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ORIGINAL ARTICLE

The Relationship Between Blood Parameters, Sleep, Anxiety and Depression Symptoms: A Retrospective Polysomnography Study

Kan Parametreleri ile Uyku, Anksiyete ve Depresyon Belirtileri Arasındaki İlişki: Retrospektif Polisomnografi Çalışması

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ABSTRACT

Objective: It is known that anxiety and depression are associated with sleep disorders and many systemic diseases. This study aims to analyse the relationship between anxiety, depression symptoms and sleep parameters among the patients subjected to polysomnographic recording.
Material and Methods: A total of 808 patients who were subjected to a polysomnographic recording were included in the retrospective cross-sectional and hospital-based study. Body mass index (BMI) was calculated. Anxiety and depression symptoms were evaluated using the Beck anxiety and Beck depression inventory. Patients were divided into groups according to anxiety and depression scores. The apnoea hypopnea index (AHI), oxygen desaturation index (ODI), and peripheral oxygen saturation (SaO2) were obtained from the polysomnographic recordings.
Results: In the study, there were 528 (65.3%) male and 280 (34.7%) female patients with the mean age of 47.64 ± 12.25 (18-82). Depression was detected in 307 (38.0%) patients according to Beck depression score. Mild anxiety symptoms were detected in 516 (63.9%), moderate anxiety symptoms in 215 (26.6%) patients and severe anxiety symptoms in 77 (9.5%) patients according to Beck anxiety score. There was a statistical difference for all polysomnographic parameters in depression and anxiety severity groups (p=0.001). In patients with depression had lower free-T3 and higher C-reactive protein (CRP) levels (p=0.001, p=0.014). The difference between thyroid stimulating hormone (TSH) and FT4 levels was determined according to the severity of the depression (p=0.037, p=0.047). CRP was higher in patients with severe anxiety (p=0.008); and free-T3 was lower in patients with moderate and severe anxiety (p=0.003, p=0.001). In the logistic regression analysis, free-T3, minimum SaO2 and BMI had an impact on anxiety (p=0.002, p=0.033, p=0.031) and depression (p=0.001, p=0.017, p=0.035).
Conclusion: Anxiety and depression symptoms are affected by numerous factors, especially sleep characteristics. Minimum SaO2, CRP and free-T3 are main predisposing factors on anxiety and depression.

Keywords: Anxiety, depression, sleep, inflammation, thyroid function

ÖZ

Amaç: Anksiyete ve depresyonun uyku bozuklukları ve birçok sistemik hastalık ile ilişkili olduğu bilinmektedir. Bu çalışmada polisomnografik kayıtlaması yapılan hastalarda anksiyete ve depresyonun uyku sırasındaki hipoksi, inflamasyon ve tiroid fonksiyonları ile ilişkisinin incelenmesi amaçlanmıştır.
Gereç ve Yöntem: Retrospektif kesitsel, hastane tabanlı çalışmaya polisomnografi kaydı yapılan 808 hasta dahil edildi. Vücut kitle indeksi (VKI) hesaplandı. Anksiyete ve depresyon Beck anksiyete ve Beck depresyon envanteri ile değerlendirildi. Hastalar anksiyete ve depresyon skorlarına göre gruplara ayrıldı. Polisomnografi kayıtlarından apne hipopne indeksi (AHI), oksijen desaturasyonu indeksi (ODI) ve periferik oksijen saturasyonu (SaO2) elde edildi.
Bulgular: Çalışmada yaş ortalaması 47,64 ± 12,25 (18-82) yıl olan 528 (%65,3) erkek ve 280 (%34,7) kadın hasta vardı. Üç yüz yedi (%38,0) hastada depresyon saptandı. Hastaların 516 (%63,9) sında hafif, 215 (%26,6) inde orta ve 77 (%9,5)sinde ciddi derecede anksiyete vardı. Depresyon ve anksiyete şiddeti grupları ile tüm polisomnografi parametreleri arasında fark vardı (p=0.001). Depresyon hastalarında serbest-T3 daha düşük, C-reaktif protein (CRP) daha yüksekti (p=0.001, p=0.014). Depresyon şiddetine göre TSH ve FT4 seviyesi farkı belirlendi (p=0.037, p=0.047). Şiddetli anksiyetede CRP yüksek, orta ve şiddetli anksiyetede serbest-T3 daha düşüktü (p=0.008, p=0.003, p=0.001). Lojistik regresyon analizinde serbest-T3, minimum SaO2 ve VKİ değerlerinin anksiyete (p=0.002, p=0.033, p=0.031) ve depresyon (p=0.001, p=0.017, p=0.035) üzerinde etkisi vardı.
Sonuç: Anksiyete ve depresyon uyku karakteri başta olmak üzere birçok faktörden etkilenmektedir. Özellikle minimum SaO2, CRP ve serbest-T3 bunların başında gelmektedir.

