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Association of obstructive sleep apnea syndrome with hematological parameters and comorbid diseases

Faysal Duksal

Department: Chest Diseases and Tuberculosis, University: Beyhekim Research and Training Hospital, Konya, Turkey

Abstract

Background & Objective: Obstructive sleep apnea syndrome (OSAS) has a close relationship with many diseases. Hematological parameters are simple diagnostic methods and can give an idea about severity of some diseases. The aim of this study was to examine the relationship of OSAS with comorbid diseases and relationship between OSAS severity, oxygen desaturation index (ODI) and hematological parameters. *Methods:* This retrospective and cross-sectional study was conducted by evaluating the medical files of patients who underwent polysomnography between 2012 and 2018. 1,119 patients (198 controls; 921 OSA) were participated to the research. *Results:* Congestive heart failure, hypertension (HT), asthma and chronic obstructive pulmonary diseases (COPD) were seen in 143, 424, 254 and 177 patients respectively. Severe OSAS was found more common in male. Except the patients with HT; neutrophil lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) levels were higher and lymphocyte levels were lower in patients with comorbid diseases. WBC and erythrocyte distribution width (RDW) levels were higher in patients with COPD than without COPD; PLT levels were higher in patients with asthma than without asthma. WBC level of the moderate-severe OSAS was significantly higher than the control and mild OSAS (p=0.001). Platelet distribution width (PDW) value of the OSAS was higher than the control group (p=0.005). The apnea-hypopnea index and ODI levels were higher in patients with comorbidity than without comorbidity (p=0.001).
Conclusions: It can be said that lymphopenia, high NLR, PLR, WBC, RDW and PDW may be useful markers for predicting severity of OSAS in comorbid diseases. The presence of OSAS should be detected in order to treat comorbidity appropriately.

Keywords: Comorbid diseases, inflammation, NLR, OSAS, PLR

INTRODUCTION

Partial or complete obstruction of the upper airway that occurs with repetitive periods during sleep is called as "Obstructive Sleep Apnea Syndrome" (OSAS).[1-4] OSAS has a close relationship with many illnesses and diagnostic method is polysomnography (PSG).[2,5] The underlying mechanism is not fully known; but there is an increase in inflammatory markers, especially in severe OSAS patients.[6,7] So, it is thought that as a result of chronic inflammatory process, there is intermittent hypoxia (IH) which is important in the pathogenesis of OSAS.[8] IH is the unique form of hypoxia occurring in OSAS. It is explained as short repetitive cycles of desaturation followed by rapid reoxygenation. This process activates inflammatory mechanisms, especially NF-κB-mediated pathway. As a result of these mechanisms, activation of inflammatory cells occurs and various inflammatory mediators are released. So, IH is likely to play a significant role in the pathogenesis of OSAS.[9] The effect of hematological markers about inflammation has been studied. White blood cell (WBC) and the ratio of neutrophil to lymphocyte (NLR), platelet to lymphocyte (PLR) were found as important parameters in predicting inflammation.[10,11-13]

Some indices of red blood cells (RBC) and platelets have been reported to be inflammatory biomarkers for various diseases.[14] However, there is controversial information about the relationship between these indices and severity of OSAS.[15-18] Increased erythrocyte distribution width (RDW) also contributes to platelet activation. In addition, it is an important indicator of prognosis in chronic patients and may play a role in predicting

Address correspondence to: Faysal Duksal, Department: Chest Diseases and Tuberculosis, University: Beyhekim Research and Training Hospital, Konya, Turkey. Tel: +90 505 292 04 50, Email: fduksal@gmail.com

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mortality.[19] Mean platelet volume (MPV) and platelet distribution width (PDW) are the most important indicators of platelet activity. A rise in MPV and PDW indicates a connection between coagulation and inflammation.[8,15,18]

Hemoglobin (Hb), WBC, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), RDW, platelet, PDW, MPV, NLR and PLR can be easily obtained from a complete blood count (CBC) analysis in peripheral blood and can give information about many diseases.

This study was planned with very large participation and it was aimed to examine the relationship of OSAS with comorbid diseases and the relationship between OSAS severity, oxygen desaturation index (ODI) and hematological parameters.

METHODS

Study protocol and ethical approval

This study was retrospective and cross-sectional, conducted by evaluating the medical files of patients who underwent polysomnography in Sivas Numune State Hospital Polysomnography Unit between 2012 and 2018. The Institutional Ethics Committee for Clinical Research Karatay University, approved the study (approval number: E-41901325-050.99-11867), which was in accordance with Helsinki Declaration and Good Clinical Practices Guideline. All individuals gave written consent prior to participation.

