct value was > 1000 fold in copies/mL.[10] Therefore, comparing Ct values between different laboratories may produce a completely useless result. The Ct value can be used to compare one result to another only if studied in the same laboratory. The fact that all PCR tests were performed in a single laboratory in this study made the comparison of children and adults feasible.

This study showed that viral load in children was higher than in adults. A point to note, Ct values may not be equal to the presence of the contagious virus, which can only be established by cell culture tests. This was not done here and therefore it is necessary to evaluate the results of this study with caution. Considering that there are contradictory reports on viral load in children as compared to adults, a more definite conclusion can be reached by studying viral cultures in a cohort with a high number of cases that are currently in the early stages of the infection.

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## Ethics approval statement

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## Patient consent statement

Not needed.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jinf.2022.08.025.

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