Anahtar kelimeler: Anksiyete, depresyon, uyku, inflamasyon, tiroid

Introduction

The prevalence of depression and anxiety is high, with around 30% of society being affected by this disorder at some point in their lives (1). It is quite challenging to use only a single etiological factor to describe a disorder that has such high prevalence. This disorder is linked to many systemic, inflammatory, psychic and structural factors. Sleep and sleep-associated disorders are the leading ones. Primary and secondary sleep disorder rates are higher in patients with anxiety and depression (2). However, several studies indicated a weak or non-existent relationship between anxiety and depression, and polysomnographic results (3). In contrast, studies indicated that there was no relationship between obstructive sleep apnoea (OSA) and depressive symptoms (4). This situation points out a complex, yet causative relationship between anxiety and depression with sleep parameters. Especially in depression, fatigue, cognitive complaints and lack

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of motivation make it difficult to diagnose comorbid disorders (5). Relationship between thyroid hormones and depression and the fall in depressive symptoms, which result from triiodothyronine treatment, has been known (6). Nevertheless, an absence of a relationship between hypothyroidism and depression was shown in a case-control study, two cross-sectional society-based studies and a patient study. Moreover, some of the above studies emphasise the relationship between reverse hypothyroidism and depression and anxiety (7-12). The relationship between inflammation and depression was indicated in many studies (13). However, there are fewer studies, which assess the relationship between anxiety and inflammation. In these studies, it was particularly demonstrated that anxiety is related to the increase in systemic inflammation (13-15). Although there is more evidence showing a cross-sectional relationship between depressive symptoms and inflammation, there are fewer studies, which evaluate its relationship with anxiety.

Anxiety and depression symptoms are affected by numerous factors. Different results were obtained from the studies in literature evaluation. The results of the studies are limited. In addition, these studies are in small patient groups. For this reason, it was aimed to evaluate the effect of nocturnal sleep parameters, thyroid functions and systemic inflammation on anxiety and depression symptoms in a large patients group exanimated with polysomnography. Ultimately, we aimed to evaluate the cross effects of different parameters on sleep and anxiety/depressive symptoms.

Methods

It was designed as a retrospective clinical study (between the years of 2014 and 2018). All patient in the polysomnography unit were screened in these years. The study protocol was approved by local ethics committee of university (approval number: 2021/338). After ethical approval, permission was obtained from the hospital management for the data. The Helsinki declaration and Good Clinical Practices (GCP) were complied with during the study.

The data of 1360 patients were analysed in the study. All patients in the polysomnography unit without exclusion criteria were included in the study. Polysomnography indication and pre-diagnosis were not evaluated. After the evaluation of diseases, drugs and blood parameters, the patients who had systemic infection, and endocrinological, haematological, respiratory and psychiatric diseases were excluded from the study. Because it is known that these diseases can affect respiratory parameters, anxiety and depression scores. A total of 808 patients' data were analysed. Patients' number, exclusion parameters and groups are shown in the figure 1. Age, gender, height and weight of the patients were recorded. Body mass index (BMI) = Weight (kg) / height2 (m2) formula was used for calculations. Blood tests were routinely performed before polysomnography in this unit. In addition, some scales were routinely applied to the patients after the blood test. These were Beck anxiety scale, Beck depression scale, Epworth sleepiness scale, Pittsburgh Sleep Quality Index etc. However, Beck anxiety and Beck depression scales were employed for this study.

