Asymptomatic infection by SARS 2 coronavirus: invisible but invincible

Reply to Malagón-Rojas et al.

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Malagón-Rojas et al. comments on the need for a widely accepted definition of asymptomatic carriers and pre-symptomatic patients and to report asymptomatic individuals in official COVID-19 statistics are well acknowledged (Nikolai et al. 2020).

Malagón-Rojas et al. show in a longitudinal follow-up of 202 airport employees that no significant differences in Ct values were observed when comparing asymptomatic and symptomatic patients (median Ct 33.4 vs. 34.1 in asymptomatic and symptomatic patients, respectively). Their findings are consistent with another study that examined asymptomatic individuals and symptomatic patients (Long et al. 2020).

The virus load is assessed semi-quantitatively by the cycle threshold (Ct) value, which corresponds to the number of amplification cycles in the diagnostic RT-PCR assays. Ct values decrease with increasing viral loads and high Ct values correspond to low viral loads (Nikolai et al. 2020). In addition, the duration of virus detectability serves as an indicator of infectivity. Several SARS-CoV-2 PCR assays use a Ct cut-off value of <40 for positivity, and in the early stages of infection patients usually have Ct values of 20-30 (Young et al. 2020). A recent narrative systematic review suggests that lower Ct values are associated with poorer outcomes and thus beneficial in predicting the clinical prognosis of COVID-19 patients (Rao et al. 2020). Higher Ct values normally correlate with lower viral loads. However the Ct values are not directly proportional to the viral load, due to the dynamic range of the assay and/or the potential presence of any inhibitory factors in samples used (Rao et al. 2020; Aquino-Jarquin 2020).
The current literature gives indications of the median duration of virus shedding of 11.5 days for pre-symptomatic, 28 days for asymptomatic and 31 days for mildly symptomatic patients (Li et al. 2020). Another study using the similar gene target ORF1ab as described by Malagón-Rojas et al. shows that median Ct values during hospitalization were significantly higher in asymptomatic patients (39.0, IQR 37.5-39.5) than in asymptomatic patients during the incubation period (34.5, IQR 32.2-37.0), indicating a significantly lower viral load (Zhou et al. 2020). Long-term virus shedding was documented rather in asymptomatic than in symptomatic patients and virus shedding did not correspond to viral infectivity (Long et al. 2020).

We agree with the authors that the absence of respiratory symptoms such as sneezing or coughing limits the potential of spread by asymptomatic individuals, however, virus transmission may occur through occasional and also more frequent sneezing during the allergy season may also increase the risk (Busco et al. 2020). The risk still exists.

Asymptomatic and presymptomatic stages can currently be assigned only retrospectively, namely after the occurrence or non-occurrence of clinical symptoms and it is virtually impossible to accurately determine the extent of asymptomatic infections. The true incidence of asymptomatic infections can only be determined if closest surveillance and extensive testing is installed and continued for a period of time exceeding the estimated average incubation period of at least five days in order not to miss a possible onset of symptoms (Nikolai et al. 2020).
Asymptomatic infections are an important aspect of SARS-CoV-2 infection, in particular on the viral transmission, and globally remain a significant epidemiologic challenge, as health systems could become severely overburdened and the pandemic could continue to elude control, hitting those hardest with the least protection.

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