Participants of study

The medical files of 1,300 inpatients over the age of 18 whose sleep data were recorded in the PSG unit included to the study. Age, gender and comorbid diseases (congestive heart failure, CHF; primary hypertension, HT; asthma, chronic obstructive pulmonary disease, COPD) of the participants were recorded. Patients under 18 years old, with other chronic diseases, active systemic infection and patients with missing data excluded from the research. Most of the patients who applied with OSAS symptoms had CHF, HT, COPD and asthma. Diseases with very few numbers such as hematological diseases and endocrinological disease (Diabetes Mellitus, thyroid diseases, osteoporosis etc.) were not included to the study, considering that they would affect the statistical results. 1,119 of 1,300 participants who had suitable conditions were included in the study. Data regarding demographics, PSG, and laboratory test results were documented and analyzed. OSAS severity was classified as; simple snoring (control), mild, moderate, and severe OSAS. In addition, participants will be subdivided according to their comorbid diseases (CHF, HT, asthma, COPD).

Polysomnography studies

Polysomnography was performed overnight in a separate room with the presence of an accompanying staff member. For visual and auditory recording, Embla S4500 model PSG device was used. Four-channel electroencephalogram, electromyogram (EMG-submental], electromyogram (EMG-right-left tibialis), and two-channel electrooculogram (right-left EOG) were used for this subject. Nasal airflow and pulse oximetry were monitored overnight to determine the blood oxygen saturation level. The mean and minimum values of oxygen saturation were eveluated from the overnight records. ODI was defined and noted as the mean oxygen saturation of at least 4% below the basal value per hour. Arrangement of results were done by following the suggestions of the American Academy of Sleep Medicine.[20]

The definition of apnea-hypopnea index (AHI) was the total number of apnea and hypopnea events per hour of sleep. AHI was assessed by using the patient records of PSG and oxygen saturation. The presence of any of the following criterias was used to define hypopnea: a) a 50% decrement in airflow for at least 10 seconds, b) the oxygen desaturation of at least 3%, c) development of arousal, more than 30% reduction in airflow lasting for at least 10 seconds, d) 4% decrease in oxygen saturation. The minimum saturation level is defined as the lowest level of oxygen saturation (oxygen desaturation) detected during the night.[20] The classification of the patients was made according to their AHI values as follows: simple snoring (control): AHI <5; mild OSAS: 5≤AHI<15; moderate OSAS: 15≤AHI<30; severe OSAS: 30≤ AHI.

Laboratory studies

The results of hematologic parameters were obtained from the medical files. By dividing neutrophil to lymphocyte and platelet to lymphocyte count, NLR and PLR were measured respectively. All patients evaluated in the sleep laboratory were taken in the stable period. The hematological tests were also performed on the same day and recorded.

