

## SHORT COMMUNICATION

# The association of COVID-19 antibody with in-hospital outcomes in COVID-19 infected patients

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## Abstract

We aimed to investigate whether hospitalizations of patients who tested positive for coronavirus disease 2019 (COVID-19) antibodies are associated with reduced in-hospital mortality. Of the 2459 patients admitted due to COVID-19 and tested for antibodies, 937 (38.1%) had positive tests. After adjustment for patient characteristics and treatments, patients with positive COVID-19 antibody test had lower in-hospital mortality compared with those with negative test results (odds ratio [OR]: 0.62; 95% confidential interval [95% CI] 0.46–0.83,  $p = 0.001$ ). In conclusion, positive COVID-19 antibody test results were associated with the reduced risk of in-hospital mortality for COVID-19 patients.

## KEYWORDS

antibody, COVID-19, mortality

Coronavirus disease 2019 (COVID-19) vaccine is expected to protect against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections and severe respiratory failure due to COVID-19.<sup>1</sup> Although COVID-19 antibodies can protect from reinfection,<sup>2</sup> it is uncertain how long antibodies produced by previous infections or vaccines can work as an effective immunity.

We aimed to investigate whether hospitalizations of patients tested positive for COVID-19 antibodies are associated with reduced in-hospital mortality to clarify the necessity of check for COVID-19 antibody at the time of admission.

This retrospective study was conducted by review of the medical records of 2459 hospitalized patients who were discharged between March 1, 2020, and March 30, 2021 from the Mount Sinai Health system with laboratory-confirmed COVID-19 infection and for whom a qualitative COVID-19 antibody test was performed within 2 days after admission.

The primary outcome of interest was in-hospital mortality. Secondary outcomes were intensive care unit admission, endotracheal intubation, and acute kidney injury (AKI). AKI was defined according to KDIGO criteria.<sup>3</sup>

All vital signs and blood tests were recorded at the time of admission. We imputed missing data using multiple imputations. Inverse probability weighted analysis (IPTW) using a propensity score with trimming weights more than 10 was performed for an adjustment for baseline patients' characteristics. The following variables were used to estimate propensity scores: age, sex, race, comorbidities, laboratory test results, and treatments. In IPTW analysis, standardized mean differences in listed variables between groups of patients positive and negative for a COVID-19 antibody were mostly less than 0.20. We compared the in-hospital outcomes between the groups of patients positive and negative for a COVID-19 antibody.

In subgroup analyses, we compared the in-hospital mortality between the patients with and without positive antibody tests stratified by endotracheal intubation and oxygen saturation using IPTW analysis. All statistical analyses were performed using R (version 3.6.2).  $p$  values less than 0.05 were considered statistically significant.

Of the 2459 patients admitted due to COVID-19 and tested for antibodies, 937 (38.1%) had positive COVID-19 antibody tests. Baseline characteristics, vital signs, treatments for patients with and without positive antibody tests are reported in Table 1.

**TABLE 1** Baseline characteristics of patients admitted with COVID-19 stratified by COVID-19 antibody

	Patients without COVID-19 antibody (N = 1,522)	Patients with COVID-19 antibody (N = 937)	p value
<b>Demographics</b>			
Age (years), mean (SD)	65.6 (16.8)	64.7 (16.7)	0.23
Male, n (%)	837 (55.0)	534 (57.0)	0.35
Race/ethnicity, n (%)			
White	561 (36.9)	261 (27.9)	<0.001
African American	240 (15.8)	187 (20.0)	
Hispanic	316 (20.8)	221 (23.6)	
Asian	119 (7.8)	80 (8.5)	
Other	286 (18.8)	188 (20.1)	
<b>Comorbidities</b>			
COPD, n (%)	82 (5.4)	32 (3.4)	0.031
Hypertension, n (%)	558 (36.7)	333 (35.5)	0.60
Diabetes mellitus, n (%)			
Atrial fibrillation, n (%)	130 (8.5)	69 (7.4)	0.34
Heart failure, n (%)	136 (8.9)	72 (7.7)	0.31
Coronary artery disease, n (%)	243 (16.0)	128 (13.7)	0.14
<b>Vital signs</b>			
Temperature, median [IQR]	38.0 [37.4–38.8]	37.5 [37.2–38.4]	<0.001
Respiratory rate (/min), median [IQR]	20.0 [18.0–20.0]	20.0 [18.0–22.0]	0.70
O <sub>2</sub> saturation (%), median [IQR]	90.0 [84.0–92.0]	90.0 [86.0–93.0]	<0.001
<b>Blood tests</b>			
White blood cell (K/ $\mu$ l), median [IQR]	6.10 [4.56–8.11]	8.30 [6.40–11.50]	<0.001
eGFR (ml/min./1.73m <sup>2</sup> ), median [IQR]	69.8 [46.8–93.9]	75.4 [49.0–97.4]	0.009
C reactive protein (mg/L), median [IQR]	66.3 [28.0–119.7]	97.1 [46.4–173.0]	<0.001
D-Dimer ( $\mu$ g/ml), median [IQR]	0.94 [0.58–1.72]	1.39 [0.79–2.83]	<0.001
<b>Treatment</b>			
Therapeutic anticoagulation, n (%)	497 (32.7)	329 (35.1)	0.23
Prophylactic anticoagulation, n (%)	978 (64.3)	553 (59.0)	0.01
Steroid treatment, n (%)	1318 (86.6)	697 (74.4)	<0.001
IL-6 inhibitor, n (%)	30 (2.0)	20 (2.1)	0.90
Convalescent plasma, n (%)	698 (45.9)	83 (8.9)	<0.001
Use of remdesivir, n (%)	701 (46.1)	244 (26.0)	<0.001
<b>In-hospital outcomes</b>			
In-hospital mortality	298 (19.6)	128 (13.7)	<0.001
Intensive care unit admission	328 (21.6)	186 (19.9)	0.34
Endotracheal intubation	202 (13.3)	90 (9.6)	0.008
<b>Acute kidney injury</b>			
No acute kidney injury	1186 (78.2)	752 (80.4)	0.45

