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Letter to the Editor

SARS-CoV-2 Omicron infection is associated with high nasopharyngeal viral load

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We read with interest the article of Zheng et al. [1], who reported that a high breath emission rate of viral particles may be one of the most important reasons for justifying the higher transmissibility of the new severe acute respiratory coronavirus 2 (SARS-CoV-2) Omicron variant. Unfortunately, no direct comparison of viral load with previous SARS-CoV-2 variants has been reported in the work of Zheng et al., so that this conclusion remains intriguingly speculative.

In order to provide a direct comparison of the viral load in nasopharyngeal specimens of patients infected by Omicron and former SARS-CoV-2 variants, we retrospectively reviewed the results of SARS-CoV-2 testing conducted during two

corresponding periods of years 2021 and 2022 (i.e., between 3-9 January), characterized by local prevalence of Alpha (>95%; January 2021) and Omicron (>90%; January 2022) SARS-CoV-2 variants, respectively. Briefly, the study population consisted of all patients with a positive SARS-CoV-2 test performed between 3-9 January 2021 or 2022, respectively. Routine nasopharyngeal samples were collected according to standardized practice in subjects referred to the Pederzoli Hospital of Peschiera del Garda (Italy) for undergoing routine SARS-CoV-2 testing for presenting symptoms of coronavirus disease 2019 (COVID-19) or for reporting close contact with SARS-CoV-2 positive subjects. In both these two years SARS-CoV-2 viral load was quantified using the same method and instrumentation (Seegene Allplex SARS-CoV-2 Assay; Seegene Inc., South Korea). This multiplex real-time polymerase chain reaction (PCR) assay detects four target genes of SARS-CoV-2 (*E*, *RdRP*/*S* and *N*) within a single sample, providing test results as cycle threshold (Ct) values. Additional technical and analytical characteristics of this method are comprehensively described elsewhere [2]. The cumulative viral load that we measured in nasopharyngeal swabs was expressed as mean Ct value of the different SARS-CoV-2 genes. Final results were reported as median and interquartile range (IQR), and compared with Mann-Whitney or Chi square tests, when appropriate, using Analyse-it software (Analyse-it Software Ltd, Leeds, UK). This study was conducted as part of routine clinical laboratory operations, using pre-existing nasopharyngeal specimens collected for systematic SARS-CoV-2 diagnostic testing at the local facility, so that patient informed consent and Ethical Committee approval were unnecessary. All test results were anonymized before statistical analysis. The study was conducted in accordance with the Declaration of Helsinki, under the terms of relevant local legislation.

The total number of patients with positive SARS-CoV-2 tests was 47 in January 2021 and 118 in January 2022, respectively, thus mirroring the dramatic surge of

infections seen after local spread of the Omicron variant. Subjects with positive SARS-CoV-2 tests in 2021 were significantly older (median age, 63 years; IQR, 47-80 years) compared to those testing positive in 2022 (median age, 42 years; IQR, 25-53 years; p<0.001), whilst the sex distribution was similar (females: 68% in 2021 vs. 58% in 2022; p=0.107). The viral load measured with the Allplex SARS-CoV-2 Assay is reported in figure 1, showing that the Ct values in January 2022 (median Ct value, 27.5; IQR, 23.5-32.7) when the Omicron variant was prevalent were significantly lower than those measured during the same period of the year 2021 (median Ct value, 31.8; IQR, 26.4-37.6; p=0.007), when the Alpha variant was prevalent. Importantly, the rate of subjects with high nasopharyngeal viral load (i.e., Ct values <25) was over 2-fold higher in January 2022 than in January 2021 (45/118 vs. 10/47; Odds ratio, 2.28 and 95%CI, 1.03-5.03; p=0.041).

In conclusion, the results of our retrospective analysis provide convincing support to the suggestion that aerosols released by patients infected by SARS-CoV-2 Omicron variant may contain higher viral particles than those released by subjects infected with previous SARS-CoV-2 strains, thus providing a solid biologic background to justify enhanced transmissibility of this new linage and higher prevalence of upper respiratory tract symptoms reported in other studies [3,4].

