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Investigation of the effects of COVID-19 on muscle skeletal pain, fatigue, and hand grip strength in pregnant woman

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ABSTRACT

Aims: Hand grip strength is an important parameter that can be measured with a cheap, effective, and simple technique that can provide information about general health status. This study aimed to investigate the relationship between hand grip strength and musculoskeletal system findings and fatigue in pregnant COVID-19 patients. The data on common symptoms, laboratory findings, vaccination rates, and smoking rates of pregnant COVID-19 patients were evaluated as secondary results in the study.

Methods: The study had a cross-sectional, single-center, and retrospective case design. Demographic information, clinical findings, musculoskeletal symptoms, laboratory findings, and body temperatures of the patients were recorded. The relationship between the patient's hand grip muscle strength and the recorded data was evaluated. Myalgia severity was evaluated in kg by using the Numerical Rating Scale (NRS), physical fatigue by the Visual Analog Scale (VAS), and muscle strength by kg using a CAMRY digital hand dynamometer.

Results: The negative relationship between hand grip strength, focal muscle pain, and physical fatigue in pregnant COVID-19 patients was found to be statistically significant (P=0.010 and p=0.020 for focal muscle pain and physical fatigue, respectively). In laboratory data, a positive relationship was detected with the neutrophil/lymphocyte ratio (NLR) and neutrophil percentage, and a negative relationship was detected with lymphocyte percentage at a statistically significant level (P=0.042, p=0.027, p=0.037 for NRL, percentage of neutrophils and percentage of lymphocytes, respectively). (Statistical significance level was accepted as $p<0.05$)

Conclusion: We think that the evaluation of hand grip strength in pregnant women infected with COVID-19 will provide useful information for diagnosis, treatment, and prognosis.

Keywords: Hand grip strength, COVID-19, focal muscle pain

INTRODUCTION

COVID-19 was first identified in December 2019 for strains infected with the virus named SARS-CoV-2. Previous studies have shown that SARS-CoV-2 can affect all cells and systems with angiotensin-converting enzyme-2 (ACE-2) receptors.[1] Cough, high fever, sore throat, headache, diarrhea, muscle and joint pain, fatigue, and loss of sense of smell and taste are among the common symptoms of COVID-19.[2] Although symptoms such as myalgia, arthralgia, and fatigue are frequently detected in the acute and chronic stages of the disease, there is insufficient data on special patient groups such as pregnancy.[3]

"Hand grip muscle strength", which can be measured with an inexpensive, reliable, and noninvasive technique, is a frequently used parameter in the evaluation of the musculoskeletal system. The relationship between hand grip muscle strength and musculoskeletal symptoms and physical fatigue in pregnant COVID-19 patients was evaluated in the present study. The first aim of our study was to investigate whether hand grip strength can be used as a meaningful parameter in determining the diagnosis, treatment, and prognosis of pregnant COVID-19 patients. As secondary results of the study, the symptoms, laboratory findings, vaccination rates, and smoking status of our pregnant COVID-19 patients were evaluated.

METHODS

Study Design and Participants

This cross-sectional, single-center, retrospective case series study was conducted in Karaman Education and Research Hospital between December 2021 and May 2022. The Ethics Committee Approval was obtained from the Ethics Committee of Karamanoğlu Mehmetbey University

Faculty of Medicine with the date 29 Jun 2022, and decision no 06-2022/10. Permission was obtained from the boards of Karaman Education and Research Hospital to conduct the study in our hospital. The study was designed in line with the principles of the Declaration of Helsinki. The study was registered retrospectively on Clinicaltrials.gov with the number NCT05970874. Pregnant women who were over the age of 18, who were clinically diagnosed with COVID-19, whose throat swab samples were positive in real-time reverse transcription polymerase chain reaction analysis, who were hospitalized and treated, and who signed the written consent documents they were informed about were included in the study. Recordings were made on the first day of admissions to the wards and on the second day of afternoon admissions. Those with neurological and physical disabilities that would affect muscle strength measurements, those with psychiatric disorders, those with myopathy, those who could not read or write Turkish, those with abnormal mental status, and those who did not allow their data to be used for scientific purposes were not included in the study.

