

An Investigation of Anemia, Fatigue and Loneliness in Patients with Chronic Obstructive Pulmonary Disease and the Relationship between Them

Kronik Obstruktif Akciğer Hastalığı olan Hastaların Anemi, Yorgunluk ve Yalnızlık Durumları ve Aralarındaki İlişkilerin İncelenmesi

Tülay SAĞKAL MİDİLLİ¹, Aslı KALKIM², Halide YILMAZ³, Erol OZAN⁴

ABSTRACT

The objective of this study was to investigate anemia, fatigue and loneliness in Chronic Obstructive Pulmonary Disease (COPD) patients, and to establish the relation between them.

This study was conducted as descriptive type. The sample of the study consisted of 250 patients who were receiving treatment in the respiratory diseases service. A Patient Description Form, the COPD and Asthma Fatigue Scale (CAFS), and the UCLA Loneliness Scale were used in the collection of data.

The mean age of the patients was found to be 68.21±12.34 (min: 24, max: 93) years; 64% were aged 65 or over, 66% were male. The patients' mean hemoglobin value was found to be 12.47±1.93 (g/dl) (min: 5.40, max: 16.70), and 45.9% of the female patients, 52.1% of the males and 50% overall were anemic. The patients' mean loneliness score was 36.58±11.00, and their mean fatigue score was 81.51±16.30. It was established that 60% were lonely at a low level. Eight out of ten patients in the study were found to be fatigued. No correlation was found between patients' mean loneliness scores and mean fatigue scores ($r=0.003$, $p=0.962$); a significant correlation was found between their hemoglobin values and their mean fatigue scores ($r=0.21$, $p=0.001$), but no significant correlation was found between their hemoglobin values and their mean loneliness scores ($r=0.011$, $p=0.867$).

It was concluded that half of the COPD patients in the study were anemic, a large proportion had fatigue, and that the loneliness rate was low. It was found that patients with anemia had more fatigue.

Keywords: Chronic Obstructive Pulmonary Disease, Anemia, Fatigue, Loneliness

ÖZ

Bu çalışmanın amacı Kronik Obstruktif Akciğer Hastalığı (KOAH) olan hastalarda anemi, yorgunluk ve yalnızlık durumlarını incelemek ve aralarındaki ilişkiyi saptamaktır.

Bu çalışma tanımlayıcı tipte yapılmıştır. Araştırmanın örneklemini tedavi gören 250 KOAH hastası oluşturmuştur. Veriler Hasta Tanıtım Formu, KOAH ve Astım Yorgunluk Ölçeği (KAYÖ) ve UCLA Yalnızlık Ölçeği kullanılarak toplanmıştır.

Hastaların yaş ortalaması 68,21±12,34 (min:24, max: 93), %64'ü 65 yaş ve üzeri, %66'sının erkek olduğu saptanmıştır. Hastaların hemoglobin değeri ortalaması 12,47±1,93 (g/dl) (min:5,40, max:16,70) olarak bulunmuş olup, %50'sinde anemi olduğu, kadınlarda bu oranın %45,9, erkeklerde %52,1 olduğu bulunmuştur. Hastaların yalnızlık puan ortalaması 36,58±11,00, ve yorgunluk puan ortalaması 81,51±16,30'dur. Hastaların %60'nın düşük düzeyde yalnız olduğu saptanmıştır. Araştırmada 10 hastanın 8'i yorgun bulunmuştur. Hastaların yalnızlık puan ortalaması ile yorgunluk puan ortalaması arasında ilişki olmadığı ($r=0,003$, $p=0,962$), hemoglobin değeri ile yorgunluk puan ortalaması arasında anlamlı bir ilişki olduğu ($r=0,21$, $p=0,001$) ve hemoglobin değeri ile yalnızlık puan ortalaması arasında anlamlı bir ilişki olmadığı ($r=0,011$, $p=0,867$) ortaya çıkmıştır.

Sonuç olarak araştırmada KOAH hastalarının yarısının anemik olduğu, çoğunluğunun yorgun olduğu, ve yalnızlık oranının düşük olduğu belirlenmiştir. Anemisi olan hastaların yorgunluğunun daha fazla olduğu bulunmuştur.

