

RESEARCH ARTICLE

Does the COVID-19 seroconversion in older adults resemble the young?

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Abstract

High antibody titers have been found to correlate with the severity of coronavirus disease 2019 (COVID-19) disease. Therefore, antibody titers may be higher in older adults, whose disease is known to have a more severe course than younger ones. This study aimed to compare the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) immunoglobulin G (IgG) antibody level in the reverse transcription-polymerase chain reaction (RT-PCR) to test positive older adults with young. Patients aged ≥ 18 with positive RT-PCR and checked serum IgG antibodies between November 1, 2020 and January 13, 2021 were included. The IgG antibody levels and the time between RT-PCR positivity with the antibody levels were recorded. A total of 1071 patients were divided into two groups as Group 1 <60 years old ($n = 902$) and Group 2 ≥ 60 years old ($n = 169$). The SARS-CoV-2 IgG antibody titers were higher in Group 2 ($p = 0.001$). This height was present in the first 3 months after positive RT-PCR. While the antibody titers were compared by dividing Group 2 into the three groups according to age ranges (60–69, 70–79, and ≥ 80 years), the antibody titer was higher in ≥ 80 years patients ($p = 0.044$). High COVID-19 IgG antibody levels may be associated with the severity of the disease. Also, the humoral immunity advantage was seen in the first 3 months in the older patients, which suggests that older adults with COVID-19 may develop reinfection in the long term.

KEYWORDS

antibody, COVID-19, older adults, SARS-CoV-2, seroconversion

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19), which started in Wuhan in December 2019 and occurred due to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) factor, affected the world in a short time. Declared as a pandemic by World Health Organization on March 11, 2020.¹ The disease, known to be transmitted by droplets and contact, may occur with asymptomatic or mild symptoms, as well as critical diseases, such as sepsis, multiorgan failure, and severe respiratory failure.² The virus has an incubation period of 5–6 days (may extend from 2 to 14 days).³ Scientific studies have reported

that older adults are the most affected group by COVID-19, due to frailty and comorbidities, and they have higher morbidity and mortality.⁴

Serological testing for SARS-CoV-2 is now widely used. Detection of anti-SARS-CoV-2 antibodies (Abs) can be useful to confirm the presence of current or past infection.⁵ It has been found that some patients with undetectable ribonucleic acid (RNA) may be screened with the antibody test even in the early stages of the disease. The combination of RNA and antibody tests significantly increases the sensitivity of detecting patients.⁶ The serological testing for COVID-19 is recommended in three indications: (1) assessment

of patients with high clinical suspicion for COVID-19 with negative molecular diagnostic tests and at least 2 weeks after symptom onset; (2) evaluation of multisystem inflammatory syndrome in children; and (3) for conducting serosurveillance studies.⁷

There are two general types of Abs, neutralizing antibodies (nAbs) and nonneutralizing Abs (also known as binding Abs).⁸ Neutralization is defined as the that a nAbs binds to a viral particle and loses its infectivity. Vaccine studies are conducted on nAbs and may play an important role in controlling viral infection.⁹ However, whether individuals with anti-SARS-CoV-2 nAbs are protected against reinfection has not yet been proven by firm data. Anti-SARS-CoV-2 antibody (Ab) tests are used in routine clinical practice to measure immunoglobulin M (IgM), immunoglobulin G (IgG), or total Ab. nAbs are mostly measured for scientific researches.

During the course of COVID-19, IgM and IgG type Abs are occurring.¹⁰ The data about SARS-CoV-2 indicate that less than 40% of these Abs were encountered in the first week, and the rate of Abs in the first 15 days was 94.3% (IgM) and 79.8% (IgG).⁶ Also, it has been reported that IgM started to decrease after the third week.¹¹ Detection of IgG or total Ab 3–4 weeks after the onset of symptoms provides the highest sensitivity and the lowest rate of false-negative results compared to other immunoglobulin classes.⁷

It has been reported that IgG and IgM titers are higher in patients with severe COVID-19 disease than in nonsevere patients, but only a significant increase in IgG titer 2 weeks after symptom onset.¹¹ Asymptomatic COVID-19 infections have a weaker immune response and a faster and greater reduction of IgG (nAbs).¹¹ Besides, it was reported that as the severity of the disease increased, higher levels of nAbs were detected.¹² These findings support that serological tests may be an important complement to RNA detection during the course of the disease and maybe a good indicator of disease severity.

In this study, we aimed to compare the levels of IgG Ab against SARS-CoV-2 in the reverse transcription-polymerase chain reaction (RT-PCR) to test positive older adults with younger adults and investigate the relationship between elapsed time after the positive COVID-19 RT-PCR test and IgG Ab levels.