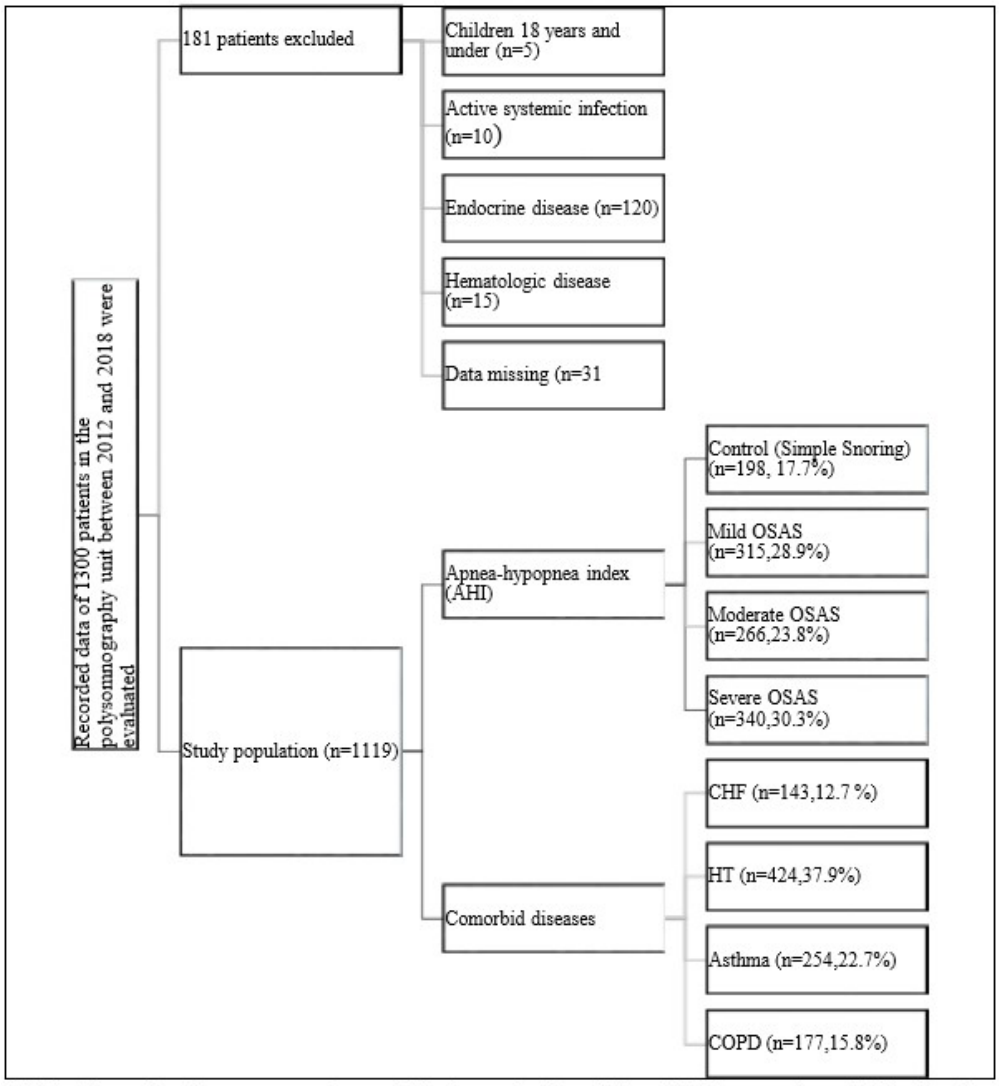
Statistical analysis

Kolmogorov-Smirnov (n>50) and Skewness-Kurtosis tests were used to check whether the continuous measurements in the study were normally distributed, and because the measurements were normally distributed, parametric tests were applied. Descriptive statistics for continuous variables in the study were expressed as; mean, standard deviation (SD), minimum, maximum; numbers (n) and percentages (%) for categorical variables. "Independent T-test" and "One-Way Analysis of Variance (ANOVA)" were used to compare the measurements according to the groups. Pearson correlation coefficients were calculated to determine the relationships between measurements. Chi-square test was used to determine the relationships between groups and categorical variables. Statistical significance with a 95% confidence interval was accepted when a p-value was below 0.05, and the SPSS (IBM SPSS for Windows, ver.24) statistical package program was used for analysis.

RESULTS

The total number of participants was 1,119 (198 controls and 921 OSAS patients); CHF, HT, asthma and COPD was seen in 143, 424, 254 and 177 patients respectively. (Figure 1) The mean age of the OSAS (50.03±11.39) was significantly higher than the control patients (42.28±12.14)

Figure 1. Flow chart regarding selection of Obstructive Sleep Apnea Syndrome patients



OSAS: Obstructive sleep apnea syndrome; CHF: Congestive heart failure, HT: Hypertension; COPD: chronic obstructive pulmonary disease

(p=0.001). The age of the moderate and severe OSAS groups was similar, and higher than mild and control group significantly (p=0.001); the age of mild OSAS group was found significantly higher than control group (p=0.001). Considering the severity of the disease, severe OSAS was more common in male (p=0.035).

The results of hematological parameters are as follows:

The WBC levels of the moderate and severe OSAS patients were detected to be similar to each other, and higher than the control, and mild OSAS patients significantly (p=0.001). Total OSAS patients had significantly higher PDW value than the control group (p=0.005). The outcomes are given in Table 1.

ODI - Mean saturation index

As the severity of OSAS increased (from mild OSAS to severe OSAS), more increases were seen in AHI and ODI values (p=0.001).

The hematologic and polysomnographic results according to comorbid diseases

The presence of severe OSAS was significantly more common in patients with comorbid disease than patients without these diseases (p=0.001); (Table 2).

