A Prospective Study on Anxiety and Blood Pressure Levels in Hemodialysis Patients During COVID-19 Pandemic

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ABSTRACT

Objective: The coronavirus disease 2019 (COVID-19) pandemic has currently been one of the leading causes of psychosocial stress throughout the world. We hypothesized that possible changes in anxiety status during the COVID-19 pandemic might affect blood pressure in hemodialysis (HD) patients.

Methods: This is an observational cross-sectional study. The Hospital Anxiety and Depression Scale (HADS) and State-Trait Anxiety Inventory (STAI) were applied to 71 prevalent HD patients. Pre-dialysis blood pressure was measured, and the systolic blood pressure measurements of 6 consecutive HD sessions were averaged. All assessments were performed both at the beginning (March) and after the end (June) of the partial lockdown, which was officially instituted by the Government in Turkey.

Results: The mean age ($\pm$SD) was 59.2 $\pm$ 14.8 years and 52% of the patients were female. The STAI-State score was higher in March than in June (44.6 $\pm$ 12.6 vs. 42.3 $\pm$ 11.5, respectively, P = .047), whereas the HADS-Anxiety, HADS-Depression, and STAI-Trait scores were not different. The pre-dialysis systolic blood pressure was significantly higher in March than in June (127.9 $\pm$ 20.3 vs. 124.8 $\pm$ 22.8 mmHg, respectively, P = .029). The change in state anxiety score from March to June was remarkable, particularly in patients not taking a beta-blocker (49.3 $\pm$ 9.6 to 43.8 $\pm$ 11.1, P = .001) and in patients younger than the median age of 64 years (48.6 $\pm$ 12.8 to 45.3 $\pm$ 12.5, P = .029). The change in blood pressure level from March to June was found to be significant only in patients not taking a beta-blocker (123.4 $\pm$ 20.2 to 118.2 $\pm$ 20.6 mmHg, P < .001), while it did not reach a statistically significant level in the others.

Conclusion: Our findings revealed an association between a higher state of anxiety and a higher blood pressure level in HD patients during the COVID-19 pandemic, which was remarkable particularly in patients not taking a beta-blocker.

Keywords: Anxiety, blood pressure, COVID-19

INTRODUCTION

Countless people around the world have faced unprecedented physical, mental and financial challenges since the coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome-2 coronavirus (SARS-CoV-2) has become a lethal pandemic.[1, 2] Among them, anxiety, which is defined as feeling a sense of danger and apprehension about the future,[2] was particularly common. Uncertainty, the fear of getting infected, social distancing, the loss of loved ones, and the loss of jobs have been the main reasons for anxiety in the general population.[3] Furthermore, individuals with high-risk profiles, such as patients with chronic diseases, are in greater distress.[4] Those who need to admit to a healthcare center regularly for reasons other than COVID-19, such as hemodialysis (HD) patients and cancer patients, might endure even higher levels of anxiety.[5]

In Turkey, the first COVID-19 case was confirmed on March 11, 2020, and with the rapid increase in the number cases and mortalities, an official partial lockdown was instituted by the Government on March 16, 2020.

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During the partial lockdown, in addition to the many strict measures taken to prevent spread of the disease, a curfew was imposed for people older than 65 and younger than 20 years old, on a whole-day basis for approximately 3 months. Everyone, except healthcare workers and the government appointed officers, was forbidden to go out during the weekends, except to restock food supplies. HD patients had to obtain a permit indicating their special status exempting them from the curfew. These strict measures were a source of distress, especially for HD patients. The curfew and partial lockdown were officially ended on June 1, 2020, after a substantial decrease in the number of COVID-19-related cases and deaths.[6]

The association between increased psychosocial stress and hypertension is an established phenomenon.[7] The probable mechanisms underlying psychosocial stress-induced hypertension are a hyperactive sympathetic system, a decreased vagal tone, the immune effects of stress-induced increase in angiotensin-2, and a maladaptive behavioral response.[8–10] Although there are data showing a relation between anxiety during the COVID-19 pandemic and a disturbance in mental health in the general population,[11] anxiety and its effect on blood pressure in HD patients are yet to be studied.

