

The effect of the COVID-19 pandemic on perimenopausal symptoms

COVID-19 pandemi sürecinin perimenopozal semptomlar üzerine etkisi

Buğra Şahin, Gizem Cura Şahin, Banuhan Şahin

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Abstract

Aim: Menopause is the period of transition from the era of female reproduction to the period of loss of reproductive ability associated with the regression of ovarian functions. Perimenopause period is; It covers premenopausal (2 years before menopause) and menopausal (first 2 years after menopause). The aim of this study was to investigate the effect of the COVID-19 pandemic on menopause symptoms of women who contracted COVID-19 infection during the perimenopausal period when they were more sensitive psychosocially to the pandemic restrictions.

Material and method: The study included 103 women aged 45-55 years, who presented at the Gynaecology and Obstetrics Clinic of Turhal State Hospital because of menopause symptoms between June 2021 and August 2021. The women were separated into 2 groups as 32 women who had contracted COVID-19 infection during the previous 6 months and recovered, and 71 women who had not had COVID-19. The groups were compared in respect of age, gravida, parity, body weight, menopause status, and not taking regular exercise using the Menopause Symptom Evaluation Scale.

Results: Menopause status ($p=0.002$), not taking regular exercise ($p<0.001$), sleep problems ($p=0.002$), hot flashes ($p<0.001$), anxiety ($p<0.001$), and joint-muscle complaints ($p=0.002$) were determined at statistically significantly higher rates in the COVID-19 group compared to the non-COVID-19 group.

Conclusion: The status of not taking regular exercise, thought to be associated with the COVID-19 pandemic restrictions, was observed to increase menopause symptoms. Hot flashes, anxiety and sleep problems in particular were found to be significant complaints in menopausal patients who had been infected with COVID-19. It must be taken into consideration that these could be associated with previous COVID-19 infection.

Key words: COVID-19, anxiety, menopause, sleep problems.

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Öz

Amaç: Menopoz; kadınların üreme çağından, over fonksiyonlarındaki gerilemeye bağlı olarak üreme yeteneğinin kaybolduğu evreye geçiş dönemidir. Perimenopoz dönemi ise; premenopozal (menopoz öncesi 2 yıl) ve menopozal (menopoz ve sonrası ilk 2 yıl) dönemleri kapsamaktadır. COVID-19 pandemisi ise tıbbi, psikolojik ve sosyal-ekonomik yönleriyle küresel halk sağlığı sorununa neden olan bir kriz durumudur. Bu çalışmada pandemi döneminde kısıtlamalara bağlı olarak psikososyal yönden hassas olan perimenopozal dönemdeki COVID-19 geçiren kadınların menopoz semptomlarının araştırılması amaçlanmıştır.

Gereç ve yöntem: Haziran 2021 ile Ağustos 2021 tarihleri arasında Turhal Devlet Hastanesi Kadın Hastalıkları ve Doğum Polikliniği'ne; 45-55 yaş aralığında perimenopozal dönemde olup menopoz semptomları nedeniyle başvuran 103 kadın çalışmaya dahil edildi. Kadınlar son 6 ay içerisinde COVID-19 hastalığı geçiren ve iyileşen 32 kadın ile COVID-19 hastalığı geçirmeyen 71 kadın olmak üzere iki ayrı gruba ayrıldı. Gruplar; yaş, gravida, parite, kilo, menopoz hali ve düzenli egzersiz yapmama durumları açısından Menopoz Semptomları Değerlendirme Ölçeği (MSDÖ) kullanılarak karşılaştırıldı.