The Beck depression inventory was used to evaluate depression symptoms. Thus, somatic, emotional, cognitive and motivational symptoms were assessed. The inventory comprises of 21 questions, which take into consideration the situation over the past week. Every question has a score, which varies from 0 to 3. Total scores change between 0 and 63. High scores are associated with increased depression (16). According to the total scores, the patients were classified as 0-13=no depression symptoms, 14-19=mild depression symptoms, 20-28=moderate depression symptoms and 29-63=severe depression symptoms.

Anxiety symptoms were assessed with the Beck anxiety inventory. In this way, presence and severity of anxiety were revealed. The inventory has 21 questions. Each question has a score from 0 to 3. Total scores change between 0 and 63. High scores are associated with increased anxiety level (17). According to the scores, the patients were classified as 0-21=mild anxiety symptoms, 22-35=moderate anxiety symptoms and 36-63=severe anxiety symptoms.

The polysomnographic test was performed in single rooms under the supervision of a technician. Voice and video were recorded during the night. An Embla S4500 model polysomnography device was used in the study. Four-channel electroencephalogram (EEG), submental electromyography (EMG), right-left tibial EMG and right-left electrooculogram (EOG) were utilised. Nasal airflow, pulse oximetry and peripheral oxygen saturation (SaO2) were recorded during the night. The data was manually assessed in line with the directions of the American Academy of Sleep Medicine (AASM) (18). Values of the apnoea hypopnea index (AHI) and oxygen desaturation index (ODI) were determined.

Blood samples were obtained between 7.00am. and 11.00am. following at least eight hours of fasting and before the polysomnographic recording. Drying tubes and the tubes with ethylenediaminetetraacetic acid (EDTA) were used for biochemical analysis and hematologic analysis, respectively. Complete blood count was examined using a Diagon kit in a Mindray BC-6800 device. Moreover, biochemical tests were analysed with the nephelometric method through a Beckman Coulter AU5800 (Beckman Coulter Inc, Hialeah) device. Inflammation was evaluated with leukocyte (K/UL), eosinophil (%), neutrophil (%), lymphocyte (%) and C-reactive protein (CRP) (mg/L). Neutrophil/lymphocyte ratio (NLR) was calculated. For thyroid functions, the thyroid stimulating hormone (TSH) (mU/L), T3 (ng/dL) and T4 (ng/dL) tests were determined.

Statistical analysis

Data were analysed with the SPSS 16.0 Package Software (Statistical Package for the Social Sciences

Inc.; Armonk, NY, ABD) programme. The Kolmogorov Smirnov test was used for normality analysis. The data were indicated with number (n), percentage (%), mean (standard deviation) or median (minimum-maximum). The mean data were compared with Student's T or Kruskal Wallis test according the results of normality test. Post-hoc analysis was performed with the Mann Whitney U test and Bonferroni Correction. The Chi-square or Fisher's exact test were applied to compare the categorical data. The relationship of the numerical data was assessed with the Spearman's correlation test. The relationship between more than two categorical data was analysed with ordered logistic regression analysis. Results were within confidence interval of 95% while significance was at $p < 0.05$.

Results

In the study, there were 808 patients whose mean age corresponded to 47.64 (12.25) (from 18 to 82). Of the patients, 528 (65.3%) were male and 280 (34.7%) were female. Demographical characteristics, polysomnographic results, emotional state and serum markers of the patients are listed in Table 1.

Table 1. Demographic characteristics, depression, anxiety symptoms and serum markers in patients (n=808)

Parameters	
Age / year, mean (SD) (min - max)	47.64 (12.25) (18-82)
Female, n (%)	280 (34.7%)
Male, n (%)	528 (65.3%)
BMI (kg/m^2), mean (SD) (min - max)	24.23 (3.00) (15.30-32.90)
Anxiety group, n (%)	
Mild symptoms	516 (63.9)
Moderate symptoms	215 (26.6)
Severe symptoms	77 (9.5)
Depression group, n (%)	
None symptoms	501 (62.2)
Mild symptoms	188 (23.3)
Moderate symptoms	40 (5.0)
Severe symptoms	79 (9.8)
Polysomnography data, median (min - max)	
Apnea-hypopnea index	14.95 (0.3-109.8)
Oxygen desaturation index	15.7 (0.2-119.9)
Average SaO_2	92.0 (79.8-98.8)
Minimum SaO_2	82.0 (50.0-95.0)
Serum markers	
Inflammatory markers, median (min - max)	
Leukocyte (K / UL)	7.80 (3.9-13.7)
Eosinophil (%)	2.0 (0.1-13.8)
Neutrophil (%)	58.5 (3.9-87.8)
Lymphocyte (%)	30.5 (5.2-55.4)
NLR	1.89 (0.13-10.84)
CRP (mg / L)	0.39 (0.01-9.80)
Thyroid function tests, median (min - max)	
TSH (mU/L)	1.58 (0.04-9.66)
FT4 (ng/dL)	1.17 (0.33-3.41)
FT3 (ng/dL)	3.20 (1.72-5.20)

