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LETTER

# Serum antibody response in critically ill patients with COVID-19

Alban Longchamp[1,2,3], Justine Longchamp[1,3], Antony Croxatto[4], Gilbert Greub[4], Bienvenido Sanchez[1*], Julie Delaloye[1*] on behalf of the Study Group



Dear Editor,

Coronavirus disease 19 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which has affected more than 7 million people. High mortality rates were reported among elderly, and those requiring mechanical ventilation in the intensive care unit (ICU) [1, 2]. Understanding virus kinetics, and host serological response to SARS-CoV-2 is crucial to guide treatment, vaccine design and epidemiological control [3]. Currently, the antibody response against SARS-CoV-2 in critically ill patients remains unknown.

We analyzed the antibody response in 28 critically Ill patients, with laboratory confirmed SARS-Cov-2 infection, admitted to Sion hospital ICU (Switzerland), between March 8th and April 4th, 2020. Only patients with serum samples available at two different time points were included. Experimental methods are described in the electronic supplementary material.

The characteristics of the cohort are summarized in Table S1-3. 27 (96%) patients required mechanical ventilation, and 5 (19%) patients died. The median (IQR) intervals from symptom onset to ICU, and hospital admission were 9 (7–12), and 6 (4–10) days, respectively (Table S1). 26 (93%) patients had available serum sample within ± 2 days of ICU admission. Of them, 15 (58%) already had virus-specific IgG antibodies. (Table S2, and Fig. 1a, b). The distribution of IgG seroconversion time from the date of ICU admission showed 2 peaks, the first one on admission, the second one about 20 days later. The median (IQR) time was 17 (1–22) days (Fig. 1b). The distribution of IgG seroconversion time, since the onset of symptoms showed only one peak, with the median (IQR) time at 10 (7–13) days (Fig. 1c). The proportion of patients with positive virus-specific IgG reached 96% over the follow-up period (Fig. 1a, and Table S2). At ICU admission, anti-N IgG levels correlated with the time from symptom onset (Fig. 1d). No association was seen between anti-N IgG levels and age, or any of the other clinical, and laboratory data assessed (Fig. S1). Interestingly, two patients had no, or weak IgG seroconversion in the ICU. One had leukemia, the other one lymphoma. They died on day 4, and 38 respectively. Patients were then split into survivors (that were discharged from the ICU), and non-survivors (that died in the ICU) in order to assess if IgG seroconversion correlates with survival. IgG levels tended to be higher in patients that remained alive (mean difference ± SD, 10.3 ± 5.5, Fig. 1e). This suggests that the antibody response correlates with virus neutralization, and functional protection [4]. Consistently, SARS-CoV-2 cycle threshold of viral RNA amplification was low during the first week of ICU stay, then gradually increased (Fig. 1f), simultaneously to the IgG seroconversion (Fig. 1g). Further large-scale studies documenting the antibody responses against different SARS-CoV-2 antigens (Protein N, protein S), and viral clearance are needed to confirm our findings.

In conclusion, similarly to mild infections [4], most patients with severe COVID-19 developed SARS-Cov-2 specific antibodies [5]. This data also suggest that the

*Correspondence: bienvenido.sanchez@hopitalvs.ch; Julie.Delaloye@hopitalvs.ch
[1] Department of Intensive Care Medicine, Centre Hospitalier du Valais Romand de l'Hôpital du Valais, (Site de Sion) Avenue du Grand-Champsec 80, 1951 Sion, Switzerland
Full author information is available at the end of the article

Alban Longchamp, Justine Longchamp, Bienvenido Sanchez and Julie Delaloye have contributed equally.

Members of study group are listed in acknowledgement section.

