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Research

Neutralizing Antibodies and COVID-19: Predicting Disease Duration and Severity After Vaccination and Infection

Nötralizan Antikorlar ve COVID-19: Aşı ve Enfeksiyon Sonrası Hastalığın Süresi ve Şiddetinin Öngörüsü

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ABSTRACT

Objective: This study aimed to explore the correlation between neutralizing antibodies post-Coronavirus disease-2019 (COVID-19) infection and vaccination with demographic characteristics, disease progression, severity, and diagnostic parameters.

Methods: A total of 80 COVID-19 patients with positive real-time polymerase chain reaction (RT-PCR) test and other diagnostic parameters were included in the study. Patients were grouped based on demographic characteristics, comorbid disease status, disease and pneumonia severity, vaccination status, intensive care requirements, and laboratory parameters used in diagnosis and follow-up. Serum samples collected on day 18 after the RT-PCR positive result were analyzed using VIDAS anti-SARS-CoV-2 immunoglobulin G (IgG) and immunoglobulin M (IgM) kits on the VIDAS analyzer (bioMérieux, France). Statistical analyses were conducted using the IBM SPSS 25.0 software package, and a significance level of less than 0.05 was considered.

Results: The results showed that patients with two or more vaccine doses had higher IgG titers compared to those with one or no dose. Patients over 65 had higher IgG titers than those younger than 65. Intensive care unit patients had lower IgG titers than ward-treated patients. Critically ill patients exhibited elevated IgM and IgG titers compared to moderate and severe cases. Additionally, patients with hypertension had higher IgG titers. A strong positive correlation was found between diagnostic biomarkers and neutralizing antibody titers.

Conclusion: Antibody titers increased with disease severity, though their neutralizing capacity remains uncertain. Our results are consistent with the literature, and our study is among the few studies that have examined the relationship between the kinetics of neutralizing antibodies and prognostic biomarkers.

Keywords: Coronavirus disease-2019, neutralizing antibody, disease severity, diagnostic biomarkers, comorbidity

ÖZ

Amaç: Bu çalışmada Koronavirüs hastalığı-2019 (COVID-19) enfeksiyonu ve aşılamasını takiben oluşan nötralizan antikorların; çalışmaya dahil edilen hastaların demografik özellikleri, hastalığın seyri, şiddeti ve diğer tanısal parametrelerle ilişkisinin incelenmesi amaçlanmıştır.

Gereç ve Yöntem: Çalışmaya gerçek zamanlı polimeraz zincir reaksiyonu (RT-PCR) testi ve diğer tanısal parametreleri pozitif 80 COVID-19 hastası dahil edilmiştir. Hastalar; demografik özellikleri, komorbid hastalık durumu, hastalık ve pnömoni şiddeti, aşılama durumları, yoğun bakım gereksinimleri, tanı ve izlemde kullanılan laboratuvar parametreleri sonuçlarına göre gruplandırılmıştır. RT-PCR pozitifliğini takiben 18. günde alınan serum örnekleri, VIDAS® Anti-SARS-CoV-2 immünoglobülin G (IgG) ve immünoglobülin M (IgM) kitleri kullanılarak VIDAS analizöründe (bioMérieux, Fransa) çalışılmıştır. İstatistiksel analizler IBM SPSS 25.0 paket programı ile yapılmış, anlamlılık düzeyi <0,05 olarak dikkate alınmıştır.

Bulgular: Hastalardan iki ve daha çok dozda aşılanmış olanların oluşturdukları IgG titreleri hiç aşı olmamış veya bir doz aşılanmış olanlara göre daha yüksek bulunmuştur. 65 yaş üzerindeki hastaların IgG titreleri Altmış beş yaş ve altı hastalara göre daha yüksektir. Yoğun bakım ünitesi'nde tedavi görenlerin IgG titreleri serviste takip edilenlere göre daha düşüktür. Kritik hastaların oluşturdukları IgM ve IgG antikor titrelerinin orta ve

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ÖZ

şiddetli hasta grubuna kıyasla daha yüksek olduğu tespit edilmiştir. Hipertansiyonu olan hastaların IgG titreleri daha yüksektir. Hastaların tanısal biyobelirteçleri ile nötralizan antikor titreleri arasındaki ilişkide CRP, ferritin, D-dimer, PLT, NLR, MLR ve PLR düzeyleriyle IgG titreleri arasında pozitif yönde yüksek düzey korelasyon gözlenmiştir. (tüm değerler için p<0,05'tir).