In the present study, we aimed to explore the possible association of anxiety during the COVID-19 pandemic with blood pressure in HD patients. We hypothesized that higher anxiety levels would be related to higher blood pressure levels, depending on the perceived distress at different time points of the pandemic.

METHODS

This is a single-center, prospective observational study that includes all prevalent adult HD patients, who had been treated for at least 3 months prior to the worldwide onset of the COVID-19 pandemic (i.e., December 2019). We intended to include all of the patients in our dialysis center; however, among the 79 eligible HD patients at our center, 2 patients did not consent to participate in the study, 2 patients transferred to another dialysis center during the study period, and 4 patients did not respond to the scales although they gave their consent; hence 71 patients were included in the study. This study was approved by Ankara University School of Medicine Ethics Committee for Clinical Studies (I3-188-20) and was carried out in accordance with the World Medical Association Declaration of Helsinki. Before inclusion, all patients gave written informed consent.

All patients were being dialyzed either thrice weekly ($n = 63$, 88.7%), or twice weekly ($n = 8$, 11.3%), for 4-hour-durations using a high-flux membrane with an appropriate dialysate.

All the assessments were performed both after the institution of the official partial lockdown was imposed, on March 16, 2020, and after it was declared lifted, on June 1, 2020.

The demographic features including education level, socioeconomic status, and medical and psychiatric comorbidities were recorded. All concomitant medications and any medication change that happened during the study period were recorded. A physical examination was done at the beginning of the HD session, in which the scales were applied. In addition to the routine monthly laboratory evaluations, the urea reduction ratio, Kt/V urea, the patients' body weight before and after each HD session, and the ultrafiltration volume were noted. There was no treatment change for this study protocol; however, all patients were checked routinely and treatment changes were made by the treating physician if needed.

In order to decrease the risk of infection, a series of preventive measures were instituted in our HD unit after the COVID-19 pandemic began, in addition to the routine standards, considering both international and local recommendations.[5, 12] The distance between dialysis machines was increased as much as possible. Entry into the dialysis unit was not allowed before the cleaning of the machines was completed. The meals served during the sessions were cancelled. Patients were not allowed to go inside the unit without masks, and their body temperatures were measured before entering the unit. All patients were informed about proper hygiene rules and social distancing, as well as the symptoms and signs of the disease. They were asked to inform the HD unit if they had noticed any symptoms or signs, and to refrain from using the transport vehicle together with the other patients.

Measures

Hospital Anxiety and Depression Scale (HADS): The HADS is a 4-point Likert-type scale and was developed to screen depression and anxiety levels in the past week in general hospital settings.[13] It was tested for reliability and validity in the Turkish

Main Points

- Countless people around the world have faced unprecedented physical, mental, and financial challenges since the coronavirus disease 2019 (COVID-19) has become a lethal pandemic. Among them, hemodialysis (HD) patients, who need to admit a healthcare center regularly for reasons other than COVID-19, might have endured even higher levels of anxiety.
- The association between increased psychosocial stress and hypertension is an established phenomenon. Although there are data showing a relation between anxiety and COVID-19 in the general population, anxiety and its effect on blood pressure in HD patients are yet to be studied.
- In this study, we have found a higher state anxiety level and a higher blood pressure in prevalent HD patients in March 2020, when the official partial lockdown was in force, compared with June 2020, when the of restrictive measures were relaxed. Once the lockdown and the stress related to it were thought to be over, the anxiety score and blood pressure levels were found to have decreased.

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context; a cut-off score of 7 was found for the depression sub-scale (HADS-D), and a cut-off score of 10 was found for an anxiety subscale (HADS-A).[14]

State-Trait Anxiety Inventory (STAI): The STAI, developed by Spielberger and Gaudry,[15] aims to measure both the state and trait anxiety levels of individuals. The Turkish version has adequate psychometric properties.[16] The instrument comprises 40 items grouped in 2 distinct categories: Sate and Trait. the STAI-1 is used to assess acute (state) distress and anxiety, while the STAI-2 is aimed at assessing distress and anxiety in general (trait). The STAI scores range from 20 to 80, and higher scores indicate higher trait anxiety.[16]