Anahtar kelimeler: Kronik Obstruktif Akciğer Hastalığı, Anemi, Yorgunluk, Yalnızlık

* Bu çalışma 2. Uluslararası Lisansüstü Eğitim Kongresi, Manisa, Türkiye'de sözel bildiri olarak sunulmuştur.

¹Dr. Öğr. Üyesi, Hemşirelik Esasları, MCBÜ Sağlık Bilimleri Fakültesi, reikimelek@hotmail.com, ORCID: 0000-0001-8303-0237

²Öğr. Gör. Dr., Halk Sağlığı Hemşireliği, Ege Üniversitesi Hemşirelik Fakültesi, aslikalkim@gmail.com, ORCID: 0000-0002-7878-5640

³Hemşire, Manisa Devlet Hastanesi Göğüs Hastalıkları Servisi, Manisa, halide.ylmz@hotmail.com, ORCID: 0000-0002-2188-5261

⁴Doç. Dr., Psikiyatri Anabilim Dalı, Manisa Hafsa Sultan Hastanesi Tıp Fakültesi, erolozan@gmail.com, ORCID: 0000-0001-5860-2803

İletişim / Corresponding Author: Tülay SAĞKAL MİDİLLİ

e-posta/e-mail: reikimelek@hotmail.com

Geliş Tarihi / Received: 15.08.2018

Kabul Tarihi/Accepted: 04.02.2019

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a disease of the lungs which causes serious health problems and which is life-threatening.¹ As well as affecting the lungs, COPD can have serious systemic effects.² The prevalence, morbidity and mortality of COPD varies between countries and between different parts of the same country.³ In the Burden of Lung Disease (BOLD) study completed in 29 countries and ongoing in eight, the total prevalence of GOLD stage II+ COPD was found to be 10.1% (11.8% in males and 8.5% in females).⁴ According to data from 2015 from the Turkish Institute of Public Health (THSK), the COPD mortality rate in Turkey is 5.9%,⁵ while it is predicted that the prevalence of COPD will increase in the next 30 years because of an increase in smoking in developing countries and a progressively aging population in developed countries, and that by 2030 deaths from COPD and related causes will reach 4.5 million a year.⁴

One of the most important physiological problems seen in COPD patients is anemia.^{2,6,7} The World Health Organization (WHO) defines anemia as hemoglobin (Hb) values of <12g/dl in females and <13g/dl in males.⁸ The latest studies report anemia rates of between 30% and 80% in COPD patients.^{2,7,9} Anemia causes physical problems such as weakness, fatigue, cachexia, eating disorders and cognitive function disorders, and problems

such as anxiety, depression, loneliness, and a deterioration in the quality of life, at the same time increasing the length of stay in hospital, the costs of health care, and mortality and morbidity rates.⁷ One of the important symptoms caused by the anemia seen in COPD patients is fatigue.⁷ In a study by Çınar and Olgun (2010), it was found that COPD patients experienced fatigue at different levels, and that their physical, mental and social functions were affected by fatigue.¹⁰ These pathophysiological changes in COPD patients cause them to experience anxiety, depression, loneliness, social isolation, helplessness and hopelessness.¹¹ In the small number of studies which have examined loneliness in COPD patients, it has been reported that these patients experience loneliness, although not at a very high level.^{11,12}

All of the psychosocial and physical problems seen in COPD patients increase their need for holistic care. These negative physical and psychosocial problems can be reduced or prevented by meeting the care needs of COPD patients and by giving them holistic care.¹¹ Thus, because COPD is a disease which can affect a patient physically and psychosocially, health professionals should assess problems such as anemia, fatigue and loneliness in these patients, take the necessary measures, and provide treatment and care where necessary.

MATERIAL AND METHOD

Aim

This study was conducted with the aim of assessing anemia, fatigue and loneliness in COPD patients, and the relationship among them.

Research Design and Sample

The study had a descriptive design. It was conducted at the inpatient respiratory diseases service of a state hospital in a city, in the western part of Turkey, between September

2016 and February 2017. The state hospital where the study was conducted was chosen by the purposive sampling method as one which was accessible to the researchers.