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Declaration of Competing Interest

The authors have no relevant competing interest to disclose in relation to this work.

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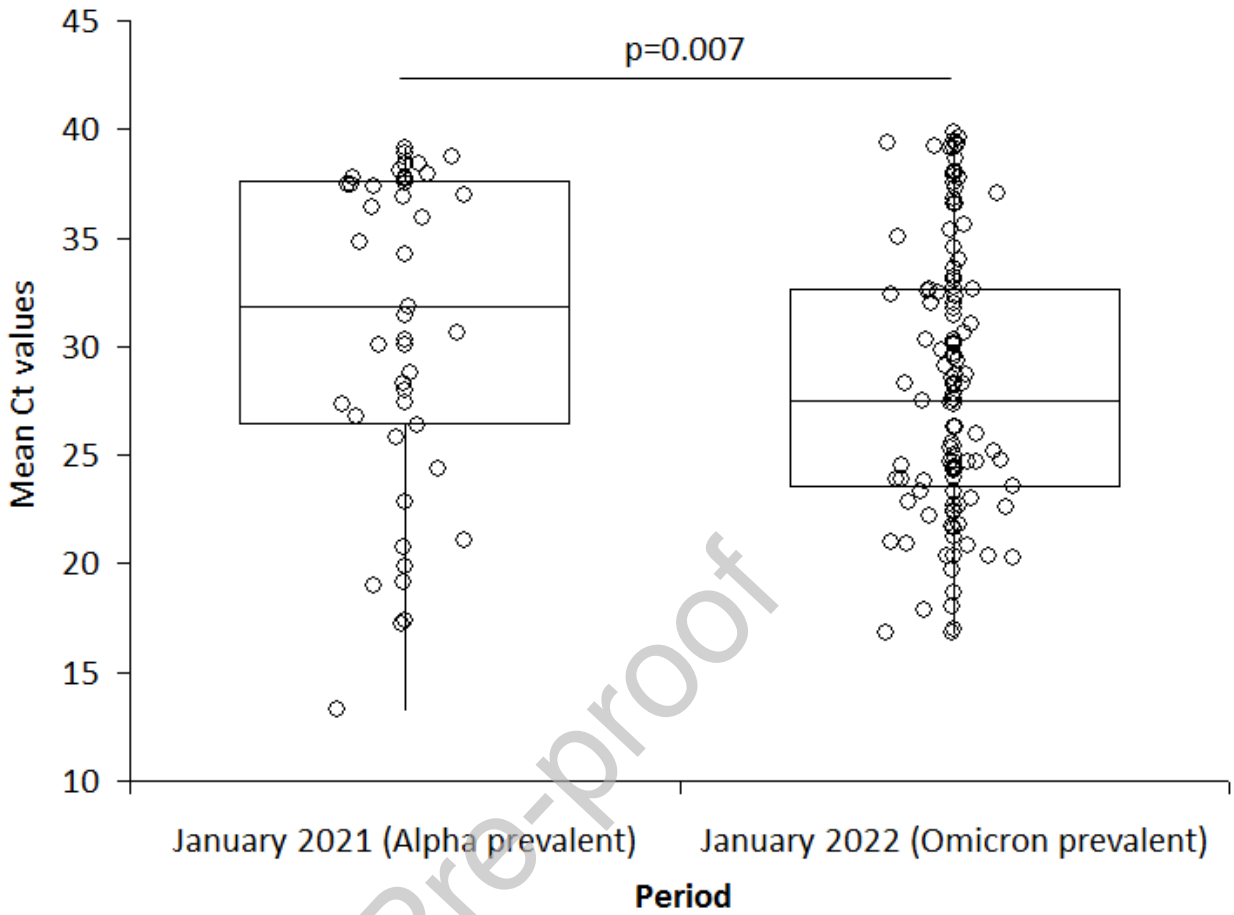

Figure 1. Nasopharyngeal viral load measured in subjects infected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) between 3-9 January 2021 (Alpha variant prevalent) and 3-9 January 2022 (Omicron variant prevalent).

Ct, cycle threshold