Blood Pressure Measurements: The HD nurses measured the systolic and diastolic blood pressure with an automatic oscillometric device on brachial arteries with appropriate cuff size, while the patient was resting in the HD chair. As per our institutional practice, 2 consecutive measurements were obtained, and their average was noted for each record. On a routine basis, 5 measurements were recorded for each HD session at the beginning, first, second, and third hour, and at the end of the session. Beginning with the session that the psychological inventories were applied, the pre-dialysis systolic blood pressure measurements of 6 consecutive HD sessions were averaged and used for statistical analyses in the present study.

Statistical Analysis
The clinical and laboratory data were expressed as percentages, means ($\pm$SD) or medians (range), as appropriate. To investigate the differences and correlations of blood pressure levels and anxiety levels over time, the independent-samples t-test, the paired-samples t-test, and Pearson and Spearman's correlation analyses were used as appropriate. A threshold value of $P < .05$ was considered as statistically significant. All analyses were done using Statistical Package for the Social Sciences (SPSS) version 23.0 (IBM SPSS Corp.; Armonk, NY, USA).

RESULTS
The mean age ($\pm$SD) was 59.2 $\pm$ 14.8 years and 52% of the patients were female. The mean duration of HD was 7.7 $\pm$ 6.3 years. The demographic features and clinical characteristics of the patients are shown in Table 1.

No patient was diagnosed positive for COVID-19 during the study period. The dosage of the medications, including antihypertensives, did not change throughout the study among those who were already receiving them; however, 3 patients needed cessation of antihypertensive medication in May or June. The dry weight, the interdialytic weight gain, and Kt/V urea values were also stable in all patients during the study period (Table 2). The hemoglobin levels increased from 10.7 $\pm$ 1.5 g/dL to 11.3 $\pm$ 1.4 g/dL (P = .003), while the other laboratory parameters were not significantly different between March and June.

Table 1. Demographic Features and Clinical Characteristics of the Patients

	Number of Patients	%
Age (years) (mean $\pm$ SD)	59.2 $\pm$ 14.8	-
Gender (female)	37	52.1
Education level		
Primary school or below	29	40.8
Secondary school	3	4.2
High school	23	32.4
University	16	22.5
HD duration (years) (mean $\pm$ SD)	7.7 $\pm$ 6.3	-
HD schedule (n, %)		
Thrice weekly	63	88.7
Twice weekly	8	11.3
Psychiatric disease requiring medication	12	16.9
Anxiety disorder	3	
Depression	8	
Sleep disturbance	1	
Patients taking any antihypertensive medication		
March	33	46.5
June	30	42.3
Patients taking combination antihypertensive treatment (n, %)	20	28.2
Type of antihypertensive medications (n, %)		
Alpha-blocker	9	12.7
Angiotensin-converting inhibitor	4	5.6
Angiotensin receptor blocker	3	4.2
Beta-blocker	38	53.5
Calcium channel blocker	20	28.2
Patients receiving an ESA (n, %)		
March	43	60.6
June	40	56.3

ESA, erythropoiesis-stimulating agent; HD, hemodialysis; SD, standard deviation.

There were 12 patients (16.9%), who were all in partial or full remission, and had a diagnosis of psychiatric disease requiring medications, as the following: atypical antidepressant, mirtazapine (n = 1); selective serotonin reuptake inhibitors, escitalopram (n = 4), sertraline (n = 5); antihistamine as a sedating medication: hydroxyzine (n = 1); and a serotonin modulator, trazodone (n = 1).