The population of the study consisted of the COPD patients under treatment at this clinic between these dates. In order to determine the size of the sample, the selection formula $n=t^2.p.q/d^2$ for the probability selection method for an unknown population was used, with a significance level of 95% and

a margin of error of 0.05. In this formula, the prevalence of anemia in COPD patients was taken as 20% as specified by Fidan et al. 2012¹³ and the size of the sample needed was determined as 246 patients. The inclusion criteria were as follows: being 18 years of age or over, having been diagnosed with COPD at least six months previously, being hospitalized in the clinic, not having any serious complications, not having any history of psychiatric illness, being literate, being able to communicate in Turkish, and agreeing to participate in the study. The sample was made up of 250 COPD patients.

Instruments and Data Collection

Three instruments were used for data collection in this study: a Patient Description Form, a COPD and Asthma Fatigue Scale, and the UCLA Loneliness Scale. The data were collected with these instruments in the clinic by researchers in face-to-face interviews.

Patient Description Form

This form was prepared by the researchers in line with the relevant literature,^{2,7,11,12,14} and consisted of 11 questions on such things as age, gender, marital status, education, duration of COPD, the existence of other chronic illnesses, duration of hospitalization, smoking and the use of alcohol, and Hb value. For patients' Hb values, the results of blood tests for the week preceding the date on which the patient participated in the study were evaluated. Hb values were recorded from the laboratory results in the records of the patients in the clinic.

COPD and Asthma Fatigue Scale (CAFS)

This scale was developed by Revicki et al. (2010) in order to show the effects of COPD and asthma on fatigue. The Turkish validity and reliability study of the scale was conducted by Yel and Ergüney (2012).¹⁵ The scale consists of 12 items and a five-point Likert scale anchored at 1 = never and 5 = very often. The total score obtained on the scale can vary from 12 to 60. The score is transformed to a value between 0 and 100. A high score signifies a high fatigue level in the person.¹⁵

The internal consistency coefficient of the scale was determined as 0.96 and the alpha value obtained in this study was determined as 0.99.

The UCLA Loneliness Scale

This scale was developed by Russell, Peplau and Cutrona (1980), and adapted to Turkish society by Demir (1989).¹⁶ It was used to investigate participants' experiences of loneliness. It consists of 20 items rated on a four-point scale range with 10 items worded in a negative direction. The total possible score on these items ranges from 20 to 80. A total score of 20–34 indicates mild loneliness, 35–48 indicates moderate loneliness, and 49–80 severe loneliness. The reliability of this scale (Cronbach's alpha) is 0.96.¹⁶ In the current study, the Cronbach's alpha for the patients was 0.95.

Ethical Considerations

Ethical approval for conducting this study was obtained the University Ethics Committee (Date:10.12.2016, Approval No:20.478.486-340). The study conformed to the principles outlines in the Helsinki Declaration. Informed consent was obtained orally and in writing from the patients taking part in the study. The information included the purpose and procedures of the study, the voluntary nature of their participation and the option to withdraw at any time.

Data Analysis

The data were evaluated via Statistical Package for the Social Sciences version 21.0 (SPSS Inc.; Chicago IL, USA). Descriptive analysis was used to assess the participants' demographic and health characteristics. The participants' Hb value, fatigue and loneliness scores for demographic and health characteristics were compared via the independent t-test one-way analysis of variance (ANOVA) and chi-square analysis. The relationships between Hb value, fatigue and loneliness scores were analyzed using Pearson's product-moment correlation. The level of significance was set at 0.05.

RESULTS AND DISCUSSION

Description of The Patients

The patients' socio-demographic characteristics are shown in Table 1. The mean age of the patients was 68.21 ± 12.34 years (ranging from 24 to 93); 66% of the participants were male, 92% were married, and 61.2% were educated to primary level. The average number of years since these patients had been diagnosed with COPD was 9.58 ± 5.38 (min = 1, max = 25) and 32.4% had another illness in addition to COPD. It was found that 7.2% of the patients smoked, 38% had stopped smoking, that 77.9% of these had not smoked for six months or more, 27.8% had smoked for 30 years, 22.2% for 50 years, and 72.2% smoked one packet a day. It was found that 1.2% of the patients drank alcohol and 8.4% had stopped drinking, and 81% of those who had stopped drinking stated that they had not drunk for six months or more. Also, 69.6% of the patients had been hospitalized for 1-5 days.

