



## The Impact of the COVID-19 Pandemic on Osteoporosis Patients

### COVID-19 Pandemisinin Osteoporoz Hastaları Üzerine Etkisi

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### Abstract

**Objective:** Osteoporosis is the most common metabolic bone disease associated with significant mortality and morbidity. The coronavirus disease-2019 (COVID-19) pandemic, which has affected the entire world, has necessitated curfews, quarantine measures, and alterations in hospital health services. Our study aimed to investigate the impact of the pandemic period on our osteoporosis patients.

**Materials and Methods:** Ninety-two previously diagnosed osteoporosis postmenopausal female patients who presented to the outpatient clinic between July 20, 2020, and October 20, 2020, were enrolled in the study. Besides the patients' demographic characteristics, the duration of osteoporosis, the osteoporosis medications they used, and whether they interrupted the treatment during the pandemic period, and if they did, the reason was questioned. In addition, fracture history, fall frequency and exercise status were recorded before and during the pandemic.

**Results:** The patients' mean age was 61±8 years. 10.9% had been exercising before the pandemic, and of these, 87.5% either reduced their exercise frequency or quit exercising during the pandemic. 20.7% of the patients before the pandemic and 17.4% during the pandemic period had a history of falling ( $p>0.05$ ). When the continuation of osteoporosis treatment was analyzed, 7 (7.6%) patients were found to have interrupted their treatments during the pandemic. Of these, one of them had interrupted treatment due to the inability to obtain the medication, one of them had interrupted treatment due to not having the necessary investigations performed, and five patients had interrupted treatment because they could not leave their homes due to restrictions. It was observed that the interruption of drug treatment was not associated with those living in urban or countryside, or the level of osteoporosis knowledge ( $p>0.05$ ).

**Conclusion:** Our study demonstrated that the COVID-19 pandemic adversely affected osteoporosis patients' medication adherence and exercise levels. Therefore, we recommend taking preventive measures of addition existing ones in similar situations.

**Keywords:** COVID-19, osteoporosis, osteoporosis treatment

### Öz

**Amaç:** Osteoporoz metabolik kemik hastalıklarının en sık görülen şekli olup, ciddi mortalite ve morbiditeye sebep olabilmektedir. Tüm dünyayı etkisi altına alan koronavirüs hastalığı-2019 (COVID-19) pandemisi sokağa çıkma yasağı, karantina uygulamaları ve hastanelerdeki sağlık hizmetlerinde değişiklikleri beraberinde getirmiştir. Çalışmamızda pandemi döneminin osteoporoz hastalarımız üzerine olan etkisini araştırmayı amaçladık.

**Gereç ve Yöntem:** 20 Temmuz-20 Ekim 2020 tarihleri arasında polikliniğe başvuran daha önceden osteoporoz tanısı almış 92 postmenopozal kadın hasta çalışmaya alındı. Hastaların demografik özelliklerinin yanı sıra; osteoporoz süreleri, kullandıkları osteoporoz ilaçlar ve pandemi dönemi tedaviyi aksatma durumları ve nedenleri sorgulandı. Bunun yanı sıra pandemi öncesi ve pandemi döneminde kırık öyküleri, düşme sıklıkları ve egzersiz durumları değerlendirildi.

**Bulgular:** Çalışmaya alınan 92 osteoporoz hastasının yaş ortalaması 61±8 idi. Pandemi öncesi hastaların %10,9'u egzersiz yapmaktaydı ve bunların %87,5'i pandemi döneminde egzersizi bıraktığını ya da azalttığını ifade etti. Pandemi öncesi hastaların %20,7'si, pandemi döneminde ise %17,4'ünün düşme öyküsü mevcuttu ( $p>0,05$ ). Hastaların osteoporoz tedavisini aksatma durumu incelendiğinde; birinin ilacı temin edemediği için, birinin gerekli tetkikleri yaptıramadığı için, beşinin kısıtlamalar nedeniyle evden çıkamadığı için tedavisini aksattığı saptandı. Tedaviyi aksatma durumunun yaşadığı yer ya da bilgi düzeyi ile ilişkisinin olmadığı görüldü ( $p>0,05$ ).