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Table 2. Comparison of Psychometric Variables, Blood Pressure Levels, and Related Parameters in March 2020, When the COVID-19 Pandemic Emerged and the Official Partial Lockdown Began, and in June 2020, When the Pandemic Began to Extinguish and the Lockdown Was Lifted

|	March	June	P
HADS-Anxiety score	7.9 ± 3.9	7.9 ± 4.4	.972
HADS-Depression score	7.9 ± 4.1	7.6 ± 3.8	.334
STAI-State score	44.6 ± 12.6	42.3 ± 11.5	**.047**
STAI-Trait score	47.9 ± 9.7	47.4 ± 8.6	.558
Pre-dialysis systolic BP	127.9 ± 20.3	124.8 ± 22.8	**.029**
Pre-dialysis BW—weekly (mean ± SD, kg)	69.9 ± 13.5	69.9 ± 13.4	.717
Post-dialysis BW—weekly (mean ± SD, kg)	67.4 ± 13.1	67.5 ± 13.2	.360
Interdialytic weight gain- weekly (% of dry-weight)	3.64 ± 1.12	3.5 ± 1.2	.567
Kt/V urea	1.63 ± 0.3	1.64 ± 0.3	.663

HADS, Hospital Anxiety and Depression Scale; STAI, State and Trait Anxiety Inventory; BP, blood pressure; BW, body weight; HD, hemodialysis; SD, standard deviation. P values of statistically significant parameters are bolded.

The STAI-State score was higher in March, when the COVID-19 pandemic emerged and the official partial lockdown began, than that in June, when the pandemic began to extinguish and the lockdown was lifted (44.6 ± 12.6 vs 42.3 ± 11.5, respectively, P = .047), (Figure 1A). The scores of HADS-Anxiety, HADS-Depression, and STAI-Trait were not significantly different between March and June (Table 2). All psychometric inventory scores were strongly correlated with each other, both in March and June. According to the HADS-Anxiety cut-off scores, 21.4% and 22.5% of the participants were considered as having high anxiety levels in March and June, respectively. According to the HADS-Depression cut-off scores, 55.7% and 52.9% of the sample participants were considered as having high depression levels in March and June, respectively.

The pre-dialysis systolic blood pressure was significantly higher in March than in June (127.9 ± 20.3 vs. 124.8 ± 22.8 mmHg, respectively, P = .029), (Table 2and Figure 1B). No statistically significant correlations were found between the STAI-State scores and the blood pressure levels, either in March or in June.

The STAI-State score in patients who were not taking a beta-blocker (n = 33, 46.5%) was significantly higher in March than those on a beta-blocker (49.3 ± 9.6 vs. 40.6 ± 13.6, respectively, P = .003). In June, the STAI-State score significantly decreased in patients who were not on a beta-blocker, (49.3 ± 9.6 to 43.8 ± 11.1, P = .001), while it remained stable in the others (40.6 ± 13.6 to 41.1 ± 11.8, P = .742).
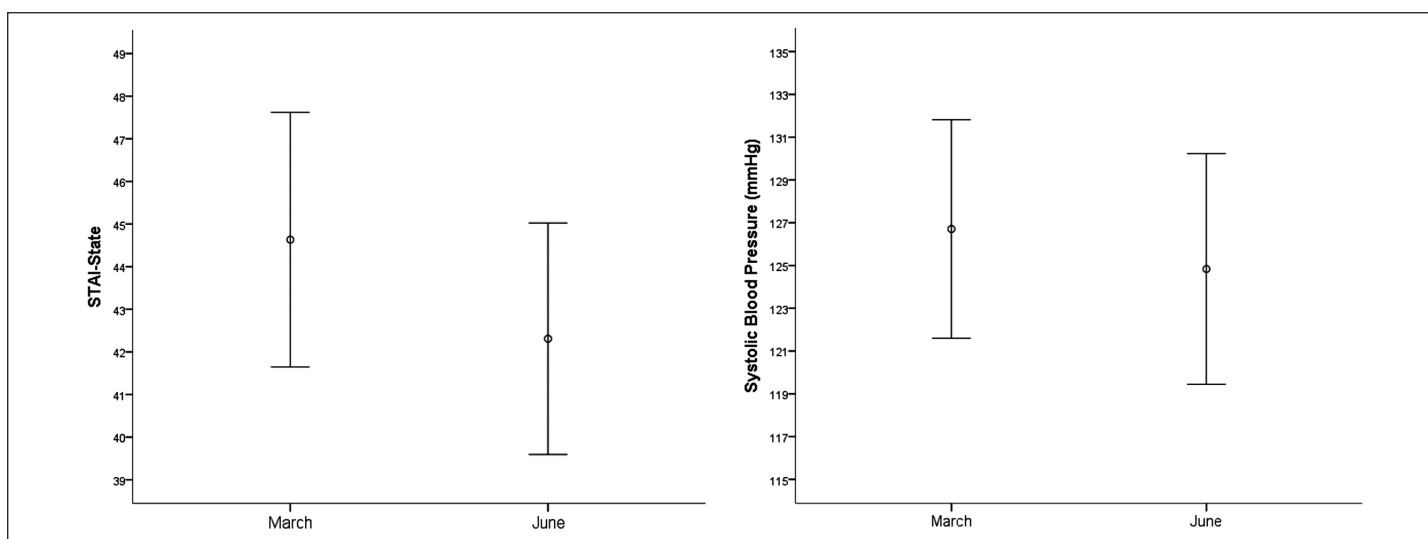
Figure 1. a,b. Comparison of the STAI-State scores and blood pressure levels in March (when the COVID-19 pandemic emerged and the official partial lockdown began) to those in June (when the pandemic began to extinguish and the lockdown was lifted). Bars represent 95% confidence intervals. (A) The STAI-State score was significantly higher in March than in June (44.6 ± 12.6 vs. 42.3 ± 11.5, respectively, P = .047). (B) Pre-dialysis systolic blood pressure was significantly higher in March than in June (127.9 ± 20.3 vs. 124.8 ± 22.8 mmHg, respectively, P = .029).