Polysomnography results indicated that ODI level was significantly higher, and mean/minimum saturation levels were lower in those with comorbid disease as compare to those without (p=0.001). WBC level of patients with COPD was higher than patients without COPD significantly (p=0.005). NLR and PLR values were detected to be significantly higher in patients with CHF (p=0.012 for NLR; p=0.001 for PLR), in patients with asthma (for NLR, p=0.014; for PLR, p=0.001) and in patients with COPD (p=0.001 both for NLR and PLR) than in patients without CHF, asthma and COPD respectively. The hematologic studies showed significantly lower HB, hematocrit, and RBC values in patients with HT (for HB, p=0.001; for hematocrit, p=0.045 and for RBC, p=0.005), and asthma (for HB and HTC p=0.001; for RBC p=0.008) compared to the patients without HT and asthma respectively. MCV and MCH levels were lower, but not significant between HT and without HT (p>0.05). In contrast, these parameteres were significantly lower in asthma than without asthma (p=0.048 and p=0.002 respectively for MCV and MCH). Furthermore, RDW value was found significanty higher in patients with HT and COPD (p=0.02 and p=0.016 respectively). PLT was significantly higher (p=0.013), but PDW and MPV were not different in patients with asthma. There was significant lymphopenia in patients with CHF, asthma and COPD (p=0.034; p=0.022; p: 0.006 respectively). The results are shown in table 3.

DISCUSSION

In the current study, ODI and hematologic parameters were studied in OSAS patients according to comorbid diseases. AHI is used to grade OSA, but may not provide information about the depth and length of the apnea.[21] On the other hand, a meaningfull relationship was stated between AHI and ODI.[21] In the current study, it was found that while the severity of the OSA increased, especially because of comorbid diseases, oxygenation decreased. As known, OSAS is usually more common in middle-aged and older adults, and comorbid diseases occur more with increasing age.[1-4] Similarly, in this study also, as the age of the patients increased, severity of OSAS and presence of comorbid diseases were found to increase. OSAS may complicate the control of comorbid diseases, therefore to improve the quality of life, the diagnosis of OSAS should be considered in these patients especially in elderly.

Inflammation is important in the pathogenesis of OSAS and there is an increase in inflammatory markers. In the previous studies, the relationship between OSAS and a high degree of WBC, NLR, PLR, MPV, PDW, RDW, and HTC was reported.[22,23] In contrast, in the current study, we did not find significant difference between total OSAS and control in terms of WBC level. However, it was higher in severe and moderate OSAS patients. In another meta-analysis also, NLR value was detected to be more elevated in OSAS patients, and the difference was bigger in severe OSAS patients. These results suggest that, NLR may be a reliable marker to detect systemic inflammation and predict disease severity in OSAS patients.[23] Another study showed that the PLR value was directly proportional to the severity of OSAS and cardiac disease.[24] In the current study, it was observed that those with the asthma, COPD and CHF had significantly higher NLR and PLR levels than those who did not have these diseases. In contrast, we did not find the same results in patients with HT. Although NLR is an inexpensive and accessible marker to identify many diseases, it should be noted that