Sonuç: COVID-19'da hastalık şiddeti arttıkça oluşturulan antikor titreleri de artmaktadır. Fakat bu antikorların nötralize edici fonksiyonları ne derece yansıttıkları konusu hala tartışmalıdır. Verilerimizin tümü literatürle paralellik göstermekle birlikte hastalıkla oluşan nötralizan antikorların miktarının özellikle prognostik biyobelirteçlerle ilişkisini de irdeleyen literatürdeki sayılı çalışmalardandır.

Anahtar Kelimeler: Koronavirüs hastalığı-2019, nötralize edici antikor, hastalık şiddeti, tanısal biyobelirteçler, komorbidite

INTRODUCTION

The gold standard for rapid detection and diagnosis of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) viral nucleic acid is real-time polymerase chain reaction (RT-PCR). The use of RT-PCR is limited due to its time-consuming and laborious nature, as well as the requirement for specialized equipment and experienced personnel. Especially in regions with limited laboratory facilities. (1). Serological tests are complementary methods that can be used when viral RNA cannot be detected. Also, these tests are preferred for rapid screening of large populations. Both molecular and serological tests are essential to guide antiviral therapy, epidemiological measures, vaccination, and ultimately disease control by implementing appropriate strategies (2,3). For the diagnosis of viral infections, it is common to use the human antibody response. In comparison with RT-PCR assays, antibody detection is generally faster, cheaper, easier to use, more accessible, and requires less laboratory expertise. In spite of these practical advantages of serological tests, the antibody responses to SARS-CoV-2 are still poorly understood and the clinical utility of these tests requires further research (4). Plasma levels of interleukin 2 (IL2), IL6, IL7, IL10, Granulocyte colony-stimulating factor, and IP10 are observed to be higher in patients with severe disease compared to those with a less severe prognosis infected with SARS-CoV-2. In these patients, MCP1, MIP1A, tumor necrosis factor alpha, lactate dehydrogenase (LDH), ferritin, C-reactive protein (CRP), and D-dimer values are high, and the lymphocyte count is low (5,6). Few studies have reported on the kinetics of neutralizing antibody (Nab) responses in severe cases, and whether this antibody response has a correlation with disease prognosis. We investigated the possible relationship between responses in severe and mild cases and various prognostic parameters to fill this gap in the literature.

METHODS

Study Design

The present study was observational and cross-sectional.

Ethical Considerations

The study was approved The study was approved Health Sciences University Hamidiye Scientific Research Ethics Board (decision no: 24/25, date: 09.07.2021). The study was conducted in accordance with the principles of the Declaration of Helsinki The study was conducted in accordance with the principles of the Declaration of Helsinki.

Informed Consent

Written informed consent was obtained from patients to participate in this study. In accordance with the regulatory procedures of the study clinic, patients gave written informed consent for the processing and publication of their medical records (anonymized) for scientific purposes.

Participants

The study analyzed 80 COVID-19 patients with positive RT-PCR results and other diagnostic tests. Patients were categorized according to demographic characteristics, comorbid disease status, severity of disease, including pneumonia, vaccination status, intensive care unit requirements, and laboratory parameters used for diagnosis and follow-up. The severity of COVID-19 was defined according to the World Health Organization (WHO) criteria as follows:

Moderate: Clinical signs of pneumonia (fever, cough, dyspnea, fast breathing) but no signs of severe pneumonia, including oxygen saturation (SpO_2) ≥90% on room air.

Severe: Clinical signs of pneumonia plus one of the following: respiratory rate >30 breaths/min, severe respiratory distress, or SpO_2 <90% on room air.

Critical: Acute respiratory distress syndrome (ARDS), sepsis, or septic shock All patients who signed the informed consent

form were included in the study. Serum samples collected on the 18th day after RT-PCR positivity were analyzed using VIDAS anti-SARS-CoV-2 immunoglobulin G (IgG) and immunoglobulin M (IgM) kits (Biomérieux, France) on the VIDAS analyzer.

Statistical Analysis

Statistical analyses were performed using the IBM SPSS 25.0 software and the significance level was set at <0.05.

