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Research Article

Assessment of the therapeutic effect and subsequent immune response in the treatment of COVID-19 with anti-SARS-CoV-2 monoclonal antibodies

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Abstract

Introduction: Over the past three decades, monoclonal antibodies have undergone a remarkable transformation—from a research tool to powerful therapeutic agents in medical practice. The monoclonal antibodies currently used in clinical practice are immunoglobulins of the "G" class (IgG).

Objective: The aim of the study is to analyze and evaluate the effect of treatment with monoclonal anti-SARS-CoV-2 IgG in patients with moderate to severe forms of complicated coronavirus infection.

Materials and methods: The study included 530 patients, of whom 243 were women and 287 were men, aged between 18 and over 80 years, who received monoclonal antibodies (mAbs) as part of their therapeutic regimen for the treatment of COVID-19. In parallel with them, the course of the disease was monitored in a control group of 255 patients (104 women and 151 men), hospitalized in the target period and not treated with mAbs.

Results: Patients treated with monoclonal antibodies within 7 days of symptoms had a shorter hospital stay compared to those treated later and to the control group. Oxygen therapy and intubation rates were significantly lower for those who received treatment early. Mortality rates were 0.42% for early treatment, 3.45% for late treatment, and 4.71% in the control group.

Conclusion: Specific monoclonal antibodies are currently the most effective safe treatment for life-threatening viral infections, supporting passive immunization as a preferred strategy against epidemics. A strong immune response is evident in treated patients by the end of the first year post-discharge. Early administration significantly reduces mortality compared to controls.

Keywords

Monoclonal antibodies, passive immunization, mAb, COVID-19, treatment, polymorbid patients, hospital stay, mortality, residual fibrosis, immunogenesis

Introduction

Over the past three decades, monoclonal antibodies (mAbs) have undergone a remarkable transformation—from being primarily research tools to becoming increasingly potent therapeutic agents in medical practice (Singh et al. 2018). Monoclonal antibodies are immunoglobulins of the IgG class (Buss et al. 2012). These antibodies, produced in this class, possess specific properties and advantages, including optimal pharmacokinetics (stability), selective pharmacodynamics, low isoimmunization activity (especially recombinant mAbs), a low toxicity profile, and scalable production for various mAbs targeting diverse antigens (Castelli et al. 2019; Malik and Ghatol 2025).

The use of monoclonal antibodies for the treatment of infectious diseases is relatively novel compared to their application in oncology and autoimmune diseases (Desoubeaux and Pelegrin 2019). Monoclonal antibodies are increasingly being utilized in the treatment of viral infections due to their ability to prevent disease progression immediately upon administration and to enhance recovery processes, regardless of whether the patient has developed an effective endogenous immune response. Due to their high specificity and multifunctionality, monoclonal antibodies are at the forefront of the therapeutic arsenal for COVID-19 treatment. They have been identified as a potentially successful therapy for preventing the progression of COVID-19 in high-risk patients prone to developing severe disease (Hwang et al. 2022).

Despite the currently conflicting opinions regarding their use, their effects on immunogenesis, and their protective role in the event of re-exposure to the virus, monoclonal antibodies were included in the therapeutic regimen for COVID-19 patients at the University Emergency

Hospital "N.I. Pirogov" in November 2021. Patients treated with monoclonal antibodies were monitored over a one-year period following administration. The effects of mAbs on disease progression were assessed using indicators such as average hospital stay, pulmonary and other organ or system complications, oxygen therapy requirements (non-invasive and invasive mechanical ventilation), mortality, and post-discharge outcomes. Additionally, individual immunogenesis (as a result of the infection) following the use of monoclonal antibodies was meticulously tracked over a one-year period.