**Sonuç:** Çalışmamız COVID-19 pandemi döneminin osteoporoz hastalarının gerek ilaç devamlılıklarını, gerekse egzersiz düzeylerini olumsuz etkilediğini gösterdi. Olası benzer durumlarda alınan tedbirlere ilave ek önlemlerin alınmasının faydalı olacağını düşünmekteyiz.

**Anahtar kelimeler:** COVID-19, osteoporoz, osteoporoz tedavisi

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## Introduction

Osteoporosis (OP) is a metabolic bone disease characterized by impairment of bone microarchitecture, decreased bone strength and bone mineral density (BMD), and elevated fracture risk (1). The consequences of the disease consist of mortality, physical disability, pain, increased fracture risk, elevated treatment costs, and impairment in the quality of life (2). Today, OP has become the seventh most prevalent disease worldwide and thus constitutes a global public health problem (3).

Coronavirus disease-2019 (COVID-19) infection due to severe acute respiratory syndrome coronavirus 2, a new coronavirus that emerged in China in late 2019, was attributed a pandemic status by the World Health Organization on March 11, 2020 (4,5). As of July 19, 2020, COVID-19 had infected 14,348,475 individuals worldwide and had caused 603,167 deaths (6). In our country, before the WHO declared a pandemic, the Ministry of Health established a Scientific Committee consisting of expert scientists on January 10, 2020. Following the first case detected in our country on March 11, 2020, the draft of the public policy's main items to be implemented was started to be prepared. Curfews and quarantine practices were enacted in the context of the prepared precautionary policies (7). Besides the imposed quarantine and travel limitations during the COVID-19 pandemic, slowing down routine hospital services has led to worries that limitations might have been encountered in treating chronic disorders (8). For example, patients with OP require long-term therapy and periodic follow-ups. Our study aimed to determine how the COVID-19 pandemic period impacted patients diagnosed with osteoporosis.

## Materials and Methods

The study was conducted among postmenopausal OP patients who presented to our outpatient clinic between July 20, 2020, and October 20, 2020. During the study period, a total of 437 OP patients visited our clinic. Patients who were newly diagnosed, male patients, premenopausal women, those the immobility due to other diseases, those who did not understand or answer the questions, and those who refused to participate in the study were excluded. The age, height, weight, education level, place of residence (urban or countryside), chronic diseases, history of COVID-19, and the duration of the OP diagnosis were questioned for the 92 female patients who met the inclusion criteria. Changes in weight during the COVID-19 pandemic were recorded. The T-scores of the total lumbar vertebrae and femur were recorded from the dual-energy X-ray absorptiometry measurements. The patients included in the study were asked about their exercising status before the pandemic. Exercises such as brisk walking, dancing, climbing stairs, and cycling for at least 30 minutes were considered as exercise. The exercise frequency was recorded as more than 3 times a week, 1-3 times a week, once a week, and less than once a week. Changes in exercise levels during the pandemic were evaluated with the options:

a) I continued the same, b) I reduced the amount of exercise, c) I stopped exercising. The occurrence and frequency of falls before and during the COVID-19 pandemic were assessed. The presence of fractures due to minimal trauma (e.g., falling from a standing height or a lower height) or unidentified trauma was questioned for both the pre-pandemic and pandemic periods. The medications they had been using for treating OP were recorded. Patients were asked whether they continued their treatment regularly during the pandemic. If they reported not being able to continue regularly, the reasons were investigated (a. I couldn't access the medication, b. I couldn't have tests done, c. I couldn't leave home due to restrictions, d. I neglected OP treatment due to other illnesses, e. other).

The patients enrolled in the study were subjected to the Osteoporosis Knowledge test (OKT). OKT is a test to assess OP awareness on various topics associated with calcium intake for OP prevention, as well as exercise and activity levels. The test was developed by Kim et al. (9) in 1991, and Kılıç and Erci (10) demonstrated the validity and reliability of the test's Turkish version in 2004.