RESULTS

The patient group included 52.5% females. Eighty-one point two percent of the patients were over 65 years of age. The average age of patients treated in the intensive care unit (ICU) is 82.4, and the average age of patients treated in the ward is 71.9. Forty percent of the patients had received at least three doses of COVID-19 vaccine, Twenty-eight point seventy-five percent were unvaccinated. Twelve point five percent of the patients were monitored and treated in the ICU; the rest in the ward. Sixty-six (82.5%) of the included patients were classified as severe or critical cases. Seventy-six point three percent of the patients had at least one comorbid condition (Table 1). Hypertension (HT) was the most common comorbidity, affecting 57.5% of the sample. The means for CRP, ferritin, procalcitonin, D-dimer, fibrinogen, neutrophil lymphocyte ratio (NLR), monocyte lymphocyte ratio (MLR), and platelet lymphocyte ratio (PLR) were significantly higher than the reference values.

Based on the Mann-Whitney U test comparing the total number of vaccinations to IgM and IgG antibody titers, patients who received 2 or more vaccinations had significantly higher IgG antibody titers than unvaccinated patients (z=-5.177; p<0.05) (Table 2).

The IgG antibody titer of patients treated in the ICU was found to be significantly lower than that of patients followed and treated in the ward (z=-2.62, p<0.05) (Table 3).

There was a significant difference between median IgM titers and patient severity, with severe patients having statistically higher IgM titers than moderate patients (χ^2=9.337; p<0.05). Similarly, the median IgG titer was higher in critically ill patients than in patients in the moderate and severe groups (χ^2=21.831; p<0.05) (Table 4).

Analysis showed no significant difference in IgM and IgG antibody titers according to comorbidity. However, a statistically significant difference was found in the analysis

Table 1. Demographic characteristics of the patients

	Patients (n=80)
Sex	
Woman n (%)*	38 (47.5)
Men n (%)	42 (52.5)
Age	
≤65 n (%)	15 (18.8)
>65 n (%)	65 (81.2)
Admission ICU**	
Yes n (%)	10 (12.5)
No n (%)	70 (87.5)
Disease severity	
Moderate n (%)	14 (17.5)
Severe n (%)	59 (73.7)
Critical n (%)	7 (8.8)
Comorbidity	
Yes n (%)	61 (76.3)
No n (%)	19 (23.7)
Vaccination status	
0-1 n (%)	23 (28.75)
2 n (%)	25 (31.25)
≥ 3 n (%)	32 (40)
***Row percentage**	
**ICU: Intensive care unit	

Table 2. Mann-Whitney U test for IgM and IgG titers by vaccination status

Antibody	Total doses	N	Q_1-Q_3 (median)	U	z	p-value
IgM	0	23	0.27-1.76 (0.43)	595	-0.643	0.52
	≥2	57	0.30-2.20 (0.80)			
IgG	0	23	1.09-23.71 (8.08)	168.5	-5.177	**0.001**
	≥2	57	49.33-57.93 (56.07)			

Table 3. Mann-Whitney U test for IgM and IgG titer based on ICU status

Antibody	ICU	N	Q_1-Q_3 (median)	U	z	p-value
IgM	No	70	0.30-2.60 (0.74)	263.5	-1.259	0.208
	Yes	10	0.22-0.87 (0.43)			
IgG	No	70	23.60-57.69 (54.56)	170	-2.61	**0.009**
	Yes	10	0.84-23.49 (3.74)			

performed between the highest rate of comorbidity (HT) and neutralizing antibodies (Nab). Patients with HT produced lower levels of IgM and IgG antibodies (z=-2.044; p<0.05, z=-7.611; p<0.05) (Table 5).

Correlation analysis was performed to examine the relationship between IgM and IgG antibody titers, and levels of biomarkers known to be prognostic for COVID-19. A moderate positive correlation was found between IgG titer and CRP level (r=0.276; p<0.05). Positive and moderate correlations were also observed between IgG titer and ferritin, D-dimer and PLT (r=0.235, p<0.05; r=0.318, p<0.05; r=0.310, p<0.05). Similarly, positive and moderate correlations were observed between NLR, MLR, and PLR values and IgG titers (r=0.201; p<0.05; r=0.247; p<0.05; r=0.547; p<0.05, respectively) (Table 6).

DISCUSSION

The primary target of SARS-CoV-2 Nab is the S antigen, comprising S1 and S2 subunits. Thus, neutralizing the RBD in the S1 region of the virus is crucial in preventing infection. However, it is unclear which immune components are most important during viral infection and what antibody levels are required for a healthy immune response (7).