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In comparison to the patients not taking a beta-blocker, the pre-dialysis systolic blood pressure level in those on a beta-blocker tended to be higher in March (123.4 ± 20.2 vs. 131.8 ± 19.9 mmHg, respectively, *P* = .082) and was significantly higher in June (118.2 ± 20.6 vs. 130.6 ± 23.2 mmHg, respectively, *P* = .021). In parallel with the STAI-state score, blood pressure level significantly decreased in patients not taking a beta-blocker (*P* = .006), while it remained stable in patients on a beta-blocker (*P* = .570).

A comparison of the patients who were younger than the median age of 64 years with the others revealed that the STAI-State score was significantly higher in younger patients than in older patients, both in March (48.6 ± 12.8 vs. 40.8 ± 11.3, respectively, *P* = .008), and in June (45.3 ± 12.5 vs. 39.4 ± 9.7, respectively, *P* = .032). The decrease in the STAI-State score was significant in younger patients (*P* = .029), while it was not significant in older patients (*P* = .455).

The pre-dialysis systolic blood pressure levels tended to be lower in patients younger than 64 years than that in the older patients both in March (126.5 ± 20.5 vs. 129.2 ± 20.4 mmHg, respectively) and in June (124.1 ± 24.5 vs. 125.6 ± 21.3, respectively). The decrease in blood pressure level did not reach a statistically significant level in any age group.

DISCUSSION

In the present single-center, prospective, observational study, we found higher state anxiety level and a higher blood pressure in the prevalent HD patients in March 2020, when the official partial lockdown and curfew due to COVID-19 pandemic were instituted and first implemented by the Turkish Government, with June 2020, when the of restrictive measures were relaxed due to the decreased count of new cases and deaths in the country. Once the lockdown and the stress related to it were thought to be over, the anxiety scores as well as blood pressure levels were found to be decreased. These differences were more remarkable particularly in patients who were not taking a beta-blocker and those younger than the median age of 64 years.

Hypertension is an established, strong, and independent risk factor for cardiovascular diseases, and considered as one of the most prominent public health issues worldwide.[17,18] Psychosocial factors have been suggested to have a role in the development of hypertension, besides the well-established risk factors such as age, race, genetic factors, dietary habits, obesity, alcohol consumption, and smoking.[17–19] Globalization and cultural changes have transformed our perception of stress, and in developed and developing countries, occupational, financial, and social stress have gained more importance as they lead to an increase in depression and anxiety.[20, 21] Eventually, globalization has created the worst scenario, a viral disease transmitting from human to human that does not yet have a cure. Both anxiety and depression are reported to be associated with

hypertension. However, there is more convincing evidence indicating an association between anxiety levels and hypertension risk.[22, 23] As an interesting example for the association between anxiety and hypertension, Dorn et al.[24] found a 1.5 fold greater risk of new-onset hypertension developing in the parents of the adolescents who were victims of the fire disaster in the Netherlands, than those in the control group.[24]