Data Collection

Age, height, weight, gestational week, weight changes during pregnancy, smoking status, comorbidities (hypertension, diabetes, goiter, rheumatological diseases), demographic data, and vaccination data were recorded. Symptoms from the onset of the disease to the moment they were registered, cough, fever, diffuse myalgia, focal muscle pain, low back pain, back pain, muster, elbow, wrist, knee, hip, and ankle joint pain, dyspnea, headache, anorexia, diarrhea, or asymptomatic presence, were questioned and recorded in the study. Complete blood count, blood glucose, D-dimer, ferritin, C-reactive protein (CRP), procalcitonin, lactate dehydrogenase (LDH), creatine kinase (CK), and isoenzyme CK-MB levels during hospitalization were analyzed.

Evaluation of Musculoskeletal Symptoms

Musculoskeletal symptoms, myalgia, and arthralgia were questioned in detail, and localizations were determined. The severity was determined by the Numerical Rating Scale (NRS), and the Visual Analog Scale (VAS) was used to assess fatigue.

Hand Grip Strength Measurements

Hand grip muscle strength was recorded when the patients were admitted to the service. Hand grip strength (HGS) was measured in kg with the CAMRY Digital Hand Dynamometer (Model No. EH101, CAMRY) with three consecutive measurements made with the dominant hand, elbows at the side, and forearm flexed at right angles. The highest measurement was included in the data.[3] For females over the age of 18, the HGS reference value determined by previous studies was accepted as 19 kg.[3]

In our study, the hand grip muscle strength of pregnant COVID-19 patients, who were deemed suitable for hospitalization, was evaluated during their hospitalization. Detailed physical examinations of the patients were performed. Arthralgia and myalgia findings were evaluated. Standard treatment protocols (Intravenous hydration, nasal O2, paracetamol) and pregnancy follow-ups were performed. Patients who required intensive care were not included in the study. Post-discharge follow-up of the patients could not be done regularly due to the pandemic and they were excluded from evaluation.

Body Temperature Measurements

The body temperatures of the patients were measured from the right and left ears using a digital tympanic thermometer during hospitalization.

Primer Outcome

The relationships of hand grip strength with musculoskeletal system symptoms and findings, laboratory values, and burnout were investigated. The effectiveness of the relationship between these parameters in determining diagnosis, treatment, and prognosis during hospitalization was evaluated.

Seconder Outcome

Common symptoms, laboratory findings, vaccination rates, and smoking status in pregnant COVID-19 patients were questioned and presented as secondary results of the study.

Statistics

The IBM Statistical Package for Social Sciences (IBM-SPSS Inc., Chicago, IL, USA) 22.0 program was used in the analysis of the data obtained in the study. The suitability of the data to the normal distribution was examined with the Shapiro–Wilk test, and the continuous variables were expressed as the mean and standard deviation or median (25-75%) according to distribution status, and categorical variables were expressed as numbers and percentages. The Spearman relationship test was used for the relationship between muscle strength and other parameters in the analysis of the continuous variables. Logistic regression analysis was used to identify possible independent risk factors for muscle strength in patients, and the statistical significance level was accepted as $p<0.05$.

RESULTS

Demographic and Clinical Findings

A total of 23 patients were included in the present study. The records of 25 patients were obtained from the system. Two patients were excluded from the statistical evaluation because of missing data. The mean age of the patients was 29±6 (years), and the mean body mass index (BMI) was 28.83±5.14 (kg/m2). The mean value of the patient's weight changes during pregnancy was 4.96±6.96 kg. Considering the weeks of pregnancy, at least 5 pregnant women and a maximum of 40 weeks were evaluated. The demographic characteristics of the patients are given in **Table 1**.

Considering the symptoms and findings of the patients, the frequency was found to be cough (82.6%), fever (52.2%), and diffuse myalgia (43.5%). Patient symptoms and findings are given in **Table 2**.

Considering the symptoms associated with the musculoskeletal system and the findings of the patients, back pain (56.5%), diffuse myalgia (43.5%), and knee arthralgia (43.5%) were found to be the most common symptoms. Patient symptoms and findings are given in **Table 2**.