The number of OP patients in a similar period of 2019 (pre-pandemic) was retrieved from the outpatient clinic records to analyze whether the number of OP patients presenting to the outpatient clinic has changed during the pandemic.

This study was approved by Aydın Adnan Menderes University Non-invasive Clinical Research Ethics Committee (decision no: 4, date: 06.08.2020). All participants were informed about their conditions and signed an informed consent form.

## Statistical Analysis

The conformity of the quantitative data to the normal distribution was analyzed with the Shapiro-Wilk test. For the quantitative variables providing the assumption of normality, t-test was used in independent groups in the intergroup comparisons and descriptive statistics were shown as mean  $\pm$  standard deviation. In the absence of normality assumption, the Mann-Whitney U test was used and descriptive statistics were given as median (25-75 percentile). The McNemar test was used to evaluate the similarity of qualitative data measured before and after, while chi-square test was used for other qualitative comparisons. Descriptive statistics were given as frequency (%). The results were considered statistically significant when  $p < 0.05$ .

## Results

Among the total of 92 female OP patients enrolled in the study, the mean age was  $61 \pm 8$  years. Table 1 presents the patients' demographic characteristics. Forty-three patients lived in the urban center (46.7%), whereas 49 lived in the countryside (53.3%). Twelve (12.9%) patients were diagnosed with COVID-19 during the pandemic. The median duration of OP diagnosis was 5 (3.25-10) years. According to BMD measurement, the median value of the patients' lumbar T score was 2.7 (2.5-3.5), and the femoral T median value was 1.9 (0.8-3.8) (Table 1).

Only ten of 92 patients (10.9%) had been exercising before the pandemic. Among these, four (4.3%) had been exercising less than once a week, 2 (2.16%) once a week and four (4.3%) 1-3 times a week (Table 2). Among the patients who were exercising, 37.5% (3.3% of the total) quit exercising during the pandemic, 50% (4.3% of the total) tapered their exercise frequency, and only 12.5% (1.1% of the total) maintained the same pattern (Table 2).

There was a fall history in 19 patients (20.7%) before this pandemic. The fall frequency was determined as less than once a week in 17 patients (18.5%), whereas it was more than once a week in 2 patient (2.2%). On the other hand, 16 (17.4%) of the patients had a history of falls during the pandemic period. While the fall frequency was less than once a week in 14 (15.2%), 2 (2.2%) had a rate of more than once a week (Table 2). There was no statistically significant difference between the falls during the quarantine period and those occurring in normal times ( $p>0.05$ ). A history of fracture was present in 16 (17.4%) patients before the pandemic, whereas in three (3.3%) patients in the pandemic period. A weight gain was observed in 27 patients (29.3%)

during the pandemic period, and this gain was 1-5 kg in 20 patients (21.7%), whereas 5-10 kg in 8 patients (8.7%).

When the patients' OP treatments were analyzed, it was seen that 8 (8.7%) patients had received medical treatment in the past and were currently being followed up, 14 (15.2%) patients received vitamin D, 12 (13.1%) were administered oral bisphosphonate, 36 (39.1%) patients had parenteral bisphosphonate and 22 (23.9%) patients received denosumab treatment. Seven (7.6%) patients were found to have interrupted their drug treatment during the pandemic period. Of those interrupting their drug treatment, one patient (1.1%) stated that it was because of not being able to obtain the medication, one (1.1%) stated that it was because of not having the necessary examinations done, and five patients (5.4%) stated that it was because they could not leave the house due to restrictions (Table 2). There was no significant difference between those living in urban centers and those living in the countryside regarding drug access ( $p>0.05$ ). The mean value of the OKT score was computed as  $14.02\pm 4.52$  and no correlation was identified between the interruption of drug treatment and OKT ( $p>0.05$ ).

The number of OP patients presenting to the outpatient clinic during the study period was 437, whereas this figure was 484 in the similar period of the previous year. Thus, it was observed that the number of OP patients presenting to the outpatient clinic declined by 9.7% during the pandemic.

