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SHORT COMMUNICATION

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Anti-SARS-CoV-2 IgG levels in relation to disease severity of COVID-19

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Abstract

The durability of infection-induced severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) immunity has crucial implications for reinfection and vaccine effectiveness. However, the relationship between coronavirus disease 2019 (COVID-19) severity and long-term anti-SARS-CoV-2 immunoglobulin G (IgG) antibody level is poorly understood. Here, we measured the longevity of SARS-CoV-2-specific IgG antibodies in survivors who had recovered from COVID-19 1 year previously. In a cohort of 473 survivors with varying disease severity (asymptomatic, mild, moderate, or severe), we observed a positive correlation between virus-specific IgG antibody titers and COVID-19 severity. In particular, the highest virus-specific IgG antibody titers were observed in patients with severe COVID-19. By contrast, 74.4% of recovered asymptomatic carriers had negative anti-SARS-CoV-2 IgG test results, while many others had very low virus-specific IgG antibody titers. Our results demonstrate that SARS-CoV-2-specific IgG persistence and titer depend on COVID-19 severity.

KEYWORDS

COVID-19, disease severity, IgG, SARS-CoV-2, serology

1 | INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can cause various outcomes that range from asymptomatic infection to serious pneumonia, acute respiratory distress syndrome, or multiple organ dysfunction, and even death.[1–7] The strength of infection-induced SARS-CoV-2 immunity has crucial implications for reinfection and vaccine effectiveness. However, the relationship between coronavirus disease 2019 (COVID-19) severity and long-term immunoglobulin G (IgG) antibody level is poorly understood. Here, we measured the longevity of SARS-CoV-2-specific IgG antibodies in survivors who had recovered from COVID-19 1 year previously.

2 | MATERIALS AND METHODS

This cohort study followed up 473 survivors of COVID-19 (including 43 individuals with asymptomatic infection) in Huanggang, Hubei, China from March 16 to March 28, 2021. These patients had been previously hospitalized from January 24 to March 18, 2020. The inclusion criteria were a previous COVID-19 diagnosis (positive reverse-transcription polymerase chain reaction result for SARS-CoV-2) and willingness and ability to provide informed consent. No SARS-CoV-2 reinfections occurred among the study population. Baseline demographic and laboratory examination results were extracted from electronic medical records.

According to the clinical manifestations, COVID-19 was classified as asymptomatic, mild, moderate, or severe (further details can be found in our previous work).[4] Serum IgG antibodies against recombinant SARS-CoV-2 nucleoprotein (N) and spike protein (S) were detected using a chemiluminescence method (AutoLumo A2000Plus; Autobio) according to the manufacturer's instructions. An antibody level of ≥1 signal to cut-off ratio (S/CO) was considered positive and a level of <1 S/CO was considered negative. Statistical analyses and preparation of figures were carried out using SPSS (SPSS Inc.) or Origin (OriginLab).

The study was approved by the Hunan Provincial People's Hospital Ethics Commission. All individuals provided written or verbal consent to participate.

3 | RESULTS

A total of 473 COVID-19 survivors participated in this study. Descriptive data for the study population are presented in Table 1. The median age was 52.5 years (standard deviation, 13.9 years); 190 patients (40.2%) were men and 283 patients (59.8%) were women. COVID-19 severity was categorized as asymptomatic (43/473, 9.1%), mild (21/473, 4.4%), moderate (356/473, 75.3%), or

TABLE 1 Characteristics of 473 survivors

Variable	All survivors (*n* = 473)	Asymptomatic cases (*n* = 43)	Mild cases (*n* = 21)	Moderate cases (*n* = 356)	Severe cases (*n* = 53)	*p* value[a]
Age, median (SD), y	52.5 ± 13.9	44.9 ± 12.7	54.2 ± 12.9	52.5 ± 13.8	57.9 ± 13.9	0.000
Age range, y						
0–19	4 (0.8)	0	0	4 (1.1)	0	0.004
20–39	87 (18.4)	18 (41.9)	3 (14.3)	59 (16.6)	7 (13.2)	
40–59	251 (53.1)	20 (46.5)	13 (61.9)	196 (55.1)	22 (41.5)	
60–79	120 (25.4)	5 (11.6)	5 (23.8)	88 (24.7)	22 (41.5)	
≥80	11 (2.3)	0	0	9 (2.5)	2 (3.8)	
Gender						
Male, no, (%)	190 (40.2)	13 (30.2)	7 (33.3)	146 (41.0)	24 (45.3)	0.414
Female, no, (%)	283 (59.8)	30 (69.8)	14 (66.7)	210 (59.0)	29 (54.7)	
The hospitalization days of discharged patients	NA	NA	8.8 ± 1.2	14.3 ± 4.2	23.9 ± 8.6	0.000
One-year after discharge IgG levels, S/CO						
<1, no, (%)	78 (16.5)	32 (74.4)	2 (9.5)	43 (12.1)	1 (1.9)	0.000
≥1, no, (%)	395 (83.5)	11 (25.6)	19 (90.5)	313 (87.9)	52 (98.1)	

Note: Data are mean (SD), or *n* (%), unless otherwise specified.

[a]Difference among all types. Differences of measurement data among asymptomatic cases, mild cases, moderate cases, and severe cases were compared with analysis of variance (ANOVA) and LSD for posthoc tests. The χ^2 test was used for categorical variables.