SD: Standard deviation, min: Minimum, max: Maximum, n: Number, %: Percentage, SaO_2: peripheral oxygen saturation, NLR: Neutrophil to lymphocyte ratio, CRP: C-reactive protein, TSH: Thyroid stimulating hormone, FT4: Free thyroxine, FT3: Free triiodothyronine

AHI and ODI in the patient group with depression symptoms (n=307) were higher than the patient group without depression symptoms (n=501) (p=0.001). Mean and minimum SaO2 of the same patient group was lower (p=0.001). The patients with depression symptoms had higher CRP level (p=0.014). There was not a statistically significant difference between the presence of depression symptoms and other systemic inflammatory parameters ($p > 0.05$). The free-T3 level was lower in the patients with depression symptoms (p=0.001). There was no statistically significant difference between TSH and free-T4 levels (p=0.051, p=0.546). Polysomnographic data, inflammatory markers and thyroid function tests of the patients are shown based on the presence of depression symptoms in Table 2.

Table 2. Polysomnography data and serum markers according to depression symptoms. Data are expressed as median (minimum-maximum), unless stated otherwise

	Depression symptoms negative group (n=501)	Depression symptoms positive group (n=307)	p-value
AHI	11.10 (0.3-106.4)	19.3 (0.4-109.8)	0.001*
ODI	11.85 (0.2-119.0)	21.1 (0.4-119.9)	0.001*
Average SaO_2	92.4 (78.6-97.6)	91.4 (76.8-98.8)	0.001*
Minimum SaO_2	83.0 (50.0-95.0)	79.0 (50.0-91.0)	0.001*
Leukocyte (K / UL)	7.7 (3.9-13.6)	7.9 (3.9-13.7)	0.586
Eosinophil (%)	2.0 (0.1-13.8)	2.1 (0.1-9.1)	0.581
Neutrophil (%)	58.2 (6.2-87.8)	58.7 (3.9-84.0)	0.900
Lymphocyte (%)	30.5 (6.8-53.3)	30.5 (5.2-55.4)	0.730
NLR	1.89 (0.23-10.84)	1.90 (0.13-7.42)	0.905
CRP (mg / L)	0.33 (0.01-8.27)	0.44 (0.01-9.80)	0.014*
TSH (mU/L)	1.65 (0.04-7.64)	1.48 (0.04-9.66)	0.051
FT4 (ng/dL)	1.19 (0.33-3.22)	1.16 (0.75-3.41)	0.546
FT3 (ng/dL)	3.31 (1.72-5.20)	3.10 (1.72-4.20)	0.001*

* Statistically significant value, n: Number, AHI: Apnea-hypopnea index, ODI: Oxygen desaturation index, %: Percentage, NLR: Neutrophil to lymphocyte ratio, CRP: C-reactive protein, TSH: Thyroid stimulating hormone, FT4: Free thyroxine, FT3: Free triiodothyronine

Difference in all polysomnographic parameters (AHI, ODI, mean and minimum SaO2) between depression symptoms groups were detected (p=0.001). As a consequence of the post-hoc analysis, AHI and ODI values were higher and mean and minimum SaO2 were lower in moderate depression symptoms than in mild depression symptoms (p=0.001). Similarly, AHI and ODI values were higher in severe depression symptoms than in mild depression symptoms (p=0.005, p=0.013). ODI of the patients with moderate depression symptoms was higher than that of the patients with severe depression symptoms (p=0.010); mean and minimum SaO2 were lower in moderate depression symptoms than in severe depression symptoms (p=0.001). A statistically significant difference in the systemic inflammatory parameters between the groups was not detected ($p > 0.05$). The difference between TSH and free-T4 levels was detected based on the severity of depression (p=0.037, p=0.047). In post-hoc analysis, patients with severe depression symptoms had higher TSH and lower free-T4 than mild depression (p=0.030, p=0.017). In patients with severe depression symptoms, the