Since the outbreak of the coronavirus pandemic in early 2020, health services have mobilized their resources primarily towards finding means of prevention, prophylaxis, and treatment of COVID-19. Their main objective has been to limit the spread of the disease, reduce complications, and minimize the consequences of the illness. Although more than three years have passed since the onset of the pandemic, there is still no unified and established standard for treatment. The vaccines introduced as preventive measures against infection, virus spread, and milder disease progression have not proven fully effective against all viral variants. While vaccine development typically takes up to ten years, exceptions are made in public health emergencies, such as the COVID-19 pandemic. However, even in such emergencies, the "First Principle of Medical Ethics" must be respected: "Primum non nocere" (First, do no harm). The period from the pandemic's onset has been marked by chaotic and often contradictory changes in treatment recommendations. This situation, driven by regulatory bodies of national health systems, placed clinical teams in one of the most challenging circumstances in recent decades. Numerous measures and medications were proposed, only to be later rejected or dismissed, creating conditions that bordered on "pharmaceutical speculation," rather than focusing efforts on the most biologically logical solution—passive immunization, or treatment with monoclonal antibodies (mAbs). Monoclonal antibodies continue to be the subject of extensive research as a potential favorable outcome for COVID-19 infection. They are particularly suited for high-risk, polymorbid patients with a positive PCR test for SARS-CoV-2, who are at risk of complications (Boivin et al. 2008).

Objective

Despite the ongoing debate regarding their use, impact on immunogenesis, and their protective role in reinfection, monoclonal antibodies have been included in the therapeutic regimen for COVID-19 patients at University Hospital "N. I. Pirogov" since November 2021. Patients treated with monoclonal antibodies were followed up for one year post-treatment, with the aim of the study focusing on several main aspects—proving their safety profile, the clinical and postclinical effect of treatment with MABs, and their influence on the intensity and durability of the immune response in patients from the target group within a one-year period after discharge. The effects of monoclonal antibodies on the course of the disease were assessed using the following parameters: average hospital stay, complications affecting the lungs and other vital organs, need for oxygen therapy (both non-invasive and invasive mechanical ventilation), mortality, and any complications after discharge. Immunogenesis following the use of monoclonal antibodies in the treatment of moderate and severe forms of complicated COVID-19 infection was closely monitored over

the course of one year. The findings of such studies are crucial for understanding the role of monoclonal antibodies in COVID-19 treatment, not only in controlling the infection but also in potentially enhancing long-term immunity in patients, helping to improve clinical outcomes.

Materials and methods

The study included 530 patients, of whom 243 were women and 287 were men, aged between 18 and over 80 years, treated with monoclonal antibodies (MABs) as part of the therapeutic regimen for COVID-19. In parallel, a control group of 255 patients (104 women and 151 men) hospitalized during the target period and not treated with MABs was also monitored. All patients were hospitalized and treated at the University Emergency Hospital "N.I. Pirogov" from 4 November 2021 to 31 March 2022.

Among patients treated with monoclonal antibodies, 80.94% (429 patients) had more than two comorbidities. The most prevalent comorbidities were cardiovascular diseases, present in 54.15% (287 patients). This group included patients with arterial hypertension, ischemic heart disease, chronic congestive heart failure, a history of acute myocardial infarction, dyslipidemias, rhythm and conduction disorders, and those with valve prostheses. Respiratory diseases (such as chronic obstructive pulmonary disease, asthma, and sleep apnea) were observed in 37.92% (201 patients). Endocrine diseases, predominantly type 1 and type 2 diabetes mellitus, were present in 40.94% (217 patients). Oncological conditions were identified as comorbidities in 10.94% (58 patients), underscoring their inclusion as an indicator for MAB therapy. Gastrointestinal, neurological, hematological, and nephrological diseases (e.g., acute kidney injury or terminal chronic kidney failure requiring hemodialysis) were documented in 17.92% (95 patients).

All patients treated with monoclonal antibodies had confirmed positive PCR tests for SARS-CoV-2 (including positive serum PCR tests) and comorbidities, which were identified as risk factors for progression to severe COVID-19.