Hb Value

The patients' mean Hb value was found to be 12.47 ± 1.93 (min = 5.40, max = 16.70); 45.9% of the females and 52.1% of the males or 50% overall were anemic. Anemia is a problem which is frequently seen in COPD patients;¹⁷ this is explained by an inflammatory reaction in which immune mediators play a role.¹³ In this study, it was determined that the patients' mean Hb values were within normal limits (12.47 ± 1.93), but that one COPD patient in two was anemic (Hb < 12 gr/dl). The prevalence of anemia varies widely according to the severity of COPD. Comeche Casanova et al. (2013) observed that 6.2% of 130 COPD patients were anemic with mean Hb values of 11.9 ± 0.95 g/dl,¹⁸ and Fidan et al. (2012) found a low anemia rate of 19.6% and Hb values of 14.2 ± 1.9 g/dl.¹³ In a study with mechanically ventilated COPD patients, Gadre et al. (2017) found an anemia rate of 79.9%.⁹ In a study by Silverback et al. (2014), it was found that 43.9% of 107 COPD patients in the

inflammation stage were anemic,⁷ and in a study by Guo et al. (2015), a mean Hb value of 10.6 ± 0.8 g/dl and an anemia rate of 31% were found.² The anemia rate observed in the present study was high compared with the literature. It is suggested that this may arise from other physiological problems or different cultural characteristics in the patients' related to different nutrition or lifestyle.

Fatigue

The average CAFS score average was 81.51 ± 16.30 (min = 33.33, max = 96.67). Eight out of ten patients in the study were found to be fatigued. One of the important symptoms restricting the activities of daily life of COPD patients is fatigue. In the present study also, a high rate of fatigue was determined in COPD patients. It is thought that this fatigue may derive from anemia in half of COPD patients. Similar to our studies, it has been observed in studies both in Turkey^{14,19-23} and in other countries²⁴⁻²⁹ that COPD patients experience fatigue. The results of these studies confirmed that fatigue was one of the major symptoms for patients with COPD.

Loneliness

The participants' loneliness mean score was 36.58 ± 11.00 (min = 21, max = 68). It was found that 19.2% participants suffered from severe loneliness, 20.8% from moderate loneliness and 60% from mild loneliness. An increase in dependence and a restriction in social activities as COPD progresses cause difficulties for the patient in fulfilling expected roles in the family and in society, anxiety, and an increase in the incidence of depression and the need for social support. Also, repeated hospitalization leads to a distancing of the patient from his or her natural environment, to a perception of being different from others, and to a feeling of loneliness.^{11,12,30} It was observed in these studies that more than half of the patients experienced low levels of loneliness. It is

thought that this may arise from most of the patients not being married and so not having social support. Similarly, it was determined in a study conducted in Turkey by Kiliçkaya and Asi Karakaş (2016) that more than half of COPD patients experienced a low level of loneliness,¹² but another study in this country found that patients' loneliness levels were high.¹¹

Table 1. The patients' description characteristics

Characteristics	n	%
Age (years)	Ort: 68.21±12.34	
≤64	90	36.0
≥65	160	64.0
Gender		
Female	85	34.0
Male	165	66.0
Marital status		
Married	230	92.0
Single	20	8.0
Educational level		
Literate	83	33.2
Primary school	153	61.2
Secondary school	13	5.2
University	1	0.4
Duration of COPD (year)		
0-1	43	17.2
2-4	57	22.8
≥5	150	60.0
The another disease		
Yes	81	32.4
No	169	67.6
Duration of stay in hospital (day)		
1-5	174	69.6
6-10	52	20.8
11 and above	24	9.6
Smoking status		
Smoking	18	7.2
No-smoking	137	54.8
Stopped smoking	95	38.0
Duration of smoking (n=18) (year)		
5 – 29	7	38.9
≥30	11	61.1
Amount of cigarettes (packet/day) (n=18)		
1	13	72.2
≥2	5	27.8
Status of alcohol drinking		
Alcohol drinking	3	1.2
No-alcohol drinking	226	90.4
Stopped alcohol drinking	21	8.4
Total	250	100.0