Bulgular: Kadınların 23'ünün premenopozal, 80'inin ise menopozal dönemde oldukları saptandı. Menopoz hali ($p=0,002$), düzenli egzersiz yapmama durumu ($p<0,001$), uyku sorunları ($p=0,002$), sıcak basması ($p<0,001$), endişe ($p<0,001$) ve eklem-kas rahatsızlığı ($p=0,002$) şikayetleri COVID-19 hastalığı geçiren grupta, COVID-19 hastalığı geçirmeyen gruba göre belirgin olarak daha yüksek oranda saptandı. Menopozda olup COVID-19 geçirenlerde egzersiz yapmama durumu ($p=0,004$), sıcak basması ($p<0,001$), endişe ($p<0,001$) ve uyku sorunları ($p<0,001$) şikayetleri daha yüksek oranda görüldü.

Sonuç: Pandemiye kısıtlamaya bağlı olduğu düşünülen düzenli egzersiz yapmama durumunun menopoz semptomlarını arttırdığı görüldü. Özellikle de sıcak basması, endişe ve uyku sorunları şikayetlerinin menopozda olan ve COVID-19 geçirenlerde önemli birer şikayet oldukları saptandı. Bu nedenle perimenopozal dönemdeki kadınların menopoz şikayetleri dikkatle dinlenmeli ve bunların geçirilmiş COVID-19 hastalığına bağlı olabileceği göz önünde bulundurulmalıdır.

Buğra Şahin, M.D. Department of Obstetrics and Gynecology, Denizli State Hospital, Denizli, Turkey, e-mail: raaakun@gmail.com (<https://orcid.org/0000-0003-0429-3085>) (Corresponding Author)

Gizem Cura Şahin, M.D. Department of Obstetrics and Gynecology, Tokat State Hospital, Tokat, Turkey, e-mail: drgizemcura@gmail.com (<https://orcid.org/0000-0001-5696-4683>)

Banuhan Şahin, Ass. Prof. Department of Obstetrics and Gynecology, Amasya University Sabuncuoglu Serefeddin Training and Research Hospital, Amasya, Turkey, e-mail: banuhansahin@gmail.com (<https://orcid.org/0000-0002-8711-1584>)

Anahtar kelimeler: COVID-19, endişe, menopoz, uyku sorunları.

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Introduction

Menopause is the period of transition from the era of female reproduction to the period of loss of reproductive ability associated with the regression of ovarian functions [1]. The World Health Organisation (WHO) definition of menopause is the permanent termination of menstruation as a result of termination of ovarian activity [1]. The menopausal period consists of the premenopausal, menopausal, and postmenopausal periods. The period when the first symptoms are seen is defined as the premenopausal period, the period when the last menstrual bleeding occurs, as the menopausal period, and the period which starts from one year after menopause and lasts until the onset of old age, as the postmenopausal period [2, 3].

The mean age of menopause worldwide is 51 years, ranging from 45-55 years. The age of menopause in developing countries is earlier than in developed countries. The mean age in Turkey is 47 years [4].

In the menopause period, hormonal, physical, and emotional changes occur in women associated with reductions in oestrogen hormone [5]. Short-term problems experienced in menopause are vasomotor, atrophic, and psychological changes, and the long-term changes are cardiovascular diseases and osteoporosis [5, 6]. The new coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 virus was declared a global pandemic on 11 March 2020 by the WHO [7]. Complex interactions based on biological gender, complementary sex chromosome, reproductive tissues, and the concentration of sex steroid hormones (oestrogen, progesterone, and testosterone) play a multi-dimensional role in COVID-19 outcomes [8].

Although various studies have investigated common sensitivity factors (old age, gender, comorbidities) to virus infections, very little is known about the relationship between the clinical outcomes of COVID-19 hospitalised patients and menopause status (premenopause,

postmenopause) [9-11]. As has been previously reported, a significant change has been shown in the concentration of plasma sex hormones (reduced oestrogen and progesterone) in postmenopausal women compared to those in the premenopausal period [12]. In addition, oestrogen and/or progesterone can regulate the congenital and acquired immune response [13, 14]. There also remains uncertainty about whether or not there are different COVID-19 outcomes in women before and after menopause [15, 16].