Previous research on HD patients has reported high anxiety and depression rates ranging from 12% to 52%.[25] Thoughts of recent traumatic events might trigger anxiety or depression, and a psychosocial burden, especially feeling a sense of danger about getting infected from dialysis centers and having several comorbidities, might have drastic mental consequences on maintenance HD patients. This concern was so significantly large that many guidelines have been published aiming to decrease the risk of contamination by SARS-CoV-2 in dialysis facilities after the emergence of the pandemic.[5, 12] Media coverage of the pandemic, in turn, possibly increases the perceived distress among these patients who already have chronic diseases.[3] Supporting this subject, in our sample, according to the HADS, we have found that 21.4% and 22.5% of the patients had high anxiety levels, and 55.7% and 52.9% of the patients had high depression levels in March and June, respectively.

Wu et al.[26] used their unique opportunity to assess the effect of COVID-19 on mental health in pregnant women through their study initiated in the beginning of December 2019, before the pandemic began. Using the Edinburgh Postnatal Depression Scale, they showed that depressive and anxiety symptoms increased after the official declaration of the epidemic in China compared to those before the epidemic began. Parallel to these findings, we demonstrated a significant decrease in both anxiety and blood pressure levels before and after the periods of official lockdown in Turkey, among HD patients.

We did not find a significant difference in the STAI-Trait, HADS-Anxiety, and HADS-Depression levels between March and June. This could be explained by the fact that each of the scales represent different time periods. For instance, the HADS-Anxiety scale measures anxiety levels in the preceding week, and the STAI-Trait scale measures anxiety levels in the recent years. In contrast, the STAI-State reflects the anxiety levels in which the blood pressure variables have been recorded. Moreover, although the follow-up assessments were applied in June 2020, when the lockdown officially ended in our country, leading us to think that the responsible stress factors had diminished, it was possible that the symptoms of anxiety were still ongoing. Nevertheless, contrary to our hypothesis, we did not find any significant correlations between anxiety and depression levels and blood pressure levels. These contradictory findings could be explained by the relatively small sample size and low power or other unexplained direct and indirect contributing factors that could interfere with blood pressure levels.

Because SARS-CoV-2 uses angiotensin-converting enzyme-2 as its receptor for entering the cells, the use of renin–angiotensin–aldosterone system blockers as antihypertensive medication was a discrete point of interest. The preclinical data suggesting the inhibition of angiotensin-2 receptor blockers ameliorates the stress,[27] hypertension, and stress-induced hypertension drew the attention to a possible relation between antihypertensive medications and anxiety levels. Therefore, we checked the antihypertensive medication records. We found that using beta-blockers was associated with a lower STAI-State score. The STAI-State score was higher in March in patients who did not take a beta-blocker. A probable underlying reason for this finding could be the possible protective effect of beta-blocker medications on blood pressure levels via the sympathetic system to mitigate the effects of perceived stress.[28, 29]

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Less is known regarding the prevalence and impact of anxiety disorders in HD patients.[30] In the general population, it is known that older individuals have a lower prevalence of anxiety than younger individuals.[31] Similarly, in our older HD patients, both anxiety and blood pressure levels were lower than in the younger patients. This might be evidence that younger patients have been more affected because they perceive the stress more than older ones.

The results of our study need to be interpreted with its limitations. First, this was a single-center study with a relatively small sample size. Second, no data revealing perceived distress associated with the COVID-19 pandemic have been obtained, since our findings indirectly revealed perceived distress among patients in our sample. Third, we did not have the chance to apply these scales in non-dialysis populations who did not have to go to the health care facilities during the lockdown.

In conclusion, anxiety and blood pressure levels were found to be high in prevalent HD patients, possibly concerning perceived distress in the COVID-19 pandemic. Because stress is a significant risk factor for elevated blood pressure, revealing the exact underlying mechanisms of stress-induced hypertension might be beneficial in the amelioration of long-term cardiovascular diseases and their outcomes. Hence, further studies with higher subject counts are needed.