COPD: Chronic Obstructive Pulmonary Disease

Hb Value, Fatigue, and Loneliness Mean Scores According to The Characteristics of COPD Patients' Characteristics

It was found that the Hb values of males ($t=3.079$, $p=0.002$), those with an education level of primary school or higher ($Z=2.009$, $p=0.046$), and smokers ($t= 11.421$, $p=0.03$) were higher. Marital status, duration of COPD, the existence of another disease and duration of hospitalization were found to have effect on Hb values ($p>0.05$, Table 2). It was found in this study that while the anemia rate in males (52.1%) was higher than in females, Hb values were somewhat higher in males (12.71 ± 2.05) than in females (11.99 ± 1.58). Similarly, some other studies have found the rates of anemia in males to be greater than in females.^{13,31} However, it was found in a study of patients with COPD by Silverberg et al. (2014) that female patients were more anemic than males.⁷ According to the WHO, there is a difference of 1 g/dl in the Hb values of males and females in the diagnosis of anemia,⁸ and this is similar to the difference in mean Hb values in this study. Smoking is one of the most significant causes of COPD.³² In a study of patients with COPD by Silverberg et al. (2014), it was found that patients who smoked were more anemic than non-smoking patients.⁷ However, it was found in the present study that the Hb values of smokers were higher. It is thought that the small number of smokers in the study ($n=18$) may have produced this result.

Females ($t= 2.061$, $p=0.040$) and those with a duration of COPD of five years or more ($F= 3.239$, $p=0.041$) were found to be more fatigued ($p<0.05$). Marital status, educational level, the existence of another disease, duration of stay in hospital and smoking were found to have no effect on the fatigue score ($p>0.05$, Table 2). In the present study, it was found that fatigue in females was higher than in males, and that patients who have had the illness for more than five years experience fatigue more severely than those who have had it for less than five years. There are many studies in the literature stating that gender is related to fatigue in patients with COPD.^{14,21,33} The finding that fatigue is higher in females than in males is supported by the findings of previous studies.^{14,21} It is thought that the many responsibilities which women have in the family in Turkish society and the

greater incidence of disease-related anemia in women than in men may cause women to be more fatigued.

It was found that males ($t = 2.198$, $p = 0.029$) and those who were literate ($t = 2.764$, $p = 0.006$) had higher loneliness scores, and that marital status, duration of COPD, the existence of another disease, duration of hospital stay and smoking had no effect on the

loneliness score ($p > 0.05$, Table 2). It was found in this study that male patients and those with a low level of education experienced a greater level of loneliness. It is thought that, as stated in the literature,³⁴ this may arise from physical, social and economic changes with advancing age, an increase in the experience of loss, and from the greater dependence on others of male patients compared to females.

Table 2. The relationship between COPD patients' characteristics and Hb value, Fatigue, Loneliness scores (n=250)