The aim of this study was to investigate menopause symptoms during the COVID-19 pandemic in women who had contracted COVID-19 infection and recovered within the previous 6 months, who were in the perimenopausal period when there is psychosocial sensitivity

Material and method

Approval for this descriptive, cross-sectional study was granted by the Clinical Trials Ethics Committee of Tokat Gaziosmanpaşa University (decision no: 21-KAEK-145). The study included 103 women aged 45-55 years, who presented at the Gynaecology and Obstetrics Clinic of Turhal State Hospital because of menopause symptoms between June 2021 and August 2021. Patients were excluded from the study if they had undergone total abdominal hysterectomy+bilateral salpingo-oophorectomy (TAH + BSO), if they had active COVID-19 infection, or if they had had COVID-19 infection other than in the last 6 months. The women were separated into 2 groups as 32 women who had contracted COVID-19 infection during the previous 6 months and recovered, and 71 women who had not had COVID-19. The patients were also separated into 2 groups as 80 in the menopause period and 23, who were in the premenopause period.

The groups were compared in respect of age, gravida, parity, body weight, menopause status, and not taking regular exercise using the Menopause Rating Scale (MRS), which

evaluates symptoms of hot flashes, cardiac disorder, sleep problems, listlessness, irritability, anxiety, physical and mental fatigue, sexual problems, urinary problems, vaginal dryness, and joint-muscle disorders.

For all the patients who presented at the Gynaecology and Obstetrics Polyclinic with menopausal complaints, the responses to the questions of the MRS were recorded. The MRS was developed by Schneider, Heineman and Potthoff [17] in 1992 to determine the severity of menopausal complaints and the effect on quality of life. The scale was modified in 1996, and the Turkish version was named the Menopause Symptoms Evaluation Scale.

The scale was adapted to Turkish to be used in clinical applications for the quantitative evaluation of

- measurement of the severity of menopausal complaints experienced during the menopause period,

- comparison of the level of menopausal symptoms experienced by women under different conditions,

- comparisons of the severity of symptoms before and after treatment in the menopause period,

- determination of the effect of menopausal symptoms on quality of life,

- changes in menopausal symptoms.

The scale is presented in supplement 1.

Supplement 1: The Menopause Symptoms Evaluation Scale.

- 1- Hot flashes, sweats
- 2- Heart disorders (palpitations)
- 3- Sleep problems (problems falling asleep, waking early)
- 4- Listlessness
- 5- Irritability
- 6- Anxiety
- 7- Physical – mental fatigue (loss of concentration)

- 8- Sexual problems (anhedonia)
- 9- Urinary problems (urinary incontinence)
- 10- Vaginal dryness, burning (vaginitis)
- 11- Joint-muscle disorders (rheumatismal complaints)

Normally, the scale is formed of 11 items referring to menopausal complaints, which are scored on a Likert-type scale as 0: none, 1: mild, 2: moderate, 3: severe, and 4: very severe. Total points range from 4-44. However, the scale used in this study was in the form of “present/absent” responses, and these were recorded for each participant.

Statistical analysis

Data obtained in the current study were analyzed statistically using SPSS vn. 16.0 software (Statistical Package for Social Sciences, Chicago, IL, USA). Descriptive statistics were stated as mean \pm standard deviation (SD) values for continuous variables and as number (n) and percentage (%) for categorical variables. In the paired group comparisons, the Independent Samples t-test, the Mann Whitney U-test, Normality test, or the Chi-square test were used. A value of $p < 0.05$ was accepted as statistically significant.

Results

Evaluation was made of the data of a total of 103 perimenopausal women, comprising 32 who had contracted COVID-19 infection within the previous 6 months and 71 who had not had COVID-19. The study participants were also separated into 2 subgroups as 80 in menopause and 23 in premenopause. The mean age was determined as 51 ± 3.88 years in the group who had had COVID-19 and 49.9 ± 3.11 years in the group that had not had COVID-19 ($p = 0.097$), and as 50.76 ± 3.46 years in the menopause group and 48.43 ± 2.39 years in the premenopause group ($p = 0.003$). The women in the menopausal period were seen to be statistically significantly older than the women in premenopause (Tables 1, 2).