TSH level was higher than in moderate depression (p=0.029). A difference in free-T3 between the groups was not discovered (p=0.058). Polysomnographic data, inflammatory markers and thyroid function tests of the patients are summarised based on the severity of depression symptoms in Table 3.

Table 3. Polysomnography data and serum markers according to depression degree. Data are expressed as median (minimum-maximum), unless stated otherwise

	Mild symptoms (n=188)	Moderate symptoms (n=40)	Severe symptoms (n=79)	p-value
AHI	24.45 (0.4-109.8)	13.30 (0.4-108.1)	17.2 (1.7-107.2)	0.001*
ODI	24.90 (0.7-119.9)	12.15 (0.4-117.6)	19.4 (0.7-112.2)	0.001*
Average SaO_2	91.05 (76.8-98.8)	92.8 (85.9-95.2)	91.30 (77.7-96.6)	0.001*
Minimum SaO_2	78.0 (51.0-91.0)	85.0 (70.0-91.0)	79.0 (50.0-90.0)	0.001*
Leukocyte (K / UL)	7.9 (3.9-13.7)	8.25 (5.0-13.1)	7.7 (4.0-13.1)	0.316
Eosinophil (%)	2.2 (0.2-9.1)	1.9 (0.5-5.1)	1.95 (0.1-7.8)	0.202
Neutrophil (%)	58.8 (4.2-84.0)	57.2 (33.3-74.4)	58.65 (3.9-74.6)	0.850
Lymphocyte (%)	30.45 (5.2-50.8)	30.35 (8.7-49.5)	30.8 (10.4-55.4)	0.989
NLR	1.88 (0.14-7.42)	1.94 (0.93-6.06)	1.88 (0.13-5.39)	0.968
CRP (mg / L)	0.47 (0.01-9.80)	0.34 (0.01-8.90)	0.42 (0.03-7.05)	0.367
TSH (mU/L)	1.41 (0.04-7.92)	1.27 (0.27-3.95)	1.72 (0.29-9.66)	0.038*
FT4 (ng/dL)	1.17 (0.75-3.41)	1.17 (0.77-2.03)	1.10 (0.84-3.0)	0.047*
FT3 (ng/dL)	3.11 (1.72-4.20)	3.20 (2.65-3.90)	3.06 (2.18-3.61)	0.058

* Statistically significant value, n: Number, AHI: Apnea-hypopnea index, ODI: Oxygen desaturation index, %: Percentage, NLR: Neutrophil to lymphocyte ratio, CRP: C-reactive protein, TSH: Thyroid stimulating hormone, FT4: Free thyroxine, FT3: Free triiodothyronine

Table 4. Polysomnography data and serum markers according to anxiety symptoms level. Data are expressed as median (minimum-maximum), unless stated otherwise

	Mild symptoms (n=516)	Moderate symptoms (n=215)	Severe symptoms (n=77)	p-value
AHI	11.15 (0.3-108.1)	22.20 (0.4-109.8)	17.40 (1.7-107.2)	0.001*
ODI	12.0 (0.2-119.0)	23.5 (0.4-119.9)	19.6 (0.7-112.2)	0.001*
Average SaO_2	92.4 (78.6-97.6)	91.4 (76.8-98.8)	91.1 (77.7-96.6)	0.001*
Minimum SaO_2	83.0 (50.0-95.0)	79.0 (50.0-91.0)	79.0 (50.0-90.0)	0.001*
Leukocyte (K / UL)	7.7 (3.9-13.6)	8.00 (3.9-13.7)	7.7 (4.0-13.1)	0.234
Eosinophil (%)	2.0 (0.1-13.8)	2.1 (0.2-9.1)	2.0 (0.1-7.8)	0.602
Neutrophil (%)	58.2 (6.2-87.8)	58.9 (4.2-84.0)	58.2 (3.9-74.6)	0.926
Lymphocyte (%)	30.50 (6.8-53.3)	30.40 (5.2-50.8)	30.8 (10.4-55.4)	0.963
NLR	1.89 (0.23-10.84)	1.90 (0.14-7.42)	1.86 (0.13-5.39)	0.997
CRP (mg / L)	0.34 (0.01-8.90)	0.44 (0.01-9.80)	0.47 (0.03-7.05)	0.016*
TSH (mU/L)	1.65 (0.04-7.64)	1.44 (0.04-8.58)	1.60 (0.27-9.66)	0.061
FT4 (ng/dL)	1.19 (0.33-3.22)	1.17 (0.75-3.41)	1.13 (0.84-3.0)	0.339
FT3 (ng/dL)	3.31 (1.72-5.20)	3.11 (1.72-4.20)	3.07 (2.18-3.80)	0.001*