Characteristics	n	%	Hb Value (X±SD)	Fatigue Scores (X±SD)	UCLA Scores (X±SD)
Gender					
Female	85	34.0	11.99±1.58	84.20±13.06	34.60±9.46
Male	165	66.0	12.71±2.05	80.13±17.62	37.61±11.61
t			3.079	2.061	2.198
p			0.002*	0.040*	0.029*
Marital Status					
Married	230	92.0	12.45±1.91	81.85±16.34	36.37±10.79
Single	20	8.0	12.68±2.19	77.67±15.72	39.10±13.30
Z			0.451	1.402	0.654
p			0.652	0.161	0.513
Educational level					
Literate	83	33.2	12.12±1.92	83.57±13.24	39.37±11.63
Primary school and above	167	61.2	12.64±1.93	80.49±17.57	35.20±10.44
t			2.009	1.550	2.764
p			0.046*	0.123	0.006*
Duration of COPD (years)					
0-1	43	17.2	12.16±1.97	79.26±16.91	36.65±11.54
2-4	57	22.8	12.65±2.06	77.72±18.57	34.32±9.14
≥5	150	60.0	12.49±1.88	83.60±14.91	37.43±11.43
F			0.809	3.239	1.661
p			0.447	0.041*	0.192
The another diseases					
Yes	81	32.4	12.40±1.94	81.28±16.18	36.68±10.78
No	169	67.6	12.50±1.93	81.63±16.41	36.54±11.14
t			0.393	0.160	0.095
p			0.695	0.873	0.924
Duration of stay in hospital (day)					
1-5	174	69.6	12.60±1.99	81.37±16.16	36.08±10.68
6-10	52	20.8	12.31±1.95	83.46±16.52	36.40±11.18
11 and above	24	9.6	11.87±1.25	78.33±16.99	40.63±12.51
χ^2			4.662	3.115	2.981
p			0.097	0.211	0.225
Smoking status					
Smoking	18	7.2	13.61±2.78	73.15±22.99	39.11±14.20
No-smoking	137	54.8	12.19±1.94	81.53±16.10	35.68±10.76
Stopped smoking	95	38.0	12.66±1.64	83.07±14.74	37.41±10.65
χ^2			11.421	2.282	1.267
p			0.03*	0.320	0.531

COPD: Chronic Obstructive Pulmonary Disease, Hb: Hemoglobin, * $p < 0.05$

Table 3. Correlations between Hb value and Fatigue, Loneliness

Variables	1 (r)	2 (r)	3 (r)
Hb value (1)	-		
Fatigue (2)	0.21*	-	
Loneliness (3)	0.011	0.003	-

Hb: Hemoglobin, * $p \leq 0.001$

Relationship of Hb value to Fatigue and Loneliness

A weak, statistically significant relationship was found between Hb value and fatigue ($r=0.21$, $p=0.001$), but there was no statistically significant relationship between Hb value and loneliness ($r=0.001$, $p=0.867$, Table 3), nor was there a statistically significant relationship between fatigue and loneliness ($r=0.003$, $p=0.962$). A positive correlation was found in the study between patients' Hb values and their fatigue. Studies have shown a negative effect on gas exchange, exercise capacity, dyspnea and walking distance in COPD patients with anemia compared to those without anemia. Also, low Hb values in COPD patients can affect pulmonary ventilation functions and the effect of ventilation.^{2,7} This may be why these patients experience more fatigue.

Fatigue in patients with COPD had a significant impact on their ability to perform the routine activities of daily living.³⁵ In COPD patients in an advanced stage of the disease, participation in outside activities may be restricted, social relationships may weaken and the risk of isolation may increase, and this may be particularly seen in those who live alone.^{12,30} Other studies have found that fatigue in COPD patients is positively correlated with anxiety and depression¹⁴ or loneliness and depression,¹¹ while in the present study no correlation was found between patients' Hb values and loneliness or between fatigue and loneliness. This finding can be explained by the fact that most patients in this study did not experience the problem of loneliness and that they had the social support to enable them to cope with it.

CONCLUSION VE RECOMMENDATIONS

In conclusion, the study is important in that it shows that anemia and fatigue are frequently encountered problems in COPD patients, and that there is a relationship between the two problems. Loneliness is a psychosocial problem expected in COPD patients, but it was not seen to be a significant

problem for the patients in this study group. In line with these results, it is recommended that anemia and fatigue should be assessed in COPD patients and that space should be allocated to these problems in treatment and nursing care plans before they affect patients' activities of daily life.

REFERENCES

1. World Health Organization. Chronic respiratory diseases. Available from: <http://www.who.int/respiratory/copd/en/> (Erişim tarihi: 02.03.2018).
2. Guo J, Zheng C, Xiao Q, Gong S, Zhao Q, Wang L, et al. (2015) Impact of anaemia on lung function and exercise capacity in patients with stable severe chronic obstructive pulmonary disease. *BMJ Open*, 5:e008295. doi:10.1136/bmjopen-2015-008295.
3. Türk Toraks Derneği'nin GOLD 2017 KOAH Raporuna Bakışı, Available from: <http://toraks.org.tr/uploadFiles/book/file/1042017161917-tumu.pdf>(Erişimtarihi: 19.04.2018).
4. Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017. Available from: <http://goldcopd.org> (Erişim tarihi: 08.03.2018).
5. Türkiye Halk Sağlığı Kurumu 2015 Faaliyet Raporu. Available from: http://www.saglikaktuel.com/d/file/thsk_2015_faaliyet_raporu.pdf.