The first monoclonal antibody regimen used was a combination of casirivimab and imdevimab. The second product administered was regdanvimab, a recombinant human IgG1 monoclonal antibody. Based on a benefit-risk analysis for each patient, these therapies were administered as a single intravenous infusion. Subsequently, treatment for COVID-19 was continued according to the therapeutic protocol of the University Emergency Hospital "N.I. Pirogov," based on clinical symptoms, laboratory results, and imaging findings. Patients treated with monoclonal antibodies were divided into two subgroups: those who received the medication within 7 days of symptom onset (472 patients) and those who received it after 7 days (58 patients). Significant differences were observed between these groups in terms of average hospital stay, subsequent oxygen therapy requirements, intubation rates, and mortality.

Results

The average hospital stay (Table 1) for the control group was 2.15 times longer than for patients treated with monoclonal antibodies within 7 days of symptom onset. A longer hospital stay increases treatment costs and places a greater burden on healthcare facilities. Additionally, prolonged hospitalization poses a higher risk of nosocomial infections for patients.

Table 1. Average hospital stay in the control and target groups.

	Average hospital stay
Patients treated with monoclonal antibody up to day 7 of first symptoms	8.8 days
Patients treated with monoclonal antibody after 7 days from first symptoms	14.5 days
Control group of patients	19 days

The need for oxygen therapy (Table 2), non-invasive ventilation, and invasive mechanical ventilation is a key criterion for determining the severity of COVID-19 infection. Among the control group, 63.14% of patients (161 out of 255) required oxygen therapy, compared to only 6.78% (32 out of 472) of patients who received monoclonal antibodies during the early stages of their COVID-19 infection. The intubation rate in the control group was 13 times as high as that observed in patients treated with monoclonal antibodies. This disparity implies not only greater consumption of material resources but also significant demands on human resources. A higher intubation rate correlates with longer hospital stays, increased treatment costs, and, most importantly, a higher likelihood of unfavorable outcomes.

The mortality rate (Fig. 1) among the control group of patients with a positive PCR test for SARS-CoV-2 who did not receive monoclonal antibodies as part of their therapeutic regimen was 11 times higher compared to patients who received monoclonal antibodies within the first seven days of symptom onset. Mortality appears to be the most definitive indicator of the role of monoclonal antibodies in treating COVID-19 infection in patients with comorbidities and an expectedly more severe disease progression. The beneficial effect of monoclonal antibodies is evident even in patients who received casirivimab/imdevimab or regdanvimab after the seventh day of

Table 2. Proportional representation of non-invasive and invasive oxygen therapy in the control and target groups.

	Patients on oxygen therapy and non-invasive ventilation	Intubated patients on mechanical ventilation
Treated with monoclonal antibody by day 7 of first symptoms	6.78% (32 out of 472 patients)	0.64% (3 out of 472 patients)
Treated with monoclonal antibody after 7 days from first symptoms	55.17% (32 out of 58 patients)	6.90% (4 out of 58 patients)
Control group	63.14% (161 out of 255 patients)	8.24% (21 out of 255 patients)

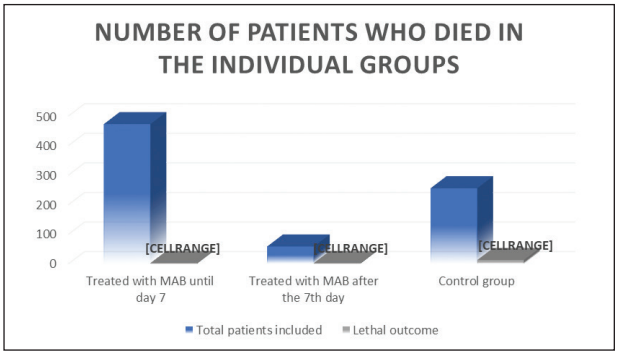

Figure 1. Hospital mortality in the control and target groups.

symptom onset. Among these patients, the mortality rate was 1.36 times lower than in the control group.