Most individuals infected with COVID-19 produce Nab through humoral immunity mechanisms. However, the

Table 4. Kruskal-Wallis test for IgM and IgG titers by disease severity

Antibody	Disease severity	N	Q_1-Q_3 (median)	χ^2	s.s	p-value
IgM	Moderate	14	0.14-0.43 (0.24)	9.337	2	0.009
	Severe	59	0.34-2.46 (0.83)			
	Critical	7	0.30-8.62 (0.49)			
IgG	Moderate	14	0.25-4.20 (1.62)	21.831	2	**<0.001**
	Severe	59	32.41-57.46 (54.64)			
	Critical	7	58.91-59.80 (59.37)			

Table 5. Mann-Whitney U test for IgM and IgG titers in relation to the presence of HT

Antibody	HT*	N	Q_1-Q_3 (median)	U	z	p-value
IgM	No	34	0.36-4.30 (1.06)	572	-2.044	0.041
	Yes	46	0.24-1.79 (0.51)			
IgG	No	34	33.04-57.99 (55.15)	0.001	-7.611	**0.001**
	Yes	46	4.81-44.79 (14.5)			

*HT: Hypertension

Table 6. Correlation analysis of IgM and IgG titers with diagnostic biomarkers

		IgM	IgG
CRP	r	0.17	0.276*
	p	0.132	**0.013**
Ferritin	r	0.043	0.235*
	p	0.704	**0.036**
PLT	r	0.015	0.31
	p	0.896	**0.005**
D-dimer	r	-0.011	0.318
	p	0.92	**0.008**
NLR	r	0.114	0.201
	p	0.316	**0.015**
MLR	r	-0.095	0.247
	p	0.402	**0.028**
PLR	r	0.122	0.145
	p	0.281	**0.015**

*p<0.05

duration and capacity of the humoral immune response is not fully known. Studies have shown that neutralizing and protective anti-SARS-CoV-2 antibodies are produced after infection, and that these antibodies reduce the risk of reinfection within 1-3 months of infection. Studies measuring Nab have shown that antibodies are detectable approximately 6 days after symptom onset, increase over the next 3-4 weeks, and that seroconversion occurs 2 weeks after infection in most patients (8).

Neutralization tests (NTs), on the other hand, provide an indication of whether antibodies produced after exposure to SARS-CoV-2 can neutralize the virus, and the level of protection provided by these antibodies in the event of subsequent exposure. NTs for detecting and measuring NAbs produced against the virus are the golden standard. The NTs assay has been conducted using SARS-CoV-2 viruses produced in cell culture. The need for specialized personnel and high-security laboratory conditions to perform these tests limits their practical use (9).

Compared to RT-PCR and NTs tests in diagnosis, antibody detection is faster, cheaper, easier to use, and therefore more accessible. Quantitative serological tests quantify the titer of the immune response by measuring antibody responses after SARS-CoV-2 infection and vaccination (10). These results are valuable tools for investigating the relationship between antibody responses and disease severity, asymptomatic infection, as well as humoral responses (11,12).

Our study investigated the kinetics of NAbs in hospitalized RT-PCR-positive patients and the association of antibody positivity with demographics, comorbidity status, disease course, severity, and other laboratory parameters.

In our study, 52.5% of the patients were female and 47.5% were male. All patients included in the study were hospitalized. Out of the 80 patients, only five (6.25%) did not produce a response (IgM and/or IgG). All these patients were female, over 65 years of age, and had at least one comorbidity (HT), were followed in the ICU, had a World Health Organization (WHO) severity of illness classification of severe, and had severe pneumonia. The remaining patients (93.75%) had detectable levels of IgM and IgG.

Research has demonstrated that age is the most important risk factor for serious illness and death from COVID-19. Upon reviewing the literature on this topic, researchers observed varying outcomes. Young et al. (13) conducted a study on 181 COVID-19 patients and found no association between patient age and levels of IgG, IgM, and IgA antibodies. A study by Luo et al. (14) of 678 COVID-19 patients found that IgM and IgG antibody titers increased significantly with age and reported that older patients had stronger immune responses to SARS-CoV-2 than younger patients. In a study in our country, it was reported that one of the factors influencing the antibody response was age, and the titers developed against the disease were found to increase with age (15). In our study, 81.2% (65/80) of the 80 COVID-19 patients were older than 65 years, similar to the study by Ozgocer et al. (15). However, according to our results, although the median IgM titer in patients over 65 years (1.76) was higher than that in patients 65 years and younger (0.57), this difference was not statistically significant ($z=-1.923$; $p>0.05$). The median IgG antibody titer (54.64) in patients over 65 years of age was statistically significant higher than the median (18.39) in patients 65 years and younger ($z=-1.824$; $p<0.05$). According to these results, our study showed that there was a correlation between IgG antibody titer and age, indicating that IgG levels increased with age.