* Statistically significant value, n: Number, AHI: Apnea-hypopnea index, ODI: Oxygen desaturation index, %: Percentage, NLR: Neutrophil to lymphocyte ratio, CRP: C-reactive protein, TSH: Thyroid stimulating hormone, FT4: Free thyroxine, FT3: Free triiodothyronine

A difference in all polysomnographic parameters (AHI, ODI, mean and minimum SaO2) was detected between in patients with anxiety symptoms groups (p=0.001). As a result of the post-hoc analysis, AHI and ODI values were higher; mean and minimum SaO2 were lower in patients with moderate and severe anxiety symptoms than in mild anxiety (p=0.001). No difference between the moderate and severe anxiety symptoms groups, and polysomnographic groups was detected (p=0.064, 0.175, 0.312, 0.681). In the systematic inflammatory parameters, only a difference in the CRP levels between the groups was detected (p=0.016). CRP level of the patients with severe anxiety symptoms was higher than that of the patients with mild anxiety (p=0.008). The Free-T3 level was determined according to the severity of anxiety and thyroid function tests (p=0.001). Free-T3 level is lower in patients with moderate and severe anxiety symptoms than mild anxiety symptoms group (p=0.003, p=0.001). Polysomnographic data, inflammatory markers and thyroid function tests of the patients are listed based on the severity of anxiety symptoms in Table 4.

According to result of the Spearman's correlation test, a positive correlation was detected between anxiety and depression scores. (p=0.001, r=0.946). As depression scores of the patients increased, AHI and ODI increased (p=0.001, r=0.199; r=0.218, respectively) and mean and minimum SaO2 decreased (p=0.001, r=-0.177, -0.212). There was a positive correlation between depression score and CRP level (p=0.011, r=0.097), a negative correlation between depression score and free-T3 (p=0.001, r=-0.219). As anxiety scores of the patients increased, AHI and ODI increased (p=0.001, r=0.228; r=0.251, respectively) and mean and minimum SaO2 decreased (p=0.001, r=-0.213, -0.247). As anxiety score increased, CRP level increased (p=0.006, r=0.105) and free-T3 decreased (p=0.001, r=-0.221).

The relationship between the depression and anxiety symptoms groups, and polysomnographic parameters, BMI, inflammatory parameters and thyroid function tests was evaluated with ordered logistic regression analysis. A parallelism was observed (p=0.525). The indexes for the ordered logistic regression model was detected as adequate. The model's Pseudo R2 value accounted for 14% of the dependent variable (Nagelkerke=0.144). When parameters of the model were examined, the effect of free-T3 (p=0.002), minimum SaO2 (p=0.033) and BMI (p=0.031) on depression groups was detected. Other data had no impact (p >0.05). Free-T3 values of the patients had a negative effect on their depression values. The likelihood of patients with high free-T3 values to go into a severe depression was 2.5 times lower. Minimum SaO2 values of the patients affected their depression values negatively. The possibility of patients with a low minimum SaO2 value of going into severe depression was 1.03 times higher. BMI values affected depression positively. The possibility of patients with higher BMIs to have a severe depression was 1.08 times higher.

