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LETTER TO THE EDITOR

# Autoantibodies in moderate and critical cases of COVID-19

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Dear Editor,

A recent article reported the useful results of autoantibodies in coronavirus disease 2019 (COVID-19).[1] We obtained additional results of autoantibodies, especially antinuclear antibody (ANA) tested by the same indirect immunofluorescence assay (IFA), in moderate and critical cases of COVID-19.

We enrolled 47 hospitalized patients with COVID-19 confirmed by real-time polymerase chain reaction (PCR), who were classified as either moderate (31 cases; pneumonia but no need for oxygenation) or critical (16 cases; pneumonia and need for oxygenation or mechanical ventilation therapy or death) based on the severity scoring system.[2] ANA and anti-cyclic citrullinated peptide (CCP) antibody were measured in serum or plasma samples within 3 weeks after PCR confirmation. ANA was evaluated by IFA using ANA HEp-2 Test System (ZEUS Scientific), and anti-CCP antibody l was measured by chemiluminescent microparticle immunoassay using ARCHITECT (Abbott Laboratories).

Table 1 shows the demographics of patients and prevalence of autoantibodies. The total positive rate of ANA was 21.3% (10/47), whereas previous studies have been 33.5% (11/33),[1] 57.5% (23/40),[3] or 50% (10/20).[4] Variability in the prevalence could be due to the small sample sizes, different assay methods, and different groups of patients enrolled. The total positive rate of anti-CCP antibody was 2.1% (1/47), which was lower than 20% (2/10)[5] reported earlier.

Pascolini et al. documented 36.3% (4/11) nucleolar and 36.3% (4/11) speckled staining among ANA-positive cases.[1] Our results revealed the same dominant patterns of 50% (5/10) nucleolar and 30% (3/10) speckled staining. However, the ANA titers were mostly weak (median, 1:40; range, 1:40–1:640), which were quite different from those of Pascolini et al.[1] (median, 1:640; range, 1:160–1:5120). In our study, 9.1% (1/11) of patients with autoantibodies and 8.3% (3/36) of patients without autoantibodies died. Hence, this finding did not reveal any significant difference between the two groups unlike those of Pascolini et al.,[1] which showed more severe prognosis in an autoantibody-positive subgroup than in an autoantibody-negative subgroup; 40% (6/15) died versus 5.5% (1/18) died, $p = 0.03$. However, all these differences between the two studies should be carefully considered because of the small numbers of patients enrolled in both studies (47 and 33), different group of patients selected (moderate and critical cases vs. cases in general medicine or subintensive care unit), difference of methods in detail, and other variables, which likely impact clinical circumstances of the studies.

Moreover, three seroconversion/seroreversion cases were found among 16 patients who were tested on consecutive samples in this study. Two ANA seroreversion cases showed all nucleolar patterns and were found only in the moderate group. One anti-CCP antibody seroconversion case was found only in the critical group. Therefore, these findings might indicate different immune responses depending on severity.

This study has some limitations due to the small number of patients and the results based on certain severity groups. Our results need to be confirmed by further larger scale studies to define the role of autoantibodies and their association with prognosis in COVID-19.

## CONFLICT OF INTEREST

All authors declared no competing interests for this work.

**TABLE 1** Demographics and prevalence of autoantibodies

| | All patients ($n = 47$) | Moderate patients ($n = 31$) | Critical patients ($n = 16$) |
|---|---|---|---|
| Age, years | 68 (25–90) | 61 (25–90) | 71 (26–85) |
| Female | 19 (40.4%) | 13 (41.9%) | 6 (37.5%) |
| Deceased | 4 (8.5%) | 0 (0.0%) | 4 (25.0%) |
| ANA (all patterns) | 10 (21.3%) | 8 (25.8%) | 2 (12.5%) |
| Nucleolar | 4 | 4 | |
| Nucleolar with dense fine speckled | 1 | 1 | |
| Speckled | 1 | 1 | |
| Speckled with cytoplasmic | 1 | 1 | |
| Proliferating cell nuclear antigen | 1 | 1 | |
| Nuclear dots | 1 | | 1 |
| Peripheral (rim) | 1 | | 1 |
| ANA titer | 1:40 (1:40–1:640) | 1:60 (1:40–1:640) | 1:40 (1:40–1:40) |
| Anti-CCP antibody | 1 (2.1%) | 0 (0.0%) | 1 (6.3%) |
| ANA seroconversion/seroreversion | 2/16 (12.5%) | 2/11 (18.2%) | 0/5 (0.0%) |
| Anti-CCP seroconversion/seroreversion | 1/16 (6.3%) | 0/11 (0.0%) | 1/5 (20.0%) |

*Note:* Data are presented as medians (ranges) or numbers (percentages).

Abbreviations: ANA, antinuclear antibody; CCP, cyclic citrullinated peptide.

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