Patients with prolonged hospital stays, severe disease progression requiring oxygen therapy, chronic illnesses, or immunocompromised status are more frequently and persistently affected by post-COVID-19 conditions. The most common symptoms of post-COVID-19 syndrome include general fatigue, dyspnea, tachypnea, cough, headache, and "brain fog" (difficulty concentrating). Persistent changes in the lung parenchyma are among the consequences of severe atypical pneumonia caused by COVID-19. Since most symptoms characteristic of post-COVID-19 conditions are subjective and difficult to measure for accurate comparison, our study focused on residual fibrosis in the study groups. Residual fibrosis was assessed through follow-up imaging studies (lung CT scans) performed during each follow-up examination.

Among patients treated with monoclonal antibodies within seven days of symptom onset who developed atypical pneumonia, 54 (11.44%) showed lung parenchymal involvement of up to 50%. Of these, two patients (0.42%) died. At the one-year follow-up, only one patient (0.21%) from this group exhibited residual fibrosis after recovering from COVID-19. In contrast, in the control group, eight patients (3.14%) presented with residual fibrosis and signs of respiratory insufficiency. Among patients who received monoclonal antibodies after seven days of symptom onset, residual fibrosis was identified in two individuals (3.45%).

An important question that remains unanswered is whether the use of monoclonal antibodies might compromise the natural course of immunogenesis in patients recovering from COVID-19 infection. For a medication to be considered effective in treating COVID-19, it must meet the following criteria: a safe profile, good tolerability, and no suppression of the development of a robust immunogenic response, which is the most reliable protective mechanism against SARS-CoV-2 reinfection.

Patients were monitored for one year after receiving monoclonal antibodies (casirivimab/imdevimab or regdanvimab), alongside a control group. Follow-up examinations after hospital discharge were conducted at the third, sixth, and twelfth months. During these follow-ups, blood samples were collected to assess the presence of SARS-CoV-2 antibodies (IgG and IgTotal). Chemiluminescent immunoassay (CLIA) and enzyme-linked immunosorbent assay (ELISA) were used to quantify anti-SARS-CoV-2 IgG and anti-SARS-CoV-2 IgTotal antibodies.

To more accurately evaluate immunogenesis following COVID-19 infection and monoclonal antibody therapy, patients were divided into four age groups as follows: 18–45 years, 46–65 years, 66–80 years, and over 80 years (Table 3).

Table 3. Age distribution of the control and target groups.

	18–45 years old	46–65 years old	66–80 years old	over 80 years old
Patients who received a monoclonal antibody	157	212	105	56
Control group	77	98	59	21

The dynamics of anti-SARS-CoV-2 IgG levels across the age groups treated with Casirivimab/Imdevimab (Fig. 2) demonstrate maximum values (technologically limited by the respective assay) in the first month following hospital discharge. A declining trend in antibody levels is observed by the third month post-discharge, which is most pronounced in patients over 80 years of age. However, these levels remain within the range of epidemiological effectiveness, as no reinfections were recorded during the one-year follow-up period.

Fig. 3 illustrates the increase in anti-SARS-CoV-2 IgTotal levels across all four age groups throughout the one-year follow-up period in patients treated with Casirivimab/Imdevimab.

Monitoring of anti-SARS-CoV-2 IgG levels in patients treated with Regdanvimab over a one-year period shows a minimal decline across all four age groups (Fig. 4).

The follow-up of anti-SARS-CoV-2 IgTotal levels in patients treated with Regdanvimab within the target pe-