The immune response to infectious diseases occurs in two ways. The acquisition of immunity can occur in two ways: the first is after exposure to the microorganism causing the infection, and the second is possible with vaccination. There have been many studies examining the Nab that develop in response to COVID-19 infection and those that develop after vaccination (16-18). While both situations develop protective antibodies against the disease, vaccination significantly reduces mortality from COVID-19 infection, especially in those with comorbidities. This reduction in mortality also leads to a decrease in transmission and severity of the disease.

Among the patients included in our study, 28.75% were never vaccinated, 31.25% were vaccinated with two doses, and 40% were vaccinated with three or more doses. When we evaluated IgM and IgG antibody titers according to total vaccination status, the median value of IgM titers did not show a significant difference total vaccine dose ($z=-0.643$; $p>0.05$). When we performed the same evaluation for IgG antibodies as in similar studies in the literature, the median IgG titer of patients who had received at least two doses of vaccine (56.07) was significantly higher than that of patients who had never been vaccinated (8.08) ($z=-5.177$; $p<0.05$).

Nab levels were found to be higher in ICU patients compared to other patients in most studies investigating the relationship between Nab levels produced by COVID-19 patients and their ICU hospitalization status (19-22). In contrast, IgG antibodies were reported to be significantly lower in ICU patients than in other patients in another study of 38 patients, of whom 11 were ICU patients (23).

Within the 80 patients included in the study, 12.5% were ICU patients who were followed in the ward. The median IgM antibody titer of ICU patients (0.43) did not differ significantly from that of other patients (0.74). However, the median IgG titer of ICU patients (3.74) was significantly lower than that of patients followed in the ward (54.56) (z=-2.16; p<0.05). Similar to the study by Sun et al. (23), our study found that critically ill COVID-19 patients being cared for in the ICU were unable to generate a sufficient level of IgG-type response. However, it is important to note that both the 80 patients in our study and the 10 patients were monitored in the ICU were of a higher mean age, compared to similar studies in the literature. Therefore, low IgM and IgG titers may have been detected in our patients, independent of COVID-19, in relation to inadequate immune response due to advanced age.

Several studies have demonstrated a correlation between the severity of COVID-19 and the antibody response. In a study of 30 COVID-19 patients, it was found that those with symptomatic and severe cases of the disease had a higher Nab response than those with asymptomatic and mild cases. Additionally, the study noted that Nab in mild cases disappeared more quickly than in severe cases (24).

A study reported significantly higher antibody titers in 285 patients in China in patients with severe COVID-19 than in those with mild and moderate disease (4). Tan et al. (25) also found a significant increase in titers with increasing severity of disease and pneumonia.

When classifying the patients in our study according to disease severity based on the WHO criteria, 14 out of 80 (17.5%) were moderate, 59 out of 80 (73.7%) were severe, and seven out of 80 (8.8%) were critical. The Kruskal-Wallis test was used to evaluate the relationship between disease severity and antibody titer. A significant relationship was found between IgM and IgG antibodies and disease severity (χ^2=9.337; p<0.05) and (χ^2=21.831; p<0.05). The levels of Nabs in the critical patient group were significantly higher than those in the severe and moderate patient groups. The Mann-Whitney U test was used to determine the significance of this difference between the paired groups (moderate-severe/critical-moderate/severe-critical). Based on this grouping, it was found that the IgM and IgG antibody titers of severe patients were significantly higher than those of moderate patients (z=-3.524; p<0.15, z=-5.633; p<0.05). While IgM levels were not significantly different between critical and moderate patients, IgG levels were significantly higher in critical patients than moderate patients (z=-0.23; p>0.0,5, z=-3.60; p<0.05). There was no statistically significant difference in IgM titers between critical and severe patients. However, IgG titers were significantly higher in critical patients than in severe patients (z=-0.312; p>0.05, z=-4.300; p<0.05). Our study found that as disease severity increased, the patients' Nab titers also increased, which is consistent with previous literature. Based on the fundamental knowledge that the neutralizing activity of antibodies is the basis of humoral immunity and not the serologically detected antibody titer, it is reasonable to assume that the lack of an adequate response, or even a delayed response, in patients with severe disease may indicate a weakness in humoral immunity, potentially leading to severe and progressive disease. In addition, the extent to which these titers reflect the neutralizing function of the antibodies is still controversial and unclear; why these patients with high titers have severe disease when they are expected to be recovering is a topic of ongoing debate.