No statistically significant difference was determined in respect of weight, gravida, and parity between the COVID-19 positive and negative groups ($p = 0.260$, $p = 0.106$,

Table 1. The age, gravida, parity, and weight values of the women with and without a history of COVID-19 infection

	COVID-19-positive	COVID-19-negative	p value
Age (years)	50.75±3.87	49.9±3.11	<i>p</i> =0.097
Gravida	2 (1-9)	3 (1-8)	<i>p</i> =0.106
Parity	2 (0-8)	2 (0-7)	<i>p</i> =0.625
Weight (kg)	75.03±14.21	72.04±10.54	<i>p</i> =0.26

Table 2. The age, gravida, parity, and weight values of the women in menopause and premenopause

	Menopause	Premenopause	p value
Age (years)	50.86±3.35	47.74±2.09	<i>p</i>=0.003
Gravida	3 (1-9)	3 (1-4)	<i>p</i> =0.099
Parity	2 (0-8)	2 (0-4)	<i>p</i> =0.288
Weight (kg)	72.9±12.68	73.22±8.33	<i>p</i> =0.386

p=0.625, respectively) (Table 1), or between the menopause and premenopause groups (*p*=0.386, *p*=0.099, *p*=0.288, respectively) (Table 2). When the women who had and had not had COVID-19 were compared according to menopause status and the menopause symptom evaluation scale, higher rates were determined in the women who had contracted COVID-19 in respect of menopause status (*p*=0.002), not taking regular exercise (*p*<0.001), anxiety (*p*<0.001), sleep problems (*p*=0.002), hot flashes (*p*<0.001), and joint-muscle pain (*p*=0.002).

No statistically significant difference was determined between the groups in respect of vaginal dryness (*p*=0.009), urinary problems (*p*=0.072), sexual problems (*p*=0.200), physical- mental fatigue (*p*=0.761), irritability (*p*=0.046), listlessness (*p*=0.464), and heart disorders (*p*=0.057) (Table 3). According to the menopause symptom evaluation scale, not taking regular exercise (*p*<0.001), vaginal dryness (*p*<0.001) urinary problems (*p*<0.001), anxiety (*p*<0.001), sleep problems (*p*<0.001) and hot flashes (*p*<0.001) were observed at a statistically significantly higher rate in the women in menopause compared to those in the premenopause period. No statistically significant difference was determined between these two groups in respect of sexual problems (*p*=0.841), physical-mental fatigue (*p*=0.545),

irritability (*p*=0.232), listlessness (*p*=0.280), heart disorders (*p*=0.027), and joint pain (*p*=0.027) (Table 4).

Discussion

Very little is known about the relationship between menopause status and the outcomes of COVID-19. In this study conducted in a single polyclinic over a 3-month period, when perimenopausal women were evaluated according to the MSES, complaints of sleep problems, hot flashes, anxiety, and joint-muscle disorders were observed at a significantly higher rate in the group that had contracted COVID-19 infection compared to the group that had not had COVID-19. In addition, vaginal dryness, urinary problems, hot flashes, anxiety, and sleep problems were determined at significantly higher rates in the menopause group compared to the premenopause group. The rate of not taking regular exercise was determined to be significantly higher both in women in the menopausal period and in women who had contracted COVID-19.