Ethics Committee Approval: Ethics committee approval was received from the Ankara University School of Medicine Ethics Committee for Clinical Studies (I3-188-20).

Informed Consent: Written informed consent was obtained from all patients who participated in this study.

Peer Review: Externally peer-reviewed.

Author Contributions: Concept - R.E.S., M.A., B.D., Ş.E.; Design - R.E.S., M.A., B.D., Ş.E.; Supervision - S.K., Ş.Ş., K.K., G.N., K.A., Ş.E.; Resource - R.E.S., M.A., B.D.; Materials - R.E.S., M.A., B.D., Ş.E.; Data Collection and/ or Processing - R.E.S., M.A., B.D., Ş.E.; Analysis and/or Interpretation - R.E.S., M.A., B.D., S.K., Ş.Ş., K.K., G.N., K.A., Ş.E.; Literature Search - R.E.S., Ş.E.; Writing - R.E.S., M.A., Ş.E., B.D.; Critical Reviews - S.K., Ş.Ş., K.K., G.N., K.A., Ş.E.

REFERENCES

1. Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. *Acta Biomed*. 2020;91(1):157–160. [CrossRef]
2. Salari N, Hosseinian-Far A, Jalali R, et al. Prevalence of stress, anxiety, depression among the general population during the COVID-19 pandemic: a systematic review and meta-analysis. *Global Health*. 2020;16(1):57. [CrossRef]
3. Duman B, Herdi O, Ilhan RS, Çolak B. COVID-19 pandemic associated misinterpretation of somatic sensations: a model for mind-body interaction. *Arch Neuropsychiatry*. 2020;57(3):169–170. [CrossRef]
4. Özdin S, Bayrak Özdin Ş. Levels and predictors of anxiety, depression and health anxiety during COVID-19 pandemic in Turkish society: the importance of gender. *Int J Soc Psychiatry*. 2020;66(5):504–511. [CrossRef]
5. Li J, Li SX, Zhao LF, Kong DL, Guo ZY. Management recommendations for patients with chronic kidney disease during the novel coronavirus disease 2019 (COVID-19) epidemic. *Chronic Dis Transl Med*. 2020;6(2):119–123. [CrossRef]
6. Türkiye Cumhuriyeti İçişleri Bakanlığı. 15 İlde Uygulanan Sokağa Çıkma Kısıtlaması 31 Mayıs 24.00 İtibariyle Sona Eriyor. 2020. (Available at: https://www.icisleri.gov.tr/15-ilde-uygulanan-sokaga-cikma-kisitlamasi-31-mayis-saat-2400-itibariyle-sona-eriyor)
7. Liu MY, Li N, Li WA, Khan H. Association between psychosocial stress and hypertension: a systematic review and meta-analysis. *Neurol Res*. 2017;39(6):573–580. [CrossRef]
8. Lambert EA, Lambert GW. Stress and its role in sympathetic nervous system activation in hypertension and the metabolic syndrome. *Curr Hypertens Rep*. 2011;13(3):244–248. [CrossRef]
9. Groeschel M, Braam B. Connecting chronic and recurrent stress to vascular dysfunction: no relaxed role for the renin-angiotensin system. *Am J Physiol Ren Physiol*. 2011;300(1):F1–F10. [CrossRef]
10. Saiki Y, Watanabe T, Tan N, Matsuzaki M, Nakamura S. Role of central ANG II receptors in stress-induced cardiovascular and hyperthermic responses in rats. *Am J Physiol*. 1997;272(1 Pt 2):R26–R33. [CrossRef]
11. Rajkumar RP. COVID-19 and mental health: a review of the existing literature. *Asian J Psychiatr*. 2020;52:102066. [CrossRef]
12. Burgner A, Ikizler TA, Dwyer JP. COVID-19 and the inpatient dialysis unit: managing resources during contingency planning pre-crisis. *Clin J Am Soc Nephrol*. 2020;15(5):720–722. [CrossRef]
13. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand*. 1983;67(6):361–370. [CrossRef]
14. Aydemir O, Guvenir T, Kuey L, Kultur S. Validity and reliability of Turkish version of hospital anxiety and depression scale. *Turk Psikiyatr Derg*. 1997;8:280–287.

