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# Lower nasopharyngeal viral load in young SARS-CoV-2-positive subjects

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## 1. Introduction

The ongoing coronavirus disease 2019 (COVID-19) pandemic has dramatically jeopardized human health, society, and economy across the world. Despite significant advances in our understanding of the disease since the appearance of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) at the end of 2019, doubts remain especially concerning the individual infective potential and its relationship with the dynamics of contagion. The term "superspreading" was originally coined to describe a phenomenon where certain individuals can infect a very large number of persons, thus creating numerous secondary cases compared to an "average" infectious individual [1]. Reliable evidence suggests that the presence of respiratory symptoms (i.e., cough, sneeze) along with a higher viral load in the upper respiratory tract contributes to significantly boost SARS-CoV-2 transmission, and thereby promotes superspreading events [2]. Controversy remains on the role played by children and young adults, whereby it has been postulated that children, especially school-age children, may be less important drivers of SARS-CoV-2 spread than adults [3]. To provide further data, we performed a study to compare nasopharyngeal viral load in a large cohort of SARS-CoV-2-positive subjects, stratified by age.

## 2. Material and methods

The study population consisted of 301 consecutive patients (mean age 45 ± 19 years, 146 [48.5%] women) with a definitive diagnosis of SARS-CoV-2 infection, who were referred to the Laboratory Medicine Unit of the Pederzoli Hospital (Peschiera del Garda, Verona, Italy) for COVID-19 screening or diagnosis. An upper respiratory specimen (Virus swab UTM™, Copan, Brescia, Italy) was collected upon presentation by trained healthcare operators and then analyzed with Altona Diagnostics RealStar® SARS-CoV-2 RT-PCR Kit (Altona Diagnostics GmbH, Hamburg, Germany) on Bio-Rad CFX96™ Deep Well Dx Real-Time PCR Detection System (Bio-Rad Laboratories, Hercules, CA, USA). This real-time reverse transcription polymerase chain reaction (rRT-PCR) assay encompasses two distinct amplifications of SARS-CoV-2 *S* and *E* genes. Test results were positive when the cycle threshold (Ct) value of both the *S* and *E* genes was < 45, while high-risk subjects with higher viral load were defined as having a Ct value of both genes < 29.5, in keeping with the infectivity threshold previously identified by Gniazdowski et al. [4].

Test results were expressed as median and interquartile range (IQR) and compared with Mann–Whitney, ANOVA, or $Chi^2$ tests, as appropriate. Statistical analysis was carried out with the Analyse-it software (Analyse-it Software Ltd, Leeds, UK). This study was conducted as part of routine clinical laboratory operations, using pre-existing specimens collected for systematic SARS-CoV-2 diagnostic screening and testing at the local facility. Patient informed consent and Ethical Committee approval were therefore unnecessary. All test results were anonymized prior to statistical analysis. The study was conducted in accordance with the Declaration of Helsinki, under the terms of relevant local legislation.

## 3. Results

No significant difference was observed among age groups for sex ($P = 0.272$), as well as for the time between symptom onset or contact with infected people and specimen collection (ANOVA, $P = 0.110$). The main results of this investigation are shown in Fig. 1. The Ct values of both SARS-CoV-2 *S* and *E* genes in subjects aged ≤ 20 years were found to be higher than those observed in older age cohorts (Table 1). No significant difference could be observed in Ct values among other cohorts of subjects aged 21–40, 41–60, or ≥ 60 years (all $P > 0.05$; data not shown). Likewise, the rate of subjects with Ct values of both SARS-CoV-2 *S* and *E* genes < 29.5 was between 3.1 and 3.8 folds higher than the proportion observed in older age cohorts (Table 1). Notably, no significant differences in Ct values of both SARS-CoV-2 *S* (32.4 [IQR 24.0–35.7] vs. 32.1 [IQR, 23.4–35.3]; $p = 0.339$) and *E* (33.2 [IQR, 24.1–36.3] vs. 32.3 [IQR, 23.9–36.1]; $P = 0.346$) genes were observed between men and women.

## 4. Conclusion

The results of this investigation attest that the nasopharyngeal viral load in SARS-CoV-2-positive subjects aged 20 years or younger is significantly lower than in older infected people. This may contribute to partially explain why younger individuals may play a lower role in viral transmission compared to adults [3]. Notably, a previous investigation published by Bulard et al. also showed that SARS-CoV-2-positive children aged up to 17 years were less likely to generate viral growth in culture, displayed higher nasopharyngeal Ct values, and thus had a lower viral load compared to adults [5]. This would lead us to conclude that although effective preventive measures (e.g., vaccination, social distancing, regular use of face masks in closed environments, and hand hygiene) remain pivotal, partial attenuation of strict lockdown policies such as controlled reopening of schools, should be considered by policymakers [6]. Systematic testing – by means of tests able to capture higher viral loads in the upper respiratory tract – could then be utilized for timely and accurately identifying and isolating the relatively low proportion (though not insignificant) of younger superspreaders [7].

## Ethical approval

All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments.

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None.

## Contributions of authors

All authors were involved in designing the study, analyzing the data, and writing the article.

## Disclosure of interest

The authors declare that they have no competing interest.