**Table 1. The patients demographic characteristics and osteoporosis features**

	Mean ± SD	25-75 percentil
Age (year)	61±8	-
Weight (kg)	67.26±12.12	-
Height (cm)	157.14±5.99	-
BMI	27.19±4.39	-
Osteoporosis knowledge level	14.02±4.52	-
Osteoporosis duration	-	5 (3.25-10)
<b>DXA (T-score)</b>		
Lomber	-	2.7 (2.5-3.5)
Femur	-	1.9 (0.8-3.8)
	<b>n (%)</b>	
<b>Educational status</b>		
Illiterate	18 (19.6)	-
Secondary education	58 (63.1)	-
High school	10 (10.9)	-
Under/postgraduate	6 (6.4)	-
<b>Living place</b>		
Urban center	43 (46.7)	-
Countryside	49 (53.3)	-
<b>Co-morbidity</b>		
Absense	25 (27.2)	-
Hypertension	17 (18.5)	-
Rheumatic disease	9 (9.8)	-
Malignancy	6 (6.5)	-
Diabetes mellitus	-	-

BMI: Body mass index, DXA: Dual X-ray absorptiometry, SD: Standard deviation

**Table 2. Exercise, falling and treatment conditions of patients**

	n (%)
Exercise in before pandemic	10 (10.9)
Less than 1 per week	4 (4.3)
Once a week	2 (2.2)
1-3 per week	4 (4.3)
Falling in before pandemic	19 (20.7)
<1 time per week	17 (18.5)
≥1 time per week	2 (2.2)
Falling in pandemic	16 (17.4)
<1 time per week	14 (15.2)
≥1 time per week	2 (2.2)
<b>Treatment of osteoporosis</b>	
In untreated follow-up	8 (8.7)
Vitamin D	14 (15.2)
Oral bisphosphonate	12 (13.1)
Prenteral bisphosphonate	36 (39.1)
Denosumab	22 (23.9)
Disrupting treatment	7 (7.6)
Inability to obtain medicine	1 (1.1)
Failure to do inspections	1 (1.1)
Due to restrictions	5 (5.4)

## Discussion

Measures such as curfews and physical isolation imposed throughout the COVID-19 pandemic led people to stay indoors and live in confined spaces. Various studies have shown that individuals' exercise levels declined due to such restrictions (11,12). The significance of exercising for treating OP has been clearly emphasized (13). However, exercise routines may differ among different societies. Only 10.9% of the patients with OP enrolled in our study had been regularly exercising before the pandemic. Daşkapan and Atalay (14), in their study conducted on 208 women in our country, reported that 69.7% of the participants did not exercise. According to the National Disease Burden Report of Turkey, the physical inactivity rates in women aged 15-29, 30-44, 45-59, and 60-69 years were determined as 70.0%, 68.7%, 80.0%, and 40.0%, respectively (15). Our OP patients' pre-pandemic exercise data were found to be lower compared to these studies. This situation indicated that our OP patients need to be informed more about exercise, and maybe programs are needed to be prepared in this direction. Half of our exercising patients discontinued exercising during the pandemic, 37.5% tapered their exercise frequency, and only 10% continued with similar exercise regimens. When we consider our entire patient population, 12.5% of our patients were affected by the pandemic regarding exercise.

Our study did not reveal any significant difference between before and after the pandemic regarding our patients' fall frequency. On the other hand, Kiyoshi-Teo et al. (16) indicated that the fall risk increased during the pandemic. Considering the adverse influence of sedentary life on falls, it might be thought that constraints in the pandemic period would have raised the fall risk. However, on the other hand, restrictions imposed on outdoor activities have also been shown to reduce individuals' trauma exposure (17). Therefore, the decrease in trauma exposure during the pandemic might explain why our OP patients' fall frequency remained unchanged and new fractures occurred in only three patients during this period. However, considering that our study data covered the first ten months of the pandemic, we suggest that these rates might have changed in the later pandemic periods, as the restrictions lasted longer, and that studies covering these periods are also warranted.