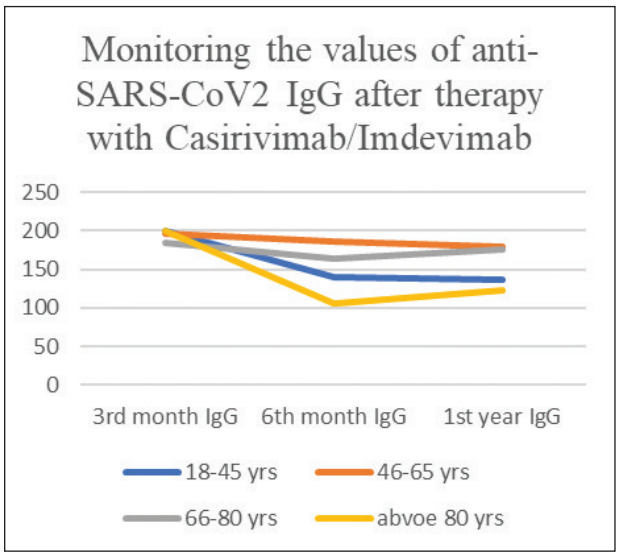

Figure 2. One-year anti-SARS-CoV-2 IgG dynamics in those treated with Casirivimab/Imdevimab.

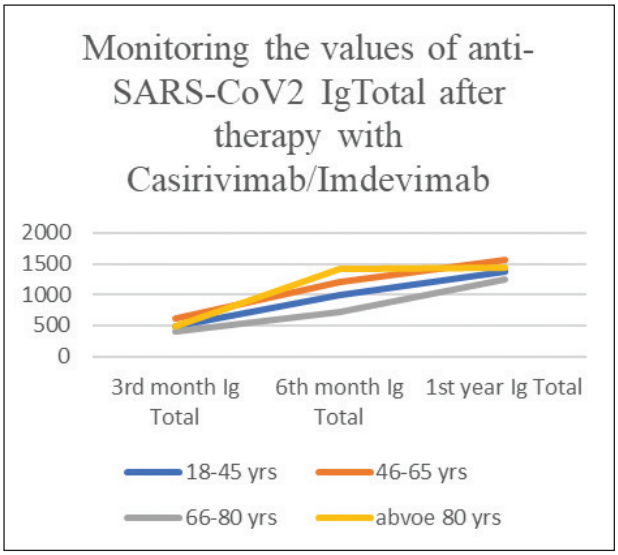

Figure 3. One-year anti-SARS-CoV-2 IgG Total dynamics in age groups.

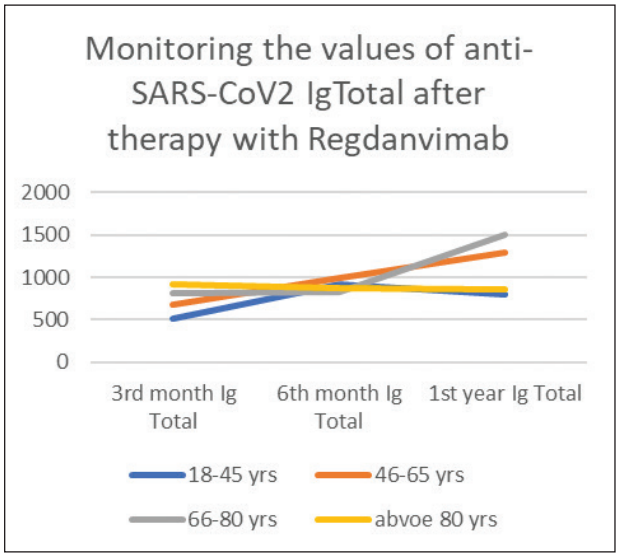

Figure 5. One-year anti-SARS-CoV-2 IgTotal dynamics in the target age groups.

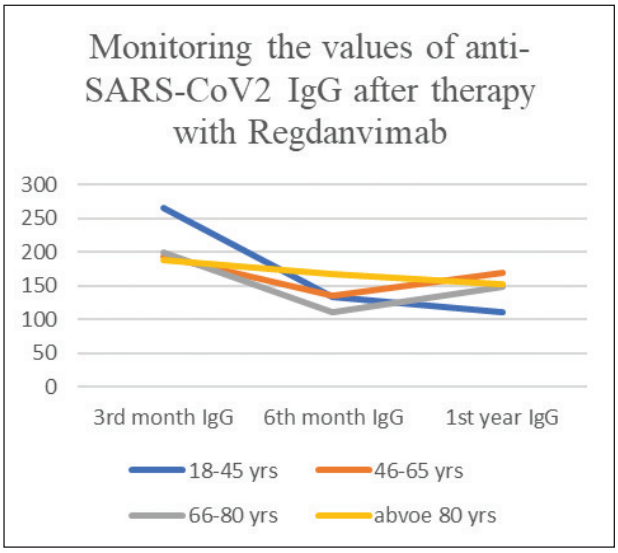

Figure 4. One-year anti-SARS-CoV-2 IgG dynamics in the target age groups.