Facial redness, night sweats, and hot flashes are known to be vasomotor symptoms [18]. In Turkey, approximately 80% of women have complaints of hot flashes [3]. If the effect of exercise on hot flashes is examined, it can be seen that Elavsky and McAuley reported that women in the menopausal period who had a

Table 3. The MSES findings, menopause status, and exercise levels of the women with and without a history of COVID-19 infection

		COVID-19-positive n (%)	COVID-19 -negative n (%)	p value
Joint-muscle pain	Present	17 (16.5)	16 (15.53)	p=0.002
	Absent	15 (14.56)	55 (53.39)	
Hot flashes	Present	25 (24.27)	25 (24.27)	p<0.001
	Absent	7 (6.79)	46 (44.66)	
Heart disorders	Present	20 (19.41)	30 (29.12)	p=0.057
	Absent	12 (11.65)	41 (39.8)	
Sleep problems	Present	26 (25.24)	35 (33.98)	p=0.002
	Absent	6 (5.82)	36 (34.95)	
Listlessness	Present	16 (15.53)	30 (29.12)	p=0.464
	Absent	16 (15.53)	41 (39.8)	
Irritability	Present	28 (27.18)	49 (47.57)	p=0.046
	Absent	4 (3.88)	22 (21.35)	
Anxiety	Present	30 (29.12)	38 (36.89)	p<0.001
	Absent	2 (1.94)	33 (32.03)	
Physical-mental fatigue	Present	15 (14.56)	31 (30.09)	p=0.761
	Absent	17 (16.5)	40 (38.83)	
Sexual problems	Present	10 (9.7)	14 (13.59)	p=0.2
	Absent	22 (21.35)	57 (55.33)	
Urinary problems	Present	21 (20.38)	33 (32.03)	p=0.072
	Absent	11 (10.67)	38 (36.89)	
Vaginal dryness	Present	17 (16.5)	19 (18.44)	p=0.009
	Absent	15 (14.56)	52 (50.48)	
Menopause status	Present	31 (30.09)	49 (16.5)	p=0.002
	Absent	1 (0.97)	22 (21.35)	
Regular exercise	Present	3 (2.91)	26 (25.24)	p=0.004
	Absent	29 (28.15)	45 (43.68)	

high level of physical activity experienced fewer vasomotor problems [19]. That study, which was conducted in Berlin, determined a positive relationship between regular physical exercise and a decrease in problems in the menopausal period. In another study that evaluated the relationship between climacteric symptoms and the level of physical activity, it was seen that intense physical exercise was less effective on menopausal symptoms, and mild physical exercise when gardening, in the workplace, or when carrying something was more effective on menopausal symptoms. Those taking regular exercise felt more comfortable and were reported to experience less severe and less frequent climacteric symptoms [20]. In the current study, hot flashes were seen more in menopausal women and those who had had COVID-19, which was thought to be associated

with a reduction in oestrogen and insufficient physical activity during the pandemic.

Sleep problems was one of the most important complaints seen in the menopausal period following night sweats and hot flashes. Approximately 75% of women experience hot flashes in the menopausal period, and the prevalence of sleeplessness has been reported to range from 14% to 53% [21-23]. In an online-based study conducted during the COVID-19 pandemic, there was seen to be an increase in mental health diseases such as depression. The prevalence of depression in that study was found to be 18.5%, anxiety 24.6%, and poor sleep quality 69.5% [24]. In the current study, sleep problems were observed at a higher rate in women in the menopausal period and in those who had had COVID-19.

Table 4. The MSES findings and exercise levels of the women in menopause and premenopause