Table 1. Demographic characteristics of the patients

Demographic feature	Mean± SD or Median (Percentile 25-75)	Minimum-Maximum
Age(years)	29±6	21-43
Height(cm)	162±7	150-178
Weight (kg)	75±14	59-103
BMI (kg/m²)	28.83±5.14	21.16-40.74
PrePre-gnancy weight(kg)	70±13	50-97
PrePre-gnancy BMI (kg/m²)	26.93±5.11	18.82-37.78
Weight gained during pregnancy (kg)	5(0-10)	(-15)-17
Pregnancy week	23(14-33)	5-40
Comorbid disease (yes/no) (%)	7(30.4%)/26 (60.6%)	
Smoking (yes/no) (%)	4(17.4%)/19(82.6%)	

Values are presented as numbers either mean ± standard deviation (SD) or median. BMI: Body Mass Index.

Table 2. Patient symptoms and findings

Symptoms and Signs	Yes, n (%)	No, n (%)
Cough	19(82.6%)	4(17.4%)
Fever	12(52.2%)	11(47.8%)
Common myalgia	10(43.5%)	13(56.5%)
Low back pain	7(30.4%)	16(69.6%)
Focal muscle pain	8(34.8%)	15(65.2%)
Back pain	13(56.5%)	10(43.5%)
Shoulder arthralgia	6(26.1%)	17(73.9%)
Elbow arthralgia	4(17.4%)	19(82.6%)
Wrist arthralgia	1(4.3%)	22(95.7%)
Knee arthralgia	10(43.5%)	13(56.5%)
Hip arthralgia	10(43.5%)	13(56.5%)
Angle arthralgia	4(17.4%)	19(82.6%)
Dyspnea	10(43.5%)	13(56.5%)
Headache	11(47.8%)	12(52.2%)
Anorexia	12(52.2%)	11(47.8%)
Diarrhea	3(13.0%)	20(87%)

Vaccination Status

When the patients were evaluated in terms of vaccination status, a total of 13 patients were vaccinated against COVID-19. Those who were vaccinated in the last three months, 6 months, or before were evaluated as of the hospitalization date. The vaccination information of the patients is given in **Table 3**.

Table 3. Covid-19 vaccination status of the patients

Vaccination Status	Yes, n(%)	No, n(%)
Vaccination Situations	13 (56.5%)	10 (43.5%)
Vaccination of the last three months	5 (11.7%)	18 (78.3%)
Getting vaccinated more than six months ago	4 (17.4%)	19 (82.6%)
Sinovac	2 (8.7%)	21 (91.3%)
BioNTech	11 (47.8%)	12 (52.2%)

Laboratory Findings

The laboratory parameters of the patients are given in **Table 4**.

Fatigue, myalgia, muscle strength, and temperature parameters of the patients were also examined and are given in **Table 5**.

Table 4. Patient laboratory parameters

Laboratory parameters	Mean± SD or Median (Percentile 25-75)	Minimum-Maximum
WBC count, (106/L)	8870(6290-11130)	4970-14570
Lymphocyte count, (106/L)	1460(980-1850)	210-3380
Neutrophil count, (106/L)	7140(5000-8190)	2760-11950
Hemoglobin, (g/L)	11.83±1.83	6.90-14.30
Platelet count, (106/µL)	230000(193000-247000)	125000-287000
CRP (mg/L)	14.2(8.4-19.4)	0.6-76.8
CK, (µg/L)	45(32-54)	18-260
CKMB, (µg/L)	10.9(8.0-12.0)	4-25.7
Ferritin, (µg/L)	19.20(9.40-58.90)	5.1-230
LDH, (U/L)	163(157-190)	113-285
D-dimer (U/L)	950(450-1736)	170-2472
Procalcitonin (ng/mL)	0.07(0.01-0.09)	0.01-0.5
Platelet/Neutrophil	152.17(103.42-204.13)	78.86-595.24
Neutrophil/Lymphocyte	4.85(2.53-8.21)	1.31-24.81
Lymphocyte percentage, (%)	15.44(9.79-25.60)	3.64-38.16
Neutrophil percentage, (%)	77.85(66.85-80.98)	49.91-90.29
Blood glucose mg/dl	98(88-133)	77-153

Values are presented as numbers either mean ± standard deviation (SD) or median. WBC: White blood cell, CRP: C-reactive protein, CK: Creatine kinase, CKMB: Creatine kinase myocardial band, LDH: Lactate dehydrogenase

Table 5. Patient fatigue, myalgia, muscle strength, and temperature parameters

Characteristic Feature	Mean± SD or Median (Percentile 25- 75)	No, n(%)
Myalgia NRS	5(2-7)	1-9
fatigue VAS	6(4-8)	1-10
Muscle strength kg	21.9(16.1-27.1)	6.7-31.1
Tc right side, (°C)	37.0±0.6	35.6-7.9
Tc left side, (°C)	37.0±0.5	35.8-38

Values are presented as numbers either mean ± standard deviation (SD) or median. Numerical Rating Scale (NRS), Visual Analog Scale (VAS), Tc: Core body temperature (Tc)

Relationship of Data with Muscle Strength

HGS was evaluated in pregnant women infected with COVID-19. Values below the determined reference value (19 kg) were found in 8 patients (34.8%). Fifteen patients (65.2%) were not considered to have low HSG.