HT is the most common comorbidity associated with COVID-19 pneumonia and disease severity. It is one of the most important risk factors associated with mortality. In a study evaluating the immune response of infected and vaccinated healthcare workers, comorbidities such as HT, immunosuppression, autoimmune disease, and cardiac disease were associated with lower antibody responses (26). The incidence of HT in the population increases with age, and it is difficult to evaluate HT as an age-independent risk factor.

In our study, 76.3% of the patients had comorbidities, while 23.7% did not. The most common comorbidities were HT (57.5%), diabetes melitus (37%), cardiac diseases (coronary artery disease and congestive heart failure) (36.5%), pulmonary diseases (chronic obstructive pulmonary disease, asthma) (17.5%), chronic renal failure (7.5%) and cerebrovascular diseases (6.25%). There was no significant difference in IgM and IgG antibody titers between patients with comorbidities and those without comorbidities (z=-1.131; p>0.05, z=-0.334; p>0.05). This may be due to the low number of patients without comorbidities (19/80). However, when we examined the relationship between HT, the most common comorbidity, and antibody titers, patients with HT had significantly lower IgM antibody titers compared to those without HT (z=-2.044; p<0.05) similarly, the IgG titer of patients with HT was significantly lower than that of patients without HT (z=-7.611; p<0.05). This result is significant because it confirms that HT, a common comorbidity in COVID-19 patients, impairs the immune response.

The most commonly used biomarkers to determine the prognosis of the disease in COVID-19 are CRP, ferritin, D-dimer, fibrinogen, lymphocytes, procalcitonin, hemoglobin, platelet, and LDH. There are many studies

in which NLR, MLR and PLR have also been used to predict disease severity and mortality. These studies also investigated disease severity and found these values to be higher than reference values. There are studies showing that especially CRP, ferritin, D-dimer, and NLR values increase, and lymphocyte levels decrease as the severity of the disease increases (27-29).

The average values of CRP, ferritin, procalcitonin, D-dimer, and fibrinogen, as well as NLR and MLR, in our patients were higher than the reference values. Correlation analysis examined the relationship between biomarkers predictive of disease prognosis and Nab generated during the disease. Strong positive correlations were found between CRP, ferritin, platelets, D-dimer, NLR, MLR, PLR, and IgG antibody ($r=0.276$; $p<0.05$, $r=0.235$; $p<0.05$, $r=0.310$; $p<0.05$, $r=0.318$; $p<0.05$, $r=0.201$; $p<0.05$, $r=0.247$, $p<0.05$, $r=0.145$; $p<0.05$, respectively). No correlation was observed when performing the same analysis for IgM with all these biomarkers.

CONCLUSION

Previous research has established a direct correlation between disease severity and the presence and levels of Nab. Additionally, changes in biomarkers have been strongly linked to the severity of the disease. Our study's findings align with these existing studies, further supporting the correlation. This consistency may also be attributed to the fact that a significant portion of our study's participants experienced critical, to severe forms of the disease. Since the onset of the COVID-19 pandemic, numerous studies have explored demographic differences, disease severity, risk factors, comorbidities, and the relationship between the disease and both diagnostic laboratory parameters and immune response. Our results are in harmony with this body of literature. Moreover, our study is among the few that investigate the relationship between Nab generated during COVID-19 infection and prognostic biomarkers.

However, our study has certain limitations. All patients were hospitalized, and the majority were over 65 years old. testing was limited to a single serum sample taken on the 18th day following PCR positivity. Future studies with larger and more diverse populations, including both symptomatic and asymptomatic COVID-19 patients across different age groups, will be invaluable in assessing vaccine efficacy and the duration of protection offered by Nab.

ETHICS

Ethics Committee Approval: The study was approved The study was approved University of Health Sciences Hamidiye Scientific Research Ethics Board (decision no: 24/25, date: 09.07.2021).

Informed Consent: Written informed consent was obtained from patients to participate in this study. In accordance with the regulatory procedures of the study clinic, patients gave written informed consent for the processing and publication of their medical records (anonymized) for scientific purposes.

FOOTNOTES

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Authorship Contributions

Surgical and Medical Practices: R.A.D., K.K.Y, Concept: R.A.D., K.K.Y, Design: R.A.D., K.K.Y, Data Collection or Processing: R.A.D., E.C.Ü., M.S.T., Analysis or Interpretation: R.A.D., K.K.Y, Literature Search: R.A.D., Writing: R.A.D.

Conflict of Interest: No conflict of interest was declared by the authors.

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