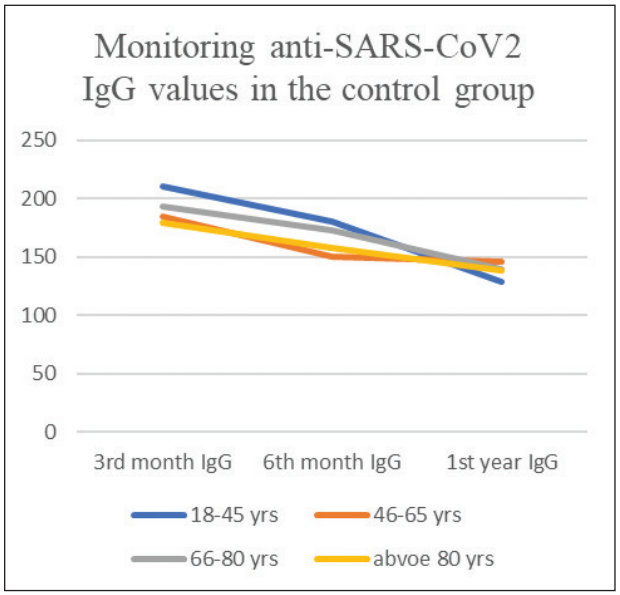

Figure 6. One-year anti-SARS-CoV-2 IgG dynamics in the control group by age.

riod reveals a distinct upward trend, most notably in the 46–65 and 66–80 age groups. In the other two age groups, anti-SARS-CoV-2 IgTotal levels remain consistently high after the sixth month of follow-up, forming a plateau-like pattern on the graph (Fig. 5).

In patients not treated with monoclonal antibodies (control group), a decline in anti-SARS-CoV-2 IgG levels was observed across all age groups during the first year of follow-up, as expected. This trend correlates with the findings from a previous study conducted by our team (Fig. 6).

In the control group of patients not treated with monoclonal antibodies (mAbs), an increase in the levels of anti-SARS-CoV-2 IgTotal was observed across all age groups (Fig. 7). These results correlate with findings from our previous study, which tracked immunogenesis in patients who experienced moderate to severe forms of complicated coronavirus infection.

Discussion

During the period from hospital discharge to the first-year follow-up, no patients were rehospitalized due to a SARS-CoV-2 infection due to a PCR-confirmed SARS-CoV-2 reinfection. This finding applies both to the control group and patients who received monoclonal antibody treatment. Differences were noted in the levels of anti-SARS-CoV-2 IgG and anti-SARS-CoV-2 IgTotal between the patient groups and among different age groups.

The role of immunity following recovery from moderate or severe coronavirus infection is to prevent reinfection and severe illness. This protection is maintained regardless of the quantity of antibodies produced.