The relationship between patient demographic data and muscle strength was examined, and the results are given in **Table 6**.

Table 6. The relationship between patient demographics and muscle strength

	Relationship With Muscle Strength	
Characteristic	R value	P value
Age(years)	-0.132	0.547
Height(cm)	-0.333	0.120
Weight(kg)	-0.238	0.273
BMI (kg/m²)	-0.085	0.701
Gestational week	0.249	0.253
PrePre-gnancy weight(kg)	-0.325	0.130
Weight Gained During Pregnancy	0.115	0.600
Comorbid Disease	-0.071	0.747
Smoking	-0.104	0.637

BMI: body mass index. The Spearman correlation test was applied.
* P value is below the threshold of 0.05.

Evaluation of Laboratory Parameters

Although the negative relationship was statistically significant for the percentage of lymphocytes (p=0.037), it was not found to be significant for other parameters (p>0.05). The relationship between laboratory parameters and muscle strength is given in **Table 7**.

Table 7. Relationship between patient laboratory parameters and muscle strength

	Muscle Strength	
Laboratory parameters	R value	P value
Ferritin, (µg/L)	0.082	0.737
D-Dimer (µg FEU/L)	0.125	0.611
Procalcitonin (ng/mL)	-0.014	0.956
WBC count, × 106/L	0.155	0.480
Lymphocyte count × 106/L	-0.348	0.104
Neutrophil count × 106/L	0.226	0.300
HemoHaemoglobin, g/L	0.039	0.859
Platelet count 106/L	-0.380	0.074
CRP (mg/L)	-0.258	0.247
CK, (µg/L)	0.021	0.937
CKMB, (µg/L)	0.171	0.543
LDH, U/L	0.240	0.409
Blood sugar, g/dl	0.288	0.182
Platelet/Lymphocyte	0.175	0.423
Neutrophil/l/ Lymphocyte	0.428	0.042*
Percentage of Lymphocyte, (%)	-0.437	0.037*
Percentage of Neutrophils, (%)	0.461	0.027*

The Spearman correlation test was applied. * P value is below the threshold of 0.05.
WBC: White blood cell, CRP: C-reactive protein, CK: Creatine kinase, CKMB: Creatine kinase myocardial band, LDH: Lactate dehydrogenase

Vaccination Situations

The relationship between the vaccination status of the patients and their muscle strength was examined in the present study and was not found to be statistically significant (p>0.05). The relationship between vaccination status and muscle strength is given in **Table 8**.

Table 8. Relationship between patient COVID-19 vaccination status and muscle strength

	Muscle Strength	
Characteristic feature	R value	P value
Don't get vaccinated	-0.033	0.881
Vaccination of the last three mouths	0.143	0.515
Vaccination of the last six mouths	-0.156	0.478
Getting vaccinated more than six months ago	-0.043	0.845
BioNTech	-0.19	0.384
Sinovac	0.279	0.197
HemoHaemoglobin, g/L	0.039	0.859

The Spearman correlation test was applied.
* P value is below the threshold of 0.05.

When the relationship between the physical fatigue, myalgia, and temperature parameters of the patients and muscle strength were examined, negative relationships were detected for all parameters. This relationship was statistically significant for the fatigue parameter (p=0.020). The relationship between fatigue, myalgia temperature parameters, and muscle strength is given in **Table 9**.