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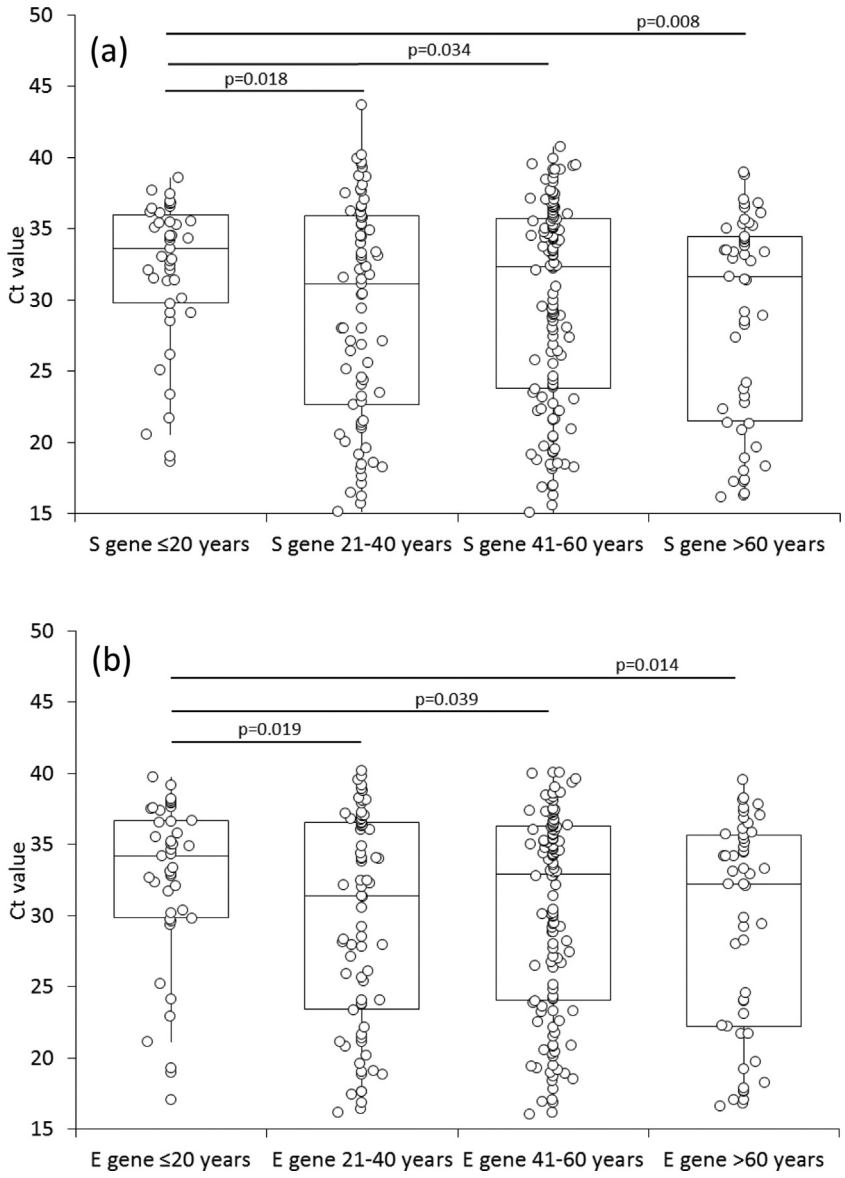


**Fig. 1.** Nasopharyngeal cycle threshold (Ct) values of severe acute respiratory syndrome coronavirus (SARS-CoV-2) *S* (a) and *E* (b) genes in a local population of SARS-CoV-2-positive subjects stratified by age group.

**Table 1**
Nasopharyngeal cycle threshold (Ct) values of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) *S* (a) and *E* (b) genes in a local population of SARS-CoV-2-positive subjects stratified by age group.

| Viral load | Age group (years) | | | | | | |
|---|---|---|---|---|---|---|---|
| | ≤ 20 | 21–40 | *P** | 41–60 | *P** | ≥ 60 | *P** |
| *n* | 43 | 75 | | 132 | | 51 | |
| Ct values (median and IQR) | | | | | | | |
| SARS-CoV-2 *S* gene | 33.6 (29.9–35.8) | 31.2 (22.7–35.9) | 0.018 | 32.4 (23.8–35.7) | 0.034 | 31.6 (21.8–34.4) | 0.008 |
| SARS-CoV-2 *E* gene | 34.2 (30.0–36.6) | 31.4 (23.6–36.5) | 0.019 | 32.9 (24.136.3) | 0.039 | 32.2 (22.2–35.5) | 0.014 |
| Ct values < 29.5 | | | | | | | |
| Rate (%) | 8/43 (18.6%) | 35/75 (46.7%) | 0.003 | 55/132 (41.7%) | 0.008 | 22/51 (43.1%) | 0.013 |
| Odds ratio (95% CI) | – | 3.8 (1.6–9.3) | 0.003 | 3.1 (1.3–7.3) | 0.008 | 3.3 (1.3–8.6) | 0.013 |

Ct: cycle threshold; IQR: interquartile range; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; *: versus ≤ 20 years.

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## Antibiotics in end-of-life care: What is the driving factor?

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In Durand M and colleagues' study, physicians prescribed antibiotics in end-of-life care settings mainly to relieve patients' symptoms [1]. However, if this was the case, there should have been a lack of knowledge on palliative care among physicians. There are treatment options to relieve end-of-life symptoms other than antibiotics. For example, fever-related lethargy and dyspnea can be managed using antipyretics [2] and morphine [3,4], respectively. It seems essential to confirm whether physicians in this study thought of using these medications instead of antibiotics. If there is a lack of knowledge among physicians, educational interventions are often beneficial to reduce inappropriate antibiotic use.

Besides, it would be important to know whether the physicians had recognized the patients' end-of-life stage at the time of antibiotic prescription. It is sometimes difficult to know the patient's prognosis, and some patients turn out to be in end-of-life stage soon before or after they die. In this context, it also seems essential to know whether the physicians in this study extended the spectrum of antibiotics in "end-of-life" care.

Recall bias often occurs in this type of questionnaire survey. More detailed information on the physicians' actions, as I mentioned above, would be helpful to analyze the driving factor for antibiotic prescription in palliative care.

### Ethical Approval

All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments.

### Disclosure of interest

The author declares that he has no competing interest.

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