2 | METHODS

2.1 | Study design and participants

The study protocol was permitted by the Biruni University Faculty of Medicine Ethics Committee and the Ministry of Health. The study was completed according to the mandates of the Helsinki Declaration. All patients were given full information about the study procedures before providing written consent.

The files of patients older than 18 years of age who admitted to the outpatient clinics of Internal Medicine and Pulmonary Diseases departments between November 1, 2020, and January 13, 2021, and who were positive for COVID-19 clinical findings (fever, cough,

muscle pain or fatigue, dyspnea, headache, diarrhea, taste and smell disorders) and COVID-19 RT-PCR test between March 18 and October 31, were retrospectively reviewed. These patients, who voluntarily checked COVID-19 serum IgG Abs between November 1, 2020, and January 15, 2021 (when vaccination applications started in our country), were included in the study. The elapsed time between the dates when serum IgG levels were measured with the positive COVID-19 RT-PCR test and Ab titers were recorded. Patient age, sex, and comorbidities were recorded. The patients with psychiatric problems, using steroids or immunosuppressive drugs, and immunosuppressive illness were excluded.

2.2 | Measurements and data collection

We collected 2 ml of venous blood from each participant between September 1 and December 31, 2020. Blood samples were tested within 4 h after blood collection at room temperature. We used an immunofluorescence assay (IFA), using COVID-19 IgG Ab IFA fast test kits (IF2084 for Getein 1600; Getein Biotech, Inc.), to evaluate the presence of serum IgG Ab against SARS-CoV-2, in accordance with the manufacturer's instructions. Briefly, each cartridge for Getein 1600 contains a specific RFID card that can calibrate automatically. Put the sample diluent at the correct position in Getein 1600, place samples in the designed area of the sample holder, insert the holder and select the right test item, Getein 1600 will do the testing and print the result automatically. The test result is displayed numerically in terms of the cut-off index (COI) value. The test result is negative for COI <1.0 and positive for COI ≥1.0.

2.3 | Statistical analysis

Our study was a retrospective cross-sectional study. The fit to a normal distribution of all data was analyzed using the Kolmogorov–Smirnov test. Categorical variables are presented as percentages, while continuous variables are presented as mean ± SD. Categorical variables were analyzed using the χ^2 test, while continuous variables in two-way groups were analyzed using the *t* test. An analysis of variance was utilized to compare multiple group means. The following post hoc evaluation was made by the Bonferroni method. Pearson's correlation was used for the numerical data. All data were tested using the SPSS 20.0 (SPSS) software, and values of *p* < 0.05 were considered statistically significant.

3 | RESULTS

A total of 1071 (female/male 449/622, mean age 42.8 ± 15.6 years) patients were included in our study. Patients below 60 years old were named as Group 1 (*n* = 902) and patients 60 years

and over were named as Group 2 ($n = 169$). The mean age of the Group 1 was 37.7 ± 10.6 , and the mean age of the Group 2 was 70.2 ± 8.1 . There was no significant difference between the groups in terms of gender and smoking history. Hypertension, Type 2 diabetes mellitus, chronic obstructive pulmonary disease/asthma, hyperlipidemia, and coronary artery disease were significantly higher in Group 2 than in Group 1 (p value of all < 0.001) (Table 1).

The count of RT-PCR was similar for screening of symptoms resembling COVID-19 until positivity. There was no difference between Groups 1 and 2 in terms of Ab positivity (Table 1). However, the COVID-19 IgG Ab titers were meaningfully higher in Group 2 ($p = 0.001$) (Figure 1).

As a result of our analysis, we found that the number of patients who checked their COVID-19 IgG Ab levels in the first month after the RT-PCR test positivity was quite high ($n = 749$), while the number of patients who checked it in the 8th month was very low ($n = 13$) (Table 2). Also, the IgG Ab titers of the patients in Group 2 in the first, second, and third months were found to be significantly higher than the patients in Group 1 ($p = 0.017$, $p = 0.002$, $p = 0.029$, respectively) (Table 2).

We compared the levels of Ab titers by dividing Group 2 patients into three groups as 60–69 years ($n = 92$), 70–79 years ($n = 51$), and ≥ 80 years ($n = 26$). The mean Ab titers were 42.5 ± 17.6 , 44.4 ± 17.7 , 52.9 ± 24.2 , respectively, and considerably higher in ≥ 80 years old patients ($p = 0.044$). Also, there was a positive correlation between age and Ab titers ($p < 0.001$, $r = 0.117$) (Figure 2).