Parallelism assumption was performed to proceed on the ordered logistic regression model in patients with anxiety groups. There was a parallelism at a statistical confidence level of 95% between the groups of dependent variables (p=0.067). The model fit indexes were found adequate. The model's Pseudo R2 value accounted for 14% of the dependent variable (Nagelkerke=0.175). In the model, the effect of free-T3

(p=0.001), minimum SaO2 (p=0.017) and BMI (p=.035) values on the anxiety groups was observed. Other parameters had no impact (p >0.05). Free-T3 values of the patients had a negative effect on their anxiety levels. The possibility of the patients with higher free-T3 value to have severe anxiety was 2.65 times lower. Minimum SaO2 values of the patients affected anxiety negatively. The possibility of the patients with a low minimum SaO2 value to have severe anxiety levels was 1.04 times higher. BMI values affected anxiety positively. The possibility of patients with high BMIs to have severe anxiety levels was 1.09 times higher.

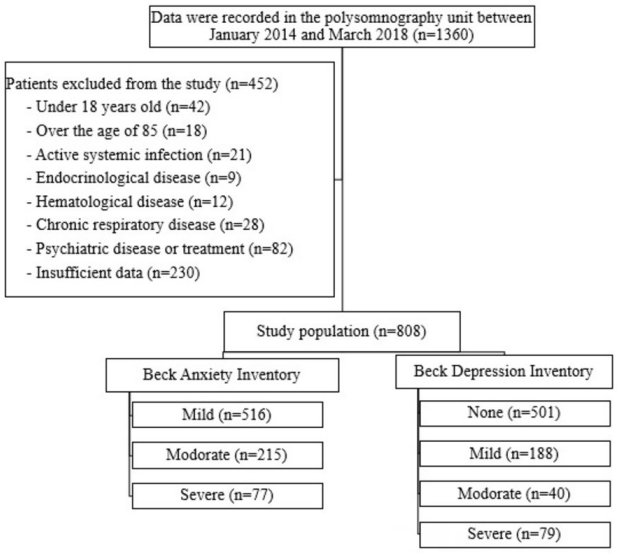

Figure 1. Study design and patient selection criteria

Discussion

In community-based studies, it is known that almost one-third of population has anxiety and depression in their lives (1). Such disorders are affected by numerous factors. Anxiety that is known as a neuropsychiatric disorder and depression are related with sleep disorders, systemic inflammation and endocrinological diseases. Emotional state and changes have different levels of impacts on these parameters (4, 6, 11, 15).

Sleep disorders may lead to substantial neuropsychiatric results. This fact may be associated with intermittent hypoxia as well as interrupted sleep. In a study of Akberzia et al., 28 patients with anxiety and 29 patients with depression were compared with a control group. There was no difference in AHI among the patients with depression. In contrast, AHI was apparently lower in patients with anxiety (p=0.0076, median 21.4 (9.6-41.3) vs. 50.5(25.1-95.3)) (19). In current study, it was detected that the severity of depression and anxiety were associated with AHI. A negative correlation between anxiety and depression with AHI was determined. Akberzia et.al. had used a hospital anxiety and depression scale (HADS) in the study (19). The Beck anxiety and depression inventory was used in the current study. Lee et.al. detected no relationship between anxiety and depression, and AHI indexes in the study. Beck anxiety and depression inventory was used and OSA patients were evaluated. However, it was observed that the patients with mild OSA had more anxiety and depression symptoms compared to the patients with severe OSA (4). The relationship between polysomnographic data and anxiety and depression was not defined clearly in the literature. In several community-onset studies which evaluated clinical data, it was revealed that there was a relationship between anxiety and depression and an increase in the AHI index and hypoxia which ultimately (2, 20). Such relationships could not be verified in some studies (21, 22). The relationship between anxiety and depression and hypoxia is not certain. The respiratory function impairment and hypoxia are known to affect emotional state. However, the data regarding cause-effect relationships is not sufficient (23). In large-scale community-onset studies, hypoxia was shown to be related to anxiety and depression (24). Higher frequency of anxiety and depression in the patients with Chronic Obstructive Pulmonary Disease (COPD), asthma and heart failure and the increase in psychogenic symptoms which occurs in line with deepening hypoxia, supports this relationship (25, 26). In current study, AHI and ODI increased and mean and minimum SaO2 decreased as anxiety and depression scores increased. Nevertheless, the correlation between them was relatively weak. It is detected that there is a casual link between anxiety and depression and sleep. However, it is impossible to explain this fact with only polysomnographic data.