Table 9. Relationship between patient fatigue, muscle strength, temperature parameters, and muscle strength

	Muscle Strength	
Characteristic feature	R value	P value
Myalgia NRS	-0.396	0.062
Fatigue VAS	-0.483	0.020*
Tc right, °C	-0.160	0.465
Tc left, °C	-0.252	0.246
BioNTech	-0.19	0.384

The Spearman correlation test was applied.
* P value is below the threshold of 0.05.
Numerical Rating Scale (NRS), Visual Analog Scale (VAS), Tc: Core body temperature (Tc)

Table 10. Relationship between patient symptoms and findings and muscle strength

	Muscle Strength	
Characteristic Feature	R value	P value
Smoking	-0.104	0.637
Cough	0.017	0.938
Fever	-0.125	0.571
Common myalgia	-0.397	0.061
Low back pain	-0.221	0.311
Focal muscle pain	-0.523	0.010*
Back pain	-0.066	0.764
Shoulder arthralgia	-0.321	0.135
Elbow arthralgia	-0.372	0.081
Wrist arthralgia	0.0001	1.000
Knee arthralgia	-0.185	0.398
Hip arthralgia	-0.218	0.317
Ankle arthralgia	0.061	0.784
Dyspnea	-0.370	0.082
Headache	-0.230	0.292
Anorexia	-0.112	0.612
Diarrhea	-0.311	0.148

The Spearman correlation test was applied. * P value is below the threshold of 0.05.

When the relationship between patient symptoms and signs and muscle strength was examined, a negative relationship was detected between focal muscle pain parameters and muscle strength at a statistically significant level (p=0.010). The relationship between patient symptoms and signs and muscle strength is given in **Table 10**.

Multivariate logistic regression analysis was applied to the study using muscle strength parameters and statistically significant and clinically significant variables. Among these independent variables, only the physical fatigue parameter was found to be significant (B value: -1.062; 95% CI: (-2.087--0.037) (p=0.043). The logistic regression model examining the risk factors for muscle strength is presented in **Table 11**.

Table 11. Relationship between significant variables and muscle strength

Risk Factor	B value (95% CI)	P value
Focal muscle pain	-5.399(-11.203- 0.406)	0.066
Neutrophil percentage, (%)	0.397(-0.343-1.138)	0.274
Lymphocyte percentage, (%)	0.177(-0.687-1.041)	0.672
Fatigue	-1.062(-2.087--0.037)	0.043*

Computer output of the logistic regression model examining risk factors for muscle strength. CI: Confidence interval. * P value is below the threshold of 0.05. * B value is the beta coefficient.

DISCUSSION

In the present study, it was found that hand grip strength was associated with the neutrophil/lymphocyte ratio, neutrophil percentage, lymphocyte percentage, focal muscle pain, and fatigue parameters in pregnant COVID-19 patients. The negative relationship between hand grip strength, focal muscle pain, and physical fatigue in pregnant COVID-19 patients was found to be statistically significant. In laboratory data, a positive relationship was detected with the neutrophil/lymphocyte ratio (NLR) and neutrophil percentage, and a negative relationship was detected with lymphocyte percentage at a statistically significant level. The clinical findings, severity of musculoskeletal symptoms, and vaccination status of pregnant COVID-19 patients were also evaluated.

In our work, the most common symptoms were cough (82.6%), back pain (56.5%), fever (52.2%), and diffuse myalgia (43.5%). In a previous study that included 108 pregnant women infected with SARS-CoV-2, the most common symptoms were fever (68%), cough (34%), fatigue (13%), and shortness of breath (12%).[4] The reason for this may be that the average gestational week for the applications in the present study was in the second trimester, and the applications in the severe disease category were not evaluated.

In our work, knee, hip, and muscular arthralgia were the most common arthralgia findings. Questioning must be done in detail because arthralgia can overlap with myalgia findings. In a previous study that examined 150 adult COVID-19 patients, the most common arthralgia findings were found to be wrist, ankle, and knee arthralgia.[5] We think that the difference in arthralgia findings occurred because our patients were young females, and the weights changed with pregnancy.

In our work, a statistically significant and positive relationship was found between hand grip strength and NRL and neutrophil percentages, and a negative relationship was detected with lymphocyte percentage. Inflammation is associated with the development and possibly poor prognosis of COVID-19. The innate immune response is characterized by the influx of neutrophils into the respiratory system in respiratory tract infections.[6] Intense neutrophil influx may lead to lymphopenia with apoptosis in lymphocytes.[7-9] In previous studies, 80% of patients who had severe COVID-19 and 25% of those who had mild infections reported lymphopenia.[10,11] In our study, a negative relationship was found between muscle strength and lymphocyte percentage, which is consistent with the results of current studies. Muscle strength is likely to decrease with disease severity in COVID-19 infection. Increased neutrophil count with the severity of inflammation may be associated with low muscle strength. In the present study, a positive relationship was found between NLR and neutrophil percentage. Muscle strength decreases with disease severity. The positive relationship that was found between NLR and neutrophil percentage and muscle strength may be associated with pregnancy physiology. Increasing neutrophil counts and decreasing lymphocyte counts are expected in pregnant women and are associated with pregnancy physiology.[12,13] It can be argued that the high number of patients in the second trimester and our evaluation of severe COVID-19 cases contributed to this result.