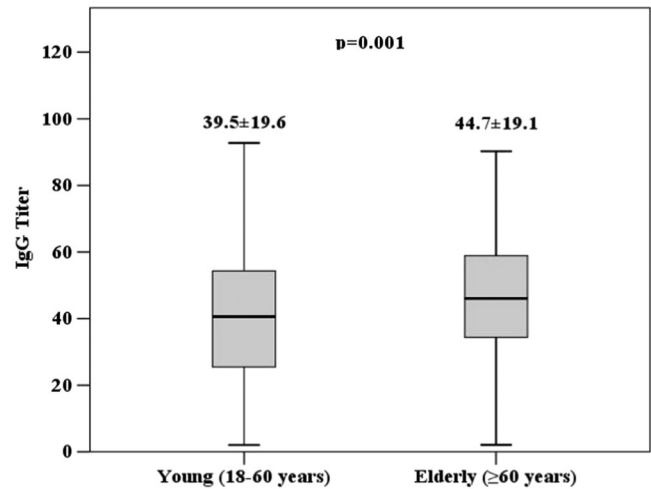


FIGURE 1 The titers of IgG antibody to SARS-CoV-2 in the young and older patients. IgG, immunoglobulin G; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

4 | DISCUSSION

In this study, comparing COVID-19 IgG Ab levels in young and older adults, IgG Ab titers to SARS-CoV-2 were found to be meaningfully higher in older adults. When the relationship between IgG Ab levels and elapsed time after the positive COVID-19 RT-PCR test was investigated, it was seen that the mean IgG Ab titer was higher in older

TABLE 1 The demographic characteristics, comorbidities, RT-PCR testing, and immunoglobulin G antibody titers to SARS-CoV-2 in the studied groups

	All patients ($n = 1071$)	Group 1 (18–59 years) ($n = 902$)	Group 2 (≥ 60 years) ($n = 169$)	p
Age (years)	42.8 ± 15.6	37.7 ± 10.6	70.2 ± 8.1	<0.001
Gender (female)	449 (41.9)	382 (42.4)	67 (39.6)	0.552
Smoking	303 (28.3)	265 (29.4)	38 (22.5)	0.077
Comorbidities				
Hypertension	414 (38.7)	297 (32.9)	117 (69.2)	<0.001
Diabetes mellitus	216 (20.2)	134 (14.9)	82 (48.5)	<0.001
COPD/Asthma	131 (12.2)	99 (10.9)	32 (18.9)	<0.001
Hyperlipidemia	120 (11.2)	61 (6.8)	59 (34.9)	<0.001
Coronary artery disease	117 (10.9)	67 (7.4)	50 (29.6)	<0.001
Count of RT-PCR screening for symptoms resembling Covid-19 until positivity	2.2 ± 2.4	2.3 ± 2.5	2 ± 2	0.201
IgG antibody positivity	1064 (99.3)	897 (99.4)	167 (98.8)	0.305
IgG antibody titer	40.3 ± 19.6	39.5 ± 19.6	44.7 ± 19.1	0.001

Note: Significant p values are indicated in bold.

Abbreviations: COPD, chronic obstructive pulmonary disease; IgG, immunoglobulin G; RT-PCR, reverse transcription-polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

	<i>n</i>	All patients (<i>n</i> = 1071)	Group 1 (18–59 years) (<i>n</i> = 902)	Group 2 (≥60 years) (<i>n</i> = 169)	<i>p</i>
1st month	749	39.3 ± 19.6	38.7 ± 19.4	44.2 ± 20.3	0.017
2nd month	165	47.2 ± 18.8	44.9 ± 18.6	55.6 ± 17.3	0.002
3rd month	54	43.7 ± 17.6	40.9 ± 17.8	53.3 ± 13.4	0.029
4th month	22	37.8 ± 19.1	35.5 ± 23.5	41.9 ± 6.3	0.455
5th month	33	28.6 ± 15.5	26.9 ± 20.4	30.6 ± 5.9	0.514
6th month	17	25.7 ± 7.8	24.2 ± 1.6	27.3 ± 11.5	0.475
7th month	18	43.5 ± 20.3	43.3 ± 21.1	43.8 ± 20.5	0.967
8th month	13	41.1 ± 26.7	31.5 ± 15.4	42.8 ± 28.5	0.602

Note: Significant *p* values are indicated in bold.

Abbreviations: IgG, immunoglobulin G; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

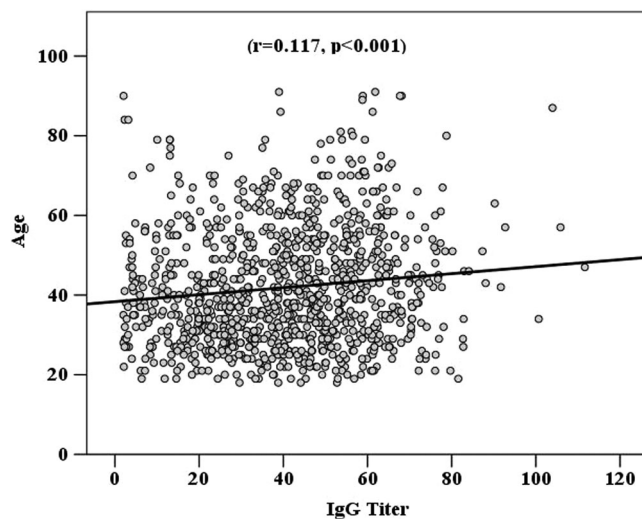


FIGURE 2 The relationship between the age and IgG antibody titers to SARS-CoV-2. IgG, immunoglobulin G; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

adults all 8 months, but this difference was significant only in the first 3 months.