Many studies associate anxiety and depression with increased systemic inflammation. The fact that anxiety and depression is present in those patients with chronic systemic disorder supports this situation. It is likely that the increased inflammatory state may induce anxiety and depression among these patients. Numerous cross-sectional studies show a relationship between increased inflammation and depression (13, 27). On the other hand, several studies indicated that there was no relationship between depression and inflammation (14, 15). Although there is solid proof of the relationship between depression and increased inflammation, the number of the studies on anxiety are fewer. Nevertheless, the relationship between anxiety and inflammation has been demonstrated by a couple of studies (28, 29). In a cohort study of Liukkonen et.al, the relationship between hs-CRP and increased anxiety and depression was proved (28). In current study, it was detected that the presence of depression was related to CRP level and that the patients with depression had higher CRP level. Although there was not difference in CRP level between the groups of depression severity, a positive correlation between depression scores and CRP levels was detected. Serum CRP level were higher in the patient group with severe anxiety. This point made us think about the relationship between the presence of depression and severity of anxiety, and increased inflammation.

For many years now, the relationship between hypothalamic-pituitary-thyroid axis and depression and anxiety has gained traction with researchers. This

originates from the fact that the symptoms in patients with hyperthyroidism resemble that of major depression (29). If we consider the fact that thyroid hormones organize the basal metabolism in all body tissues, including the brain, then this is understandable (30). Some of the studies indicate a relationship between depression and clinical and sub-clinical hyperthyroidism (4, 29). This brings the use of triiodothyronine (T3) for the patients who resist to standard treatments such as antidepressants (31). However, several community-onset studies did not find out a relationship between serum TSH levels and depression (8). The patients with depression in current study had lower free-T3 level. TSH level of the patients with severe depression was higher while free-T4 level was lower. The possibility of patients with high free-T3 value to have severe depression was found 2.5 times lower. The studies, which analyse the relationship between anxiety and thyroid functions, provided different results. In a study of Ittermann et.al, the relationship between hyperthyroidism and anxiety was detected (12). The lower free-T3 level of the patients with severe anxiety which was detected in the current study matches up with this study. The possibility of patients with high free-T3 value to have severe anxiety was 2.65 times lower. In addition, the data from a similar cross-sectional study which included 254 patients promote our results (32). In some of the cross-sectional studies, it was demonstrated that the anxiety prevalence in hyperthyroid was higher. Such studies have a comparatively lower sample size (33,34).

Conclusion

Depression and anxiety are related to numerous factors. Sleep and sleep-related respiratory disorders are the leading ones. Depression and anxiety are associated with AHI, ODI, minimum and mean SaO2. This point promotes the relationship between hypoxia and anxiety and depression. CRP, an indicator of systemic inflammation, is higher in patients with depression and severe anxiety. Thus, it makes us think about the correlation between anxiety and depression and systemic inflammation. Lower Free-T3 and higher BMI have a negative effect on depression and anxiety. These results support that anxiety and depression are complex diseases, which have a causal link with numerous factors.

Limitations of the study; first, the study has a retrospective design. However, the high number of participants makes the study powerful. Second; anxiety and depression are clinical diagnoses. But, in this study, only scales were used to evaluate the patient. Third, the level of anxiety and depression symptoms was evaluated with scales. Clinical evaluation is also required to assess the level of anxiety and depression in clinical practice. Yet, this study is a retrospective design. In addition, data should be grouped in order to perform more detailed statistical analysis. For this reason, the scale scores were grouped according to literature data. Prospective and multicenter studies should be designed to confirm these results.

Conflict of interests: The authors declare that there is no conflict of interest regarding the publication of this article.

Ethics approval: The local Ethics Committee of University (approval number: 2021/338) approved the study protocol.

Author contributions: Concept – F.E, F.D; Design – F.E, F.D; Supervision – F.E, F.D; Materials – F.D., F.E; Data collection and/or processing – F.D., F.E; Analysis and/or interpretation – F.E, F.D; Literature search – F.D., F.E; Writing – F.E, F.D; Critical review – F.E, F.D.

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