The relationship between hand grip strength and respiratory functions was examined in a previous study, and it was reported that the goodness of respiratory function was associated with increased hand grip strength.[14] A study conducted on patients over the age of 50 showed that higher grip strength was associated with a lower risk of COVID-19 hospitalization and argued that age, obesity, and muscle strength were independent risk factors for COVID-19.[15] We also found in the study that lower hand grip strength was associated with physical fatigue. More comprehensive studies are needed to determine whether hand grip strength is a parameter that can determine the prognosis of COVID-19.

The rate of smoking was found to be 17.4% in the present study. Despite all warnings about smoking, the high rate of smoking may indicate that smoking addiction is a very strong addiction.[16] The relationship between COVID-19 and smoking is not yet clear. In a large-scale meta-analysis conducted with pregnant women who had a confirmed diagnosis of COVID-19, obesity, preeclampsia, smoking, and diabetes were reported as risk factors for severe COVID-19.[17] Some publications argue that nicotine may be a potential preventive factor for COVID-19.[18,19] It was argued in these studies that smoking reduces the rate of being infected with SARS-CoV-2 but may increase the severity of the disease in infected people.

The data on vaccination rates were also given in the present study. The vaccination rate was 56.5% in pregnant COVID-19 patients who were included in the present study. The choice of vaccine is made by the individuals who will be vaccinated after the necessary information is given in our country. The preferences of the patients for the vaccine within the specified date range were mRNA vaccine (BioNTech) with 47.8% and inactivated vaccine (Sinovac) with 8.7%. There are limited data on the safety and efficacy of COVID-19 vaccines in pregnancy.[20] The relationship between the status of being vaccinated in the last 3 months, 6 months, and more than 6 months and muscle strength was also evaluated in the present study, and no significant relationship was detected. No study was detected in the literature review about muscle strength

and SARS-CoV-2 vaccines. We think that these data increase the value of the present study.

The fact that we could not reach a higher number of patients in our study can be considered a limitation. This is associated with the decreased incidence of the disease and the severity of the clinical course worldwide and in our country. Although the pandemic has reduced its severity today, it is possible to experience exacerbations or new outbreaks associated with the coronavirus family. For this reason, we believe that the data on specific patient groups, such as pregnant women, must be very valuable.

Pregnancy involves many physical, hormonal, immunological, and psychological changes.[21] Long-term studies conducted on the effects and results of a newly identified virus must be evaluated in this process, which involves many variables. Differences in individual sensitivities, variations in exposure time and frequency, and limitations in the use of radiological imaging methods and pharmacological agents limit the evidence in the literature on pregnant women.

In the present study, the data of pregnant women who had an oxygen saturation of 94 and above and needed hospitalization were analyzed. No comparisons were made regarding the severity of the disease. Imaging methods must be used objectively to compare the severity of the disease. The use of imaging methods depends on the permission of the physician, pregnant COVID-19 patients, and their spouses. Additionally, standardizing pulmonary changes regarding pregnancy physiology could not be performed in the present study because it is associated with many different variables, such as gestational week, weight change, and hormonal and immunological changes.

The fact that our sample was relatively small and we could not evaluate the severity of the disease can be considered a limitation in our study. Studies with larger samples are needed to support our results.

CONCLUSION

Handgrip strength measurement is a noninvasive, safe, and easily accessible parameter in pregnant women who have various limitations in diagnosis and treatment. We recommend that hand grip strength be evaluated at the first admission in pregnant COVID-19 patients. We hope that future studies will find results that support this idea.

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ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Karamanoğlu Mehmetbey University Ethics Committee (Date: 29.06.2022, Decision No: 06-2022/10). The study was registered retrospectively on Clinicaltrials.gov with the number NCT05970874. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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