		Menopause n (%)	Premenopause n (%)	p value
Joint-muscle pain	Present	30 (29.12)	3 (2.91)	$p=0.027$
	Absent	50 (48.54)	20 (19.41)	
Hot flashes	Present	49 (47.57)	1 (0.97)	$p<0.001$
	Absent	31 (30.09)	22 (21.35)	
Heart disorders	Present	41 (39.8)	9 (8.73)	$p=0.305$
	Absent	39 (37.86)	14 (13.59)	
Sleep problems	Present	55 (53.39)	6 (5.82)	$p<0.001$
	Absent	25 (24.27)	17 (16.5)	
Listlessness	Present	38 (36.89)	8 (7.76)	$p=0.28$
	Absent	42 (40.77)	15 (14.56)	
Irritability	Present	62 (60.19)	15 (14.56)	$p=0.232$
	Absent	18 (17.47)	8 (7.76)	
Anxiety	Present	61 (59.22)	7 (6.79)	$p<0.001$
	Absent	19 (18.44)	16 (15.53)	
Physical-mental fatigue	Present	37 (35.92)	9 (8.73)	$p=0.545$
	Absent	43 (41.74)	14 (13.59)	
Sexual problems	Present	19 (18.44)	5 (4.85)	$p=0.841$
	Absent	61 (59.22)	18 (17.47)	
Urinary problems	Present	51 (49.51)	3 (2.91)	$p<0.001$
	Absent	29 (28.15)	20 (19.41)	
Vaginal dryness	Present	36 (43.95)	0	$p<0.001$
	Absent	44 (42.71)	23 (22.33)	
Regular exercise	Present	6 (5.82)	23 (22.33)	$p<0.001$
	Absent	74 (71.84)	0	

One of the atrophic changes that occurs with insufficient oestrogen is urogenital complaints, which is one of the most frequently seen problems in the menopause period [25]. The results of a study in the USA reported that sexual problems were experienced by 27% of menopausal women, changes in emotional state by 19-29%, vaginal problems by 6-13%, and urinary system problems by 17% [6]. In a 2005 study conducted in Istanbul by Arikian [26], 30% of women were found to have experienced problems associated with connective tissue changes such as dry skin, itching, joint pain, and prolapse. In the women in the menopausal period in the current study, there were seen to be more problems of vaginal dryness and urinary complaints. However, no significantly higher rate of sexual problems was determined in the menopausal group.

By leading to a series of mental changes in the central nervous system, hormonal changes in menopause are thought to affect mood state

and behaviour. Some of these complaints are feeling bad, sad, and weepy, listlessness, changes in mood, irritability, feeling tense, being quick to anger, restlessness, panic, reduced general performance, poor memory, difficulties in concentration, and forgetfulness [27]. In a study in Taiwan of 3359 women aged 40-55 years, a high rate of anxiety symptoms related to menopause was determined in 145 women [28]. Recent studies of the psychological and social effects of COVID-19 have shown that the disease led to radical changes in living conditions in many societies, and there was reported to be a relationship with negative psychological outcomes [29]. For example, in a study in China of 1210 subjects during the COVID-19 pandemic, 16.5% of the study participants were found to have depression symptoms at a moderate to severe level, and 28.8% had moderate to severe anxiety symptoms [30]. In the current study, anxiety was determined more in the women in the menopausal period and in those who had had COVID-19.

It has been reported that 25% of COVID-19 symptomatic patients have myalgia and general weakness. Although some data have shown that the formation of muscle pain is not increased with COVID-19 severity, myalgia in patients with abnormal computed tomography (CT) or radiographic imaging finding is a significant predictive factor for disease severity [31, 32]. In the current study, the complaint of muscle-joint pain was seen at a higher rate in the women with a history of COVID-19 infection.

There were some limitations to this study, primarily that the low number of patients in both groups prevented significant results being reached in the comparisons of some parameters. Therefore, there is a need for further studies with greater numbers of patients.

In conclusion, the results of this study showed that menopause symptoms were increased by not taking regular exercise, which was thought to be due to the pandemic restrictions. The complaints of hot flashes in particular, anxiety, and sleep problems were each determined to be significant complaints in women in menopause and those who had contracted COVID-19 infection. Therefore, the menopause complaints of perimenopausal women should be listened to carefully and it must be considered that these could be associated with a history of COVID-19 infection.

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

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Contributions of authors

B.S., G.C.S. and B.S. conceptualized and designed the article. B.S., G.C.S. and B.S. designed the material-method section. B.S., G.C.S. and B.S. collected the data. B.S., G.C.S. and B.S. evaluated the data in the results section. The discussion section of the article was written by B.S., G.C.S. and B.S. In addition, all authors discussed the study and approved its final version.