SARS-CoV-2 Viral loads and serum IgA/IgG immune responses in critically-ill COVID-19 patients

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This article has undergone peer-review and has been accepted for publication in the Journal Intensive Care Medicine (ICM). This is not yet the definitive version of the manuscript as it will undergo copyediting and typesetting before it is published in its final form with a DOI.

DOI : 10.1007/s00134-020-06157-5

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Funding/support: none
To the Editor:

The pandemic of Coronavirus disease 2019 (COVID-19) caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) represents the greatest global public health crisis that occurred during the last decades. Among hospitalized patients, up to 25% will develop acute respiratory failure and the acute respiratory distress syndrome (ARDS) and require intensive care unit (ICU) admission. The median duration between onset of symptoms and ICU admission ranges from 7 to 12 days [1], suggesting a gradual deterioration in the majority of cases. Although the clinical characteristics of patients requiring ICU admission have now been well described [2-4], their viro-immunological features are still unknown. Whether a higher titer of SARS-CoV-2 specific antibodies may reduce viral RNA load in upper respiratory samples and eventually mitigate the course of infection in patients admitted in the ICU has not been established. We examined the relationship between SARS-CoV-2 viral loads collected from nasopharyngeal swabs on ICU admission, concomitant SARS-CoV-2 specific IgA and IgG antibody titers, and day-28 mortality.

This is a prospective monocenter study, which included all patients diagnosed with RT-PCR-confirmed SARS-CoV-2 infection consecutively admitted in the medical ICU at Henri Mondor Hospital, Créteil, France, between March 8, 2020, and March 26, 2020. The study has received the approbation of an institutional review board (Comité de Protection des Personnes Ile de France II; reference number: 3675-NI). Informed consent was obtained from all patients or their relatives. Nasopharyngeal swabs and sera were collected from patients within 48 hours of ICU admission. The cycle threshold values of RT-PCR were used as indicators of the viral load of SARS-CoV-2 RNA in nasopharyngeal specimens, with lower cycle threshold values corresponding to higher viral load. IgA and IgG antibodies against SARS-CoV-2 spike protein subunit 1 (S1) were quantified in patients’ serum using ELISAs (Euroimmun Medizinische Labordiagnostika, Lübeck, Germany) and expressed in arbitrary units (AU). The primary clinical outcome was day-28 mortality.

Twenty-five patients (mean age 60±14 years; males 80% (n=20/25)) were admitted in the ICU for severe SARS-CoV-2 infection during the study period. The median time elapsed between the first symptoms and ICU admission was 9 days [6-12]. Invasive mechanical ventilation was required in 96% (n=24/25) of patients during ICU stay and the mortality at day-28 of ICU admission was 32% (n=8/25) (Supplemental Table 1). There was a significant correlation between the time elapsed between the first symptoms and ICU admission and the titer of both anti-S1 IgA (Spearman’s r=0.70; p<0.001) and anti-S1 IgG (r=0.68; p<0.001) measured in sera obtained upon ICU admission (Figures 1A and 1B). No correlation was found between the absolute counts of peripheral B or T lymphocytes and the titers of anti-S1 IgA (r=0.002, p=0.99 and r=0.10, p=0.624, respectively) or IgG (r=0.12, p=0.56, and r=0.13, p=0.53, respectively). There was also no correlation between peripheral B or T lymphocyte counts and viral loads (r=0.34, p=0.093 and r=0.24, p=0.247, respectively). We observed an inverse correlation between the viral load obtained from nasopharyngeal swabs and the serum level of...
LETTER TO THE EDITOR

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References


Figure 1. A) Correlation between the number of days since onset of symptoms and intensive care unit (ICU) admission and the serum titer of anti-S1 IgA, expressed in arbitrary units (AU) (Spearman’s \( r=0.70; \) p<0.001; \( r^2=0.40 \)); B) Correlation between the number of days since onset of symptoms of SARS-CoV-2 infection and ICU admission and the serum titer of anti-S1 IgG (AU) (Spearman’s \( r=0.68; \) p<0.001, \( r^2=0.22 \)); C) Correlation between the serum titer of anti-S1 IgA (AU) and the SARS-CoV-2 viral load measured in nasopharyngeal swabs (expressed in cycle threshold value, Ct) (Spearman’s \( r=0.69; \) p<0.001; \( r^2=0.35 \)); D) Correlation between the serum titer of anti-S1 IgG (AU) and the SARS-CoV-2 viral load measured in nasopharyngeal swabs (expressed in Ct) (Spearman’s \( r=0.72; \) p<0.0001; \( r^2=0.29 \)); Note that the x-axis of panels C and D is inverted so as to reflect that the RT-PCR Ct is inversely correlated with RNA viral load; E) Comparisons of serum anti-S1 IgA titers obtained upon ICU admission between patients who were alive at day-28 of ICU admission and patients who died; F) Comparisons of serum anti-S1 IgG titers obtained upon ICU admission between patients who were alive at day 28 of ICU admission and patients who died; Continuous lines represent the lines of best fit of the linear regressions and the dotted lines show their 95% confidence intervals; Horizontal lines represent the median value; p-values displayed in panels E and F come from the Mann-Whitney test.