6. Pavliša G, Labor M, Purić H, Hećimović A, Jakopović M, Samaržija M. (2017). Anemia, hypoalbuminemia, and elevated troponin levels as risk factors for respiratory failure in patients with severe exacerbations of chronic obstructive pulmonary disease requiring invasive mechanical ventilation. *Croat Med J.*, 58,395-405.
7. Silverberg DS, Mor R, Weu MT, Schwartz IF, Chernin G. (2014). Anemia and iron deficiency in COPD patients: prevalence and the effects of correction of the anemia with erythropoiesis stimulating agents and intravenous iron. *BMC Pulm Med.*, 14, 1-8.
8. de Benoist B, Erin McLean, Egli I, Cogswell M (Eds). *Worldwide prevalence of anaemia 1993 2005 WHO Global Database on Anaemia*. Geneva: WHO, 2008. Available from: http://www.who.int/vmnis/publications/anaemia_prevalence/en/index.html
9. Gadre SK, Jhand AS, Abuqayyas S, Wang X, Guzman J, Duggal A. (2017). Effect of anemia on mortality in mechanically ventilated patients with chronic obstructive pulmonary disease. *J Intensive Care Med.*, Jan 1:885066617739561..
10. Çınar S, Olgun N. (2010). Determining of fatigue and sleep disturbance in patients with Chronic Obstructive Pulmonary Disease. *J Nurs Sci.*, 2, 24-31.
11. Kara M, Mirici A. (2004). Loneliness, depression, and social support of Turkish patients with chronic obstructive pulmonary disease and their spouse. *J Nurs Scholarsh.*, 36, 331-6.
12. Kiliçkaya C, Asi Karakaş S. (2016). The effect of illness perception on loneliness and coping with stress in patients with Chronic Obstructive Pulmonary Disease (COPD). *Int J of Caring Sci.*, 9, 481-8.
13. Fidan A, Tokmak M, Kiral N, Şener Cömert S, Saraç G, Salepci B, et al. (2012). Bir sistemik hastalık olarak KOAH ile anemi birlikteliği. *Solunum Dergisi*, 14,18-26.
14. Karakurt P, Ünsal A. (2013). Fatigue, anxiety and depression levels, activities of daily living of patients with chronic obstructive pulmonary disease. *Int J Nurs Pract.*, 19, 221–31.
15. Yel F., Ergüney S. (2012). Kronik Obstrüktif Akciğer Hastalığı ve Astım Yorgunluk Ölçeğinin Kronik Obstrüktif Akciğer Hastalığında Geçerlik ve Güvenirlik Çalışması. Atatürk Üniversitesi Sağlık Bilimleri Enstitüsü İç Hastalıkları Hemşireliği Anabilim Dalı (Yüksek lisans Tezi), Erzurum.
16. Demir A. (1989). Validity and reliability of UCLA loneliness scale. *Turkish Journal of Psychology* 1989; 23,14–18.
17. Similowski T, Agustí A, Mac Nee W, Schönhofer B. (2006). The potential impact of anaemia of chronic disease in COPD. *Eur Respir J.*, 27, 390-6.
18. Comeche Casanova L, Echave-Sustaeta JM, García Luján R, Albarrán Lozano I, Alonso González P, Llorente Alonso MJ. (2013). Prevalence of anaemia associated with chronic obstructive pulmonary disease. Study of associated variables. *Arch Bronconeumol*, 49, 383–7.
19. Arslan S, Oztunc G. (2016). The effects of a walking exercise program on fatigue in the person with COPD. *Rehabilitation Nursing* 41, 303-12.
20. Şahin ZA, Dayapoğlu N. (2015). Effect of progressive relaxation exercises on fatigue and sleep quality in patients with chronic obstructive lung disease (COPD). *Complement Ther Clin Pract.*, 21, 277-81.