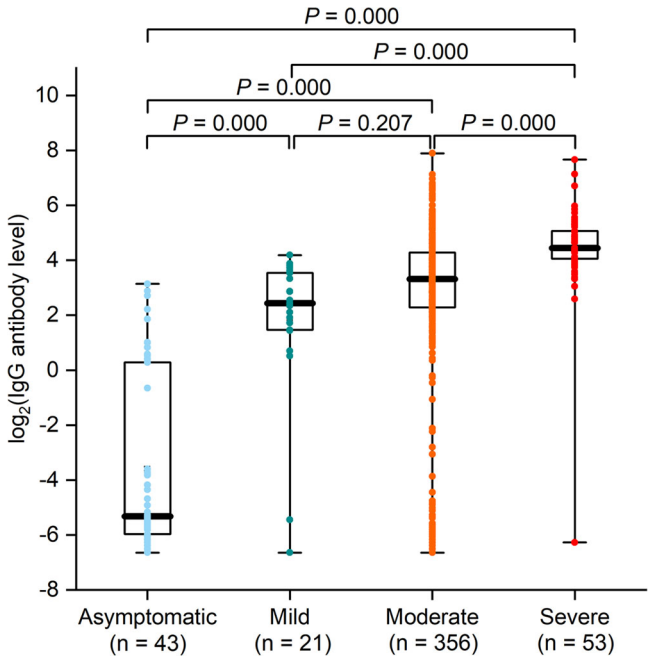

FIGURE 1 IgG antibody responses against SARS-CoV-2. Comparison of the level of IgG against SARS-CoV-2 between asymptomatic, mild, moderate, and severe patients. The boxplots show medians (middle line) and third and first quartiles (boxes), while the whiskers show 1.5× the interquartile range (IQR) above and below the box. Numbers of patients (*n*) are shown underneath. The results were expressed as mean {log2 (Fluorescence intensity)} ± SD in different groups. Analysis of variance (ANOVA) was conducted to test the difference in means among groups. IgG, immunoglobulin G

severe (53/473, 11.2%). The clinical characteristics of the survivors are shown in Table 1.

At 1 year post-discharge, only 25.6% (11/43) of patients with asymptomatic COVID-19 had detectable SARS-CoV-2-specific IgG. By contrast, 90.5% (19/21), 87.9% (313/356), and 98.1% (52/53) of patients with mild, moderate, and severe COVID-19, respectively, tested positive for SARS-CoV-2-specific IgG (Table 1). The SARS-CoV-2-specific IgG titers of patients with mild, moderate, and severe COVID-19 at 1-year postinfection were significantly higher ($p < 0.001$) than those of patients with asymptomatic infection (Figure 1). SARS-CoV-2-specific IgG antibody titers gradually increased with the increasing severity of COVID-19.

4 | DISCUSSION

In this observational study, we evaluated SARS-CoV-2-specific IgG in 473 survivors who had recovered from COVID-19 1 year previously. Titers of SARS-CoV-2-specific IgG varied substantially and were not detectable in 78 survivors.

We found that 74.4% of recovered asymptomatic carriers were negative for SARS-CoV-2-specific IgG, while those with positive test results had very low virus-specific IgG titers. By contrast, survivors who recovered from severe COVID-19 had relatively higher anti-SARS-CoV-2 IgG titers. Similar findings have been documented for other viral infectious diseases (e.g., SARS, middle east respiratory syndrome) whose etiologies involve a significant contribution of immunopathogenesis.[8,9]

The mechanism underlying the relationship between anti-SARS-CoV-2 IgG titers and COVID-19 severity remains unclear. Severe COVID-19, caused by excessive inflammation and/or uncontrolled SARS-COV-2 replication, may lead to overproduction of antibodies. Associations between COVID-19 severity and SARS-CoV-2 viral load in plasma, nasopharyngeal, and sputum specimens were identified in a previous study.[10] Patients with more severe symptoms had higher viral loads than patients with less severe symptoms, suggesting that the initial amounts of viral antigens may contribute to stronger serological responses. Our results indicate that SARS-CoV-2-specific IgG persistence and titers depend on COVID-19 severity.

The strong humoral response to SARS-CoV-2 may be linked to the excessive immune responses of serious COVID-19, which include cytokine storms involving interleukin-1 (IL-1), IL-6, and interferon-γ.[11,12] Selective B-cell plasmablast amplification in patients with severe COVID-19 may be associated with a stronger SARS-CoV-2-specific humoral response and a decrease in peripheral naive and memory B-cell counts.[13,14] Another potential mechanism could be induction of SARS-CoV-2-specific IgG responses by enhanced and prolonged B-cell receptor stimulation. In support of this hypothesis, enhanced B-cell receptor rearrangement has been observed in individuals with severe COVID-19.[15,16]

Our study had several limitations. We did not assess viral neutralization activity in serum. Therefore, the neutralization activity of SARS-CoV-2-specific IgG was unknown. Moreover, follow-up was only for 1 year; a longer follow-up period might have yielded different results. Further studies should focus on time-dependent changes in IgG levels and identification of survivors at risk of reinfection.

In conclusion, our results showed that SARS-CoV-2-specific IgG persistence and titer depend on COVID-19 severity. Further long-term studies are needed to determine the roles of SARS-CoV-2 specific T-cell responses in survivors and to determine whether individuals with asymptomatic infection are at increased risk of re-infection. Our results also indicate that collection of convalescent plasma from COVID-19 survivors for passive antibody therapy should be conducted in those with relatively severe symptoms.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Yimin Zhu, Xiaotong Han, Yong Zeng, and Xiquan Yan developed the research question and analysis plan. Xiquan Yan, Guoqiang Chen, Zhaoxia Jin, Zhongwei Zhang, Jiangming He, Siqing Yin, Bing Zhang, Juanshu Huang, Maiying Fan, Zhenyuan Li, Fang Chen, Yong Zeng, Xiaotong Han, and Yimin Zhu participated in data collection and clinical evaluations. Xiquan Yan, Guoqiang Chen, Zhaoxia Jin, and Zhongwei Zhang were involved in data analysis. All authors were involved in the final manuscript preparation.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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