15. Gaudry E, Vagg P, Spielberger CD. Validation of the state-trait distinction in anxiety research. *Multivariate Behav Res*. 1975;10(3):331–341. [CrossRef]

16. Oner N, Le Compte A. *Durumluk Surekli Kaygi Envanteri El Kitabi.* (in Turkish) 1st ed. Istanbul: Bogazici Universitesi Yayinlari; 1983.

17. Kannel WB. Blood pressure as a cardiovascular risk factor: prevention and treatment. *JAMA*. 1996;275(20):1571–1576.

18. Whelton PK, He J, Appel LJ, et al. Primary prevention of hypertension: clinical and public health advisory from the National High Blood Pressure Education Program. *JAMA*. 2002;288(15):1882–1888. [CrossRef]

19. Markovitz JH, Matthews KA, Kannel WB, Cobb JL, D'Agostino RB. Psychological predictors of hypertension in the Framingham study: is there tension in hypertension? *JAMA*. 1993;270(20):2439–2443.

20. Kayano H, Koba S, Matsui T, et al. Anxiety disorder is associated with nocturnal and early morning hypertension with or without morning surge: ambulatory blood pressure monitoring. *Circ J*. 2012;76(7):1670–1677. [CrossRef]

21. Michal M, Wiltink J, Lackner K, et al. Association of hypertension with depression in the community: results from the Gutenberg Health Study. *J Hypertens*. 2013;31(5):893–899. [CrossRef]

22. Player MS, Peterson LE. Anxiety disorders, hypertension, and cardiovascular risk: a review. *Int J Psychiatry Med*. 2011;41(4):365–377. [CrossRef]

23. Paterniti S, Alpérovitch A, Ducimetière P, et al. Anxiety but not depression is associated with elevated blood pressure in a community group of French elderly. *Psychosom Med*. 1999;61(1):77–83. [CrossRef]

24. Dorn T, Yzermans CJ, Guijt H, van der Zee J. Disaster-related stress as a prospective risk factor for hypertension in parents of adolescent fire victims. *Am J Epidemiol*. 2007;165(4):410–417. [CrossRef]

25. Cohen SD, Cukor D, Kimmel PL. Anxiety in patients treated with hemodialysis. *Clin J Am Soc Nephrol*. 2016;11(12):2250–2255. [CrossRef]

26. Wu Y, Zhang C, Liu H, et al. Perinatal depressive and anxiety symptoms of pregnant women during the coronavirus disease 2019 outbreak in China. *Am J Obstet Gynecol*. 2020;223(2):240.e1–240. e9. [CrossRef]

27. Saavedra JM, Sánchez-Lemus E, Benicky J. Blockade of brain angiotensin II AT1 receptors ameliorates stress, anxiety, brain inflammation and ischemia: therapeutic implications. *Psychoneuroendocrinology*. 2011;36(1):1–18. [CrossRef]

28. Meli L, Chang BP, Shimbo D, et al. Beta blocker administration during emergency department evaluation for acute coronary syndrome is associated with lower posttraumatic stress symptoms 1-month later. *J Trauma Stress*. 2017;30(3):313–317. [CrossRef]

29. Burhans LB, Smith-Bell CA, Schreurs BG. Propranolol produces short-term facilitation of extinction in a rabbit model of post-traumatic stress disorder. *Neuropharmacology*. 2018;135:386–398. [CrossRef]

30. Cukor D, Cohen SD, Peterson RA, Kimmel PL. Psychosocial aspects of chronic disease: ESRD as a paradigmatic illness. *J Am Soc Nephrol*. 2007;18(12):3042–3055. [CrossRef]

31. Mackenzie CS, Reynolds K, Chou KL, Pagura J, Sareen J. Prevalence and correlates of generalized anxiety disorder in a national sample of older adults. *Am J Geriatr Psychiatry*. 2011;19(4):305–315. [CrossRef]

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