There are publications in the literature reporting that high Ab levels are associated with the severity of the COVID-19.^{13,14} In a study in which critical and noncritical COVID-19 patients were compared, found that the average Ab levels showed a marked increase since about 1 week after onset and continuously elevated during the next 2 weeks. While there was no difference between critical and noncritical patients during the first 12 days, Ab titers were higher in critically ill patients after the 12th day.⁶ The higher Ab titers in Group 2 in our study may be explained by the more severe COVID-19 of older adults. Since our study is retrospective, we do not have sufficient information on whether the patients need hospitalization, intensive care unit, and mechanical

TABLE 2 The titers of IgG antibody to SARS-CoV-2 according to months in the studied groups

ventilation. If we could strengthen the results with these data, we would have supported our hypothesis more. Many studies have reported that the mortality and morbidity of the disease are higher in older adults.^{15–17} The positive correlation between age and Ab titer level, and when Group 2 was classified among themselves, the highest average Ab titer level of patients aged ≥80 years explains this situation more clearly.

A study in the literature, evaluating the association of clinical characteristics with neutralizing Ab levels in patients who have recovered from COVID-19, reported that older adults had significantly higher nAb titers than younger patients.¹⁸ While older adults are expected to have a lower immune response due to immunocenes, it suggests that high nAb levels may be the result of strong inflammation or innate immune response. Also, in our study, the fact that the comorbidities were significantly higher in Group 2 than in the Group 1 may have led to a more severe course of COVID-19 in older adults and the resulting high Ab titers.

In our study, in the comparisons of IgG Ab titers in young and older adults made according to the time elapsed after RT-PCR positivity, it was observed that IgG Ab titers in the older patients were significantly higher in the first 3 months compared to the young adults. However, it was seen that this significance disappeared in the following months. One of the reasons for this may be the low number of patients whose Ab levels are checked after the third month. Additionally, one study showed that patients who recovered rapidly from symptomatic COVID-19 had higher Ab levels for a longer duration.¹⁹ Older adults are more likely to experience COVID-19 complications than younger people, and therefore recovery times are longer.¹⁵ Hence, another reason for the disappearing higher Ab levels significance after the 3rd month in our study may be that the Ab levels remained higher for a longer period of time because the youth recover rapidly than older. This result suggests that the older patients with COVID-19 may susceptible to re-infection in the long term.

Our study has some strengths and limitations. The initial strength of our study, the number of patients whose Ab levels have been checked is high. Meanwhile, according to our knowledge, this is the first study to compare the older and young Ab titers according to

the time elapsed after positive RT-PCR. The limitations of our study are that the number of patients in the older and young groups is not homogeneous and the number of patients who had Abs checked after 3rd months is low. Also, the correlation between age and IgG antibody levels in the older group is not high. Stronger data may be needed to say that this correlation is significant. Another deficiency of our study is that we could not check the neutralizing COVID-19 Abs because nAbs are not used routinely except for scientific studies in our country and our study is retrospective. Our findings need to be confirmed by future studies conducted with a more extensive patient cohort.

5 | CONCLUSION

In this study, where we compared the IgG Ab levels to SARS-CoV-2 in COVID-19 RT-PCR to test positive older adults with younger adults, and we investigated the relationship between time after illness onset and IgG Ab levels, we found that the mean IgG Ab titer was higher in older adults, but this situation disappeared after the 3rd month. These results support that high levels of IgG Abs to SARS-CoV-2 may be associated with the severity of the disease. Additionally, the advantage of humoral immunity seen in the first 3 months in the older patients is not continuing after the 3rd month. This suggests that reinfection may develop in the long term in older adults with COVID-19.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Rabia Bag Soytaş, Mahir Cengiz, Hakan Yavuzer, and Serap Yavuzer: Conceptualization and design of the study. **Mehmet Sami Islamoglu, Betül Borku Uysal, and Hande İkitimur:** Statistical analysis and interpretation of data. **Rabia Bag Soytaş, Hakan Yavuzer, and Serap Yavuzer:** Writing the first draft of the manuscript. **Hakan Yavuzer and Serap Yavuzer:** Revised the article. All authors reviewed and approved the final manuscript.

PEER REVIEW

The peer review history for this article is available at <https://publons.com/publon/10.1002/jmv.27106>

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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