**TABLE 1** (Continued)

	Patients without COVID-19 antibody (N = 1,522)	Patients with COVID-19 antibody (N = 937)	p value
Stage 1	117 (7.7)	57 (6.1)	
Stage 2	48 (3.2)	28 (3.0)	
Stage 3	166 (10.9)	98 (10.5)	
Length of stay, median [IQR], days	7.25 [4.04–13.8]	6.31 [3.72–11.2]	<0.001

Abbreviations: COVID-19, coronavirus disease 2019; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; HIV, human immunodeficiency virus; IL-6, interleukin-6; IQR, interquartile range; SD, standard deviation.

**TABLE 2** Risk-adjusted in-hospital mortality overall and for subgroups of patients' hospitalized with COVID-19 and tested positive or negative (reference group) for COVID-19 antibody

	Odds ratio	Confidential Interval	p value
Overall	0.68	0.50–0.91	0.01
Patients without endotracheal intubation	0.78	0.53–1.16	0.23
Patients with endotracheal intubation	0.36	0.17–0.77	0.009
Patients whose oxygen saturation $\geq$ 92%	0.96	0.35–2.66	0.94
Patients whose oxygen saturation < 92%	0.71	0.51–0.98	0.038

Abbreviation: COVID-19, coronavirus disease 2019.

Patients with antibody had lower crude in-hospital mortality and lower rates of endotracheal intubation compared to those without (Table 1). The incidences of AKI were not significantly different between these two groups of patients.

After adjustment for patient characteristics and treatment, patients with positive COVID-19 antibody test had lower in-hospital mortality compared with those with negative test results (odds ratio [OR]: 0.68; 95% confidential interval [95% CI] 0.50–0.91,  $p = 0.01$ ) (Table 2). This relationship was confirmed after multiple imputations of missing data (OR [95% CI]: 0.52 [0.68–0.88]).

In the subgroup analyses, the positive antibody was associated with decreased risk of in-hospital mortality for patients with endotracheal intubation and hypoxia (Table 2).

The recent observational study demonstrated that COVID-19 antibody decreased the risk of reinfection.<sup>2</sup> Most of the infected patients with SARS-CoV-2 develop antibodies about 1 week after symptoms onset, with the antibodies persisting for at least 3 months.<sup>4</sup> Neutralizing antibodies targeting the SARS-CoV-2 spike protein is considered to provide protection against SARS-CoV-2.<sup>5</sup> However, it remains uncertain whether the detection of antibodies is associated with the decreased risk of in-hospital death. Our study is meaningful as we demonstrated that positive antibody is associated with decreased risk of in-hospital death but may not completely prevent it.

COVID-19 vaccine is not perfect to prevent infections and severe respiratory failure.<sup>1</sup> In addition, SARS-CoV-2 infection can be recurrent and there always remains a concern about seasonal infection of SARS-CoV-2 as not all individuals are likely to receive COVID-19 vaccines. Therefore, assessing the antibody at the time of

admission due to COVID-19 can be valuable for estimating the risk of death even though patients may be vaccinated or previously infected.

There are several limitations to our study. First, this is a retrospective observational study. Antibody test was performed based on physicians' decisions, not by study protocol, resulting in selection bias. Second, we do not have information about previous COVID-19 infections, symptoms onset, and previous vaccinations against COVID-19.

In conclusion, positive COVID-19 antibody test results were associated with a reduced risk of in-hospital mortality for COVID-19 patients.

#### AUTHOR CONTRIBUTIONS

Toshiki Kuno, Mai Takahashi, and Natalia N. Egorova had full access to all the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis. Study concept and design was done by Toshiki Kuno. Data curation by Toshiki Kuno, Mai Takahashi, and Natalia N. Egorova. Acquisition, analysis, or interpretation of data by all authors. Drafting of the manuscript was done by Toshiki Kuno. Critical revision of the manuscript for important intellectual content by all authors. Statistical analysis by Toshiki Kuno and Mai Takahashi. Administrative, technical, or material support by Natalia N. Egorova. Study supervision was conducted by Natalia N. Egorova.

#### ETHICS STATEMENT

This study was approved by the institutional review boards of Icahn School of Medicine at Mount Sinai (#2000495) and conducted in accordance with the principles of the Declaration of Helsinki. The

waiver of patients' informed consent was also approved by the institutional review boards.

#### DATA AVAILABILITY STATEMENT

Research data are not shared.

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