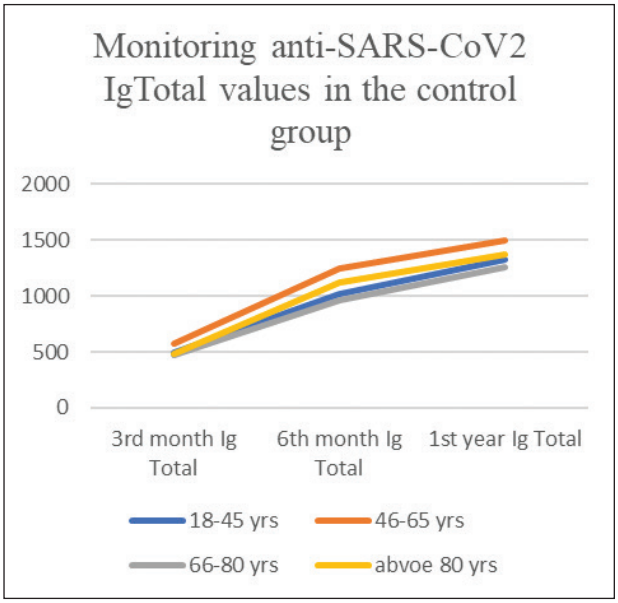

Figure 7. One-year anti-SARS-CoV-2 IgTotal dynamics in the control group by age.

This study advances our understanding of this field in several significant ways:

1. The safety profile of anti-SARS-CoV-2 monoclonal antibodies (casirivimab combined with imdevimab, as well as regdanvimab as a standalone agent) has been clearly established for treating moderate and severe COVID-19 cases in clinical practice.
2. A robust protective immune response has been conclusively demonstrated in all patients treated with monoclonal antibodies by the end of the first year following their hospital discharge.
3. It has been clearly shown that administering anti-SARS-CoV-2 monoclonal antibody therapies within the first seven days of symptom onset significantly reduces mortality rates compared to control groups that did not receive such treatments.
4. The study strongly supports the notion that, at present, the only effective treatment for life-threatening viral infections is specific monoclonal antibodies. The rapid development and deployment of the first anti-SARS-CoV-2 monoclonal antibody therapies, along with their impressive efficacy, undeniably bolster the argument that passive immunization is currently the preferred strategy in combating life-threatening viral diseases with epidemic potential.

Conclusion

Based on the results observed, several conclusions can be drawn regarding the role of monoclonal antibodies in the treatment of COVID-19 in patients with a potentially high risk of developing severe forms of the disease. Monoclonal antibodies represent a significant addition to the established therapeutic approaches for combating COVID-19, and their potential is not yet fully realized. Different classes of synthetic antibodies offer promising advantages over conventional coronavirus therapies, and further improvement and broader application in the future are expected. These drugs represent a vital reserve for future potential pandemic waves of SARS-CoV-2. Efforts in the scientific community should focus on optimizing their use in the face of continuously emerging new viral variants. The most effective defense against reinfection with COVID-19 remains naturally acquired immunity. There is no objective evidence suggesting that natural immunity is compromised following the use of monoclonal antibodies for the treatment of SARS-CoV-2 infection. On the contrary, there is even a suggestion of "vaccine-like effects" following their administration, which enhance the immune response developed during the infection. The preservation of immunogenesis—evidenced by the formation of anti-SARS-CoV-2 IgG and IgTotal antibodies—and their protective effect against future reinfection further justify including monoclonal antibodies in COVID-19 treatment protocols.

The objective benefits of using these biological agents in the appropriate indications are real. Patients treated with monoclonal antibodies experienced shorter hospital stays, fewer complications, and lower mortality rates. Additionally, residual fibrosis with symptoms of respiratory insufficiency was also lower. This is an important indicator of the patient's quality of life after recovering from a coronavirus infection. Given the large number of COVID-19 cases and survivors, post-infection quality of life remains a key criterion for evaluating the effectiveness of any given therapy.

Additional information

Conflict of interest

The authors have declared that no competing interests exist.

Ethical statements

Clinical trials: EK-01-25/20.03.2025.

The authors declared that no experiments on humans or human tissues were performed for the present study.

Informed consent from the humans, donors or donors' representatives: Clinic of Internal Diseases, UMHATEM "N. I. Pirogov" – Sofia, Bulgaria

The authors declared that no experiments on animals were performed for the present study.

The authors declared that no commercially available immortalised human and animal cell lines were used in the present study.

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Author contributions

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Data availability

All of the data that support the findings of this study are available in the main text.

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