Dinçer and Kolcu's (12) study revealed that nutritional behaviors were negatively affected, as well as physical activity declined during the pandemic period. Rapid weight gain is among the problems that may be encountered concerning these (18). In 29.3% of our OP patients, weight gain was observed during this phase of the pandemic period. Among these patients, weight gain was between 1-5 kg in 21.7% and 5-10 kg in 8.7%.

Several measures introduced in response to the COVID-19 pandemic also altered how healthcare institutions delivered services (19). For example, our study determined that the number of OP patients presenting to the outpatient clinic during the pandemic declined by 9.7% compared to the previous year's corresponding period. In addition, McCloskey et al. (20)

reported that the usage rates of the Frax website to assess OP patients' fracture risk decreased by 23.1% and 58.3% in March and April 2020, respectively, compared to the respective periods in 2019 (20). These results indicate that hospital admissions of OP patients globally declined. Most (63%) of our studied patients' OP treatments consisted of intravenous bisphosphonates or subcutaneous denosumab, whereas the remaining received oral treatments. Even though most of our patients were receiving IV/SC treatments, which were slightly more dependent on hospitalization, only 7.6% were observed to have interrupted their treatments during this period (21). Of these, one patient stated having delayed treatment due to the inability to obtain medication, one patient due to the inability to undergo tests, and five patients because they could not leave home due to restrictions. Delayed or missed access to OP treatments like intravenous or subcutaneous antiresorptives, often hospital-administered, was expected; however, this effect was minimal in our OP patients. The study by Peeters et al. (22) revealed that 45.4% and 6.3% of patients interrupted receiving their intravenous bisphosphonates and denosumab treatments, respectively. The lower interruption rate in OP treatment of our patients compared to other studies might have been related to the health measures introduced with the pandemic in our country. Among these measures, prolonging the medical report durations to reduce patient visits to health institutions and obtaining reported medications from pharmacies without needing a prescription might have been the strategies that positively influenced the results. We also think that studies involving data on subsequent pandemic processes are needed.

Until the COVID-19 pandemic, none of the guidelines contained recommendations on managing such a crisis from the perspective of providing OP treatment. However, since the onset of the pandemic, several opinions have been published (23-26). In addition, long-term protection against fractures after treatment with zoledronic acid and other oral bisphosphonates has been documented in several studies (27-30). Therefore, based on the above, even delaying a scheduled infusion for a few months is not expected to be harmful. On the other hand, if this period will last longer than 6-9 months, switching from infusion to oral bisphosphonates has been recommended (23). When denosumab administrations were delayed for seven months following the last dose, the drug's inhibitory effects on bone resorption were observed to disappear rapidly (31).

Meanwhile, in patients discontinuing treatment, rapid bone loss, increased vertebral fracture risk, and hypercalcemia might be noted by the end of one year (32). A review of current guidelines suggests that denosumab treatment postponement should not exceed one month from the scheduled injection date (31,32). A rebound bone loss and an increased fracture risk are anticipated when delayed. Therefore, patients receiving denosumab and their family members should be educated about such situations, and if such treatment is not possible, conversion to oral bisphosphonates should be recommended (23).

## Conclusion

Our study revealed that OP patients were mildly affected by the COVID-19 pandemic. Therefore, we suggest that measures such as telemedicine services, video training, and maintaining a particular clinic active for treating such patients might be helpful in addition to preventive measures undertaken in probable similar situations.

## Ethics

**Ethics Committee Approval:** This study was approved by Aydın Adnan Menderes University Non-invasive Clinical Research Ethics Committee (decision no: 4, date: 06.08.2020).

**Informed Consent:** All participants were informed about their conditions and signed an informed consent form.

**Peer-review:** Externally and internally peer-reviewed.

## Authorship Contributions

Surgical and Medical Practices: G.T.B., M.D., Concept: G.T.B., M.D., G.G., Design: G.T.B., M.D., G.G., Data Collection or Processing: G.T.B., Analysis or Interpretation: M.D., İ.K.Ö., Literature Search: G.T.B., M.D., Writing: G.T.B., M.D., İ.K.Ö.

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