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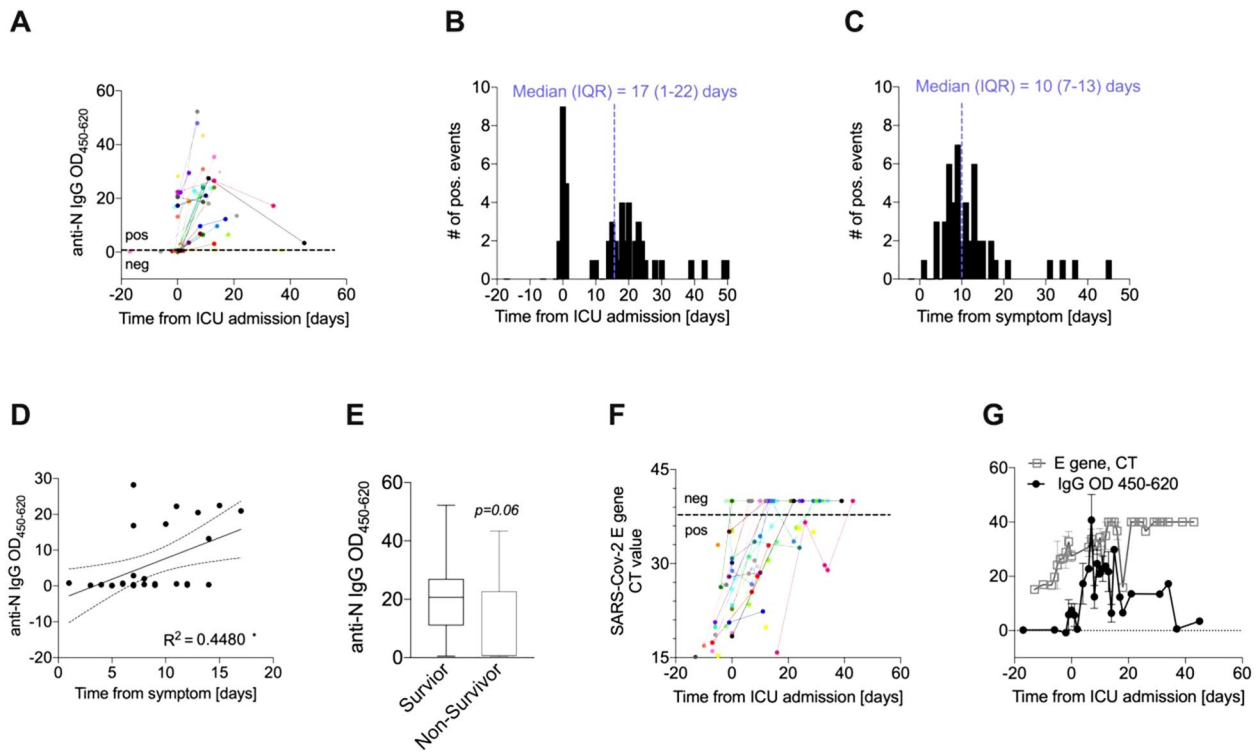


**Fig. 1** Serological profile of critically ill patients with Covid-19. **a** anti-N IgG levels in patients over time since the admission to the ICU. **b**, **c** Interval from ICU admission (**b**), and symptom onset (**c**) in samples considered positive for SARS-CoV-2-specific IgG antibodies. **d** Unparametric Spearman's correlation between anti-N IgG levels at ICU admission, and corresponding time from symptom onset with their coefficient of determination $R^2$ and *p* value. Dashed lines indicate 95% confidence intervals. (**e**) Pooled sera antibody levels in survivor versus non-survivors. **f**, **g** Individual patient SARS-Cov-2 E gene threshold cycle (CT) values since admission to the ICU (**f**), and grouped with anti-N IgG profile (**g**). Data are expressed as mean ± SD. For negative qPCR, CT values were arbitrary set at 40

severity of COVID-19 cannot be solely attributed to an impaired rate of seroconversion.

#### Electronic supplementary material

The online version of this article (https://doi.org/10.1007/s00134-020-06171-7) contains supplementary material, which is available to authorized users.


#### Author details

[1] Department of Intensive Care Medicine, Centre Hospitalier du Valais Romand de l'Hôpital du Valais, (Site de Sion) Avenue du Grand-Champsec 80, 1951 Sion, Switzerland. [2] Department of Biomedical Sciences, University of Lausanne, Lausanne, Switzerland. [3] Department of Vascular Surgery, Centre Hospitalier Universitaire Vaudois and University of Lausanne, Lausanne, Switzerland. [4] Department of Laboratory Medicine and Pathology, Institute of Microbiology, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland. [5] Service of Infectious Diseases, Institut Central Des Hôpitaux, Hôpital du Valais, Sion, Switzerland.



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#### Author contributions

AL, JL, BS, and JD designed the project. AC, GG, AD and SE performed the ELISA, and the qPCR. AL, JL, LW, AC, GG, AD, SE, and JD collected the data. AL, JL, AC, BS, and JD analyzed the data. AL, JL, LW, SJ, GG, RF, BS, and JD wrote the manuscript.

#### Compliance with ethical standards

#### Conflicts of interests

All authors declare no conflicts of interest.

## Publisher's Note




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