21. Mollaoglu M, Fertelli TK, Tuncay FO. (2011). Fatigue and disability in elderly patients with chronic obstructive pulmonary disease (COPD). *Arch Gerontol and Geriatr.*, 53, 93-8.
22. Inal-Ince D, Savci S, Saglam M, Calik E, Arikan H, Bosnak-Guclu M, et al. (2010). Fatigue and multidimensional disease severity in chronic obstructive pulmonary disease. *Multidisciplinary Respiratory Medicine.*, 5, 162-7.
23. Arikan H, Savci S, Calik-Kutucu E, Vardar-Yagli N, Saglam M, Inal-Ince D, et al. (2015). The relationship between cough-specific quality of life and abdominal muscle endurance, fatigue, and depression in patients with COPD. *Int J Chron Obstruct Pulmon Dis.*, 10, 1829–35.
24. Antoniu SA, Petrescu E, Stanescu R, Anisie E and Boiculese L. (2016). Impact of fatigue in patients with chronic obstructive pulmonary disease: results from an exploratory study. *Ther Adv Respir Dis.*, 10, 26–33.
25. Peters JB, Heijdra YF, Daudey L, Boer LM, Molema J, Dekhuijzen PNR, et al. (2011). Course of normal and abnormal fatigue in patients with Chronic Obstructive Pulmonary Disease, and its relationship with domains of health status. *Patient Educ and Couns.*, 85, 281-5.
26. Zakerimoghadam M, Tavasoli K, Nejad AK, Khoshkesht S. (2011). The effect of breathing exercises on the fatigue levels of patients with chronic obstructive pulmonary disease. *Acta Med Indones-Indones J Intern Med*, 43, 29-33.
27. Wong CJ, Goodridge D, Marciniuk DD, Rennie D. (2010). Fatigue in patients with COPD participating in a pulmonary rehabilitation program. *Int J Chron Obstruct Pulmon Dis*, 5, 319–26.
28. Eckerblad J, Tjødt K, Jakobsson P, Unosson M, Skargren E, Kentsson M, et al. (2014). Symptom burden in stable COPD patients with moderate or severe air flow limitation. *Heart Lung*, 43, 351–7.
29. Pantilat S, O’Riordan D, Dibble S, Landefeld CS. (2012). Longitudinal assessment of symptom severity among hospitalized elders diagnosed with cancer, heart failure, and chronic obstructive pulmonary disease. *J Hosp Med.*, 7, 567–72.
30. Aras A, Tel H. (2009). Kronik obstrüktif akciğer hastalığı olan hastalarda algılanan sosyal destek ve ilişkili faktörlerin belirlenmesi. *Turk Toraks Der.*, 10, 63-8.
31. Pirotte M, Guiot J, Beguin Y, Louis R. (2016). Anemia in patients with severe chronic obstructive pulmonary disease, a comorbidity more common than previously thought. *Rev Med Liege*, 71, 488-94.
32. Ekin S, Sertoğullarından B, Günbatar H, Yıldız H, Arısoy A, Özbay B. (2015). Sigara ve biomas dumanına bağlı gelişen KOAH olgularında anemi sıklığı. *Tıp Araştırmaları Dergisi*, 13, 123-7.
33. Alvarez-Gutierrez FJ, Miravittles M, Calle M, Gobartt E, Lo’pez F, Martin A, Grupo de Estudio EIME. (2007). Impact of chronic obstructive pulmonary disease on activities of daily living: result of the multicenter EIME multicenter study. *Arch. Bronchoneumol*, 43, 64–72.
34. Bilgili N. (2012). Yaşlılarda yalnızlık, uyku kalitesi ve etkileyen faktörlerin değerlendirilmesi. *Tur Geriatri Derg* 15, 82-90.
35. Christensen VL, Holm AM, Kongerud J, Bentsen SB, Paul SM, Miaskowski C, et al. (2016). Occurrence, characteristics, and predictors of pain in patients with chronic obstructive pulmonary disease. *Pain Manag Nurs* 17,107-18.