Table 1: Demographic, hematology and PSG results of OSAS patients

Variables	Total OSAS (n=921)	Control (n=198)	OSAS groups			Control vs. total OSAS p	Control vs. OSAS groups p	Between OSAS groups p
			Mild (n=315)	Moderate (n=266)	Severe (n=340)			
Age (year)								
Mean ± SD	50.03± 11.39	42.28± 12.14	47.75± 10.87	50.16± 10.72	52.09± 11.99	**0.001**	**0.001**	**0.001**
Range	(19.00-82.00)	(18.00-78.00)	(19.00-79.00)	(22.00-82.00)	(19.00-82.00)			
Gender								
M (n %)	534(57.98)	101(51.01)	181(57.99)	139(52.54)	213(62.31)	>0.05	**0.035**	**0.035**
F (n %)	387(42.01)	97(48.9%)	134(42.01)	127(47.54)	127(35.9)			
WBC $\times 10^9$/L								
Mean ± SD	8.34± 2.19	8.04± 2.2	8.01± 2.47	8.47± 2.34	8.67± 2.51	>0.05	**0.001**	**0.001**
Range	(3.90-20.5)	(4.50-18.30)	(4.10-16.60)	(3.90-20.50)	(4.20-18.80)			
RBC($\times 10^{12}$/L)								
Mean ± SD	4.98± 0.48	4.98±0.52	4.99 ± 0.52	4.99 ± 0.45	4.97 ± 0.43	>0.05	>0.05	>0.05
Range	(2.6-6.5)	(3.75-7.74)	(2.60-6.40)	(4.00-6.49)	(2.7-6.5)			
HGB(g/dL)								
Mean ± SD	4.68± 1.70	14.46± 1.69	14.68± 1.64	14.57± 1.51	14.65 ± 1.54	>0.05	>0.05	>0.05
Range	(8.4-19.70)	(8.20-18.50)	(8.40-19.20)	(10.40-18.30)	(10.60-19.70)			
HCT%								
Mean ± SD	43.55± 5.23	42.94± 4.79	43.57± 4.74	43.44± 4.19	43.24 ± 4.15	>0.05	>0.05	>0.05
Range	(26.80-66.20)	(28.10-55.10)	(26.80-66.20)	(31.70-55.30)	(32.60-60.60)			
MCV(fL)								
Mean ± SD	86.33± 7.77	86.16± 7.42	86.8094± 5.87	87.08± 5.31	86.33± 6.14	>0.05	>0.05	>0.05
Range	(41.70-102.20)	(42.70-103.80)	(44.50-102.20)	(57.60-99.70)	(41.70-99.10)			
MCH(pg)								
Mean ± SD	29.21± 2.26	29.28± 2.45	29.38± 2.19	29.32± 1.98	29.11± 2.16	>0.05	>0.05	>0.05
Range	(19.00-35.40)	(17.30-37.50)	(19.00-34.20)	(22.80-35.40)	(19.50-34.30)			
RDW%								
Mean ± SD	13.75± 1.80	13.73± 1.98	13.76± 2.01	13.59± 1.28	13.83± 1.36	>0.05	>0.05	>0.05
Range	(10.00-31.10)	(10.40-34.40)	(10.40-31.10)	(10.20-22.30)	(10.00-20.70)			
NEU%								
Mean ± SD	59.39± 9.89	59.57± 9.97	58.27± 9.84	57.96± 12.17	57.501± 12.31	>0.05	>0.05	>0.05
Range	(4.20-92.20)	(2.40-91.00)	(5.04-83.90)	(4.20-90.00)	(3.60-92.20)			
LYM%								
Mean ± SD	29.55± 8.35	29.66±8.12	30.88± 8.24	30.80± 8.77	30.68± 8.15	>0.05	>0.05	>0.05
Range	(4.00-66.90)	(5.00-52.50)	(9.50-58.40)	(4.00-55.40)	(5.20-66.90)			
PLT count ($\times 10^9$/L)								
Mean ± SD	258.99± 60.73	254.49± 64.01	254.07± 60.39	262.94± 61.82	261.73± 58.99	>0.05	>0.05	>0.05
Range	(114.00-538.00)	(120.00-487.00)	(114.00-492.00)	(127.0-538.0)	(134.00-483.00)			
PDW%								
Mean ± SD	15.86± 2.05	15.36± 2.34	16.044± 2.04	15.77± 2.07	15.78± 1.99	**0.005**	>0.05	>0.05
Range	(7.00-30.0)	(5.55-19.50)	(7.50-30.00)	(7.40-25.90)	(7.00-18.60)			
MPV(fL)								
Mean ± SD	8.61± 1.12	8.63± 1.04	8.56 ± 1.02	8.62± 1.14	8.60± 1.01	>0.05	>0.05	>0.05
Range	(5-16)	(5.90-11.50)	(8.59-12.80)	(5.00-16.00)	(5.10-11.60)			
NLR								
(Mean ± SD)	0.081± 0.05	0.082± .06	0.076±0.056	0.09± 0.087	0.084± .076	>0.05	>0.05	>0.05
Range	(0.0-0.93)	(0.01-0.47)	(0.00-0.53)	(0.00-0.88)	(0.00-0.93)			
PLR								
Mean ± SD	9.43± 5.46	9.41± 4.41	8.94± 3.78	9.75± 5.95	9.29± 3.88	>0.05	>0.05	>0.05
Range	(2.93-61)	(3.75-44.60)	(2.93-33.47)	(3.29-61.00)	(3.68-38.64)			
ODI(events/h)								
Mean ± SD	29.81± 24.0	3.87± 2.91	11.95± 8.51	23.69 ± 9.2	58.17± 26.49	**0.001**	**0.001**	**0.001**
Range	(0.5-143)	(0.00-17.60)	(0.50-115.00)	(5.70-64.40)	(8.00-143.00)			
Mean SpO2%								
Mean ± SD)	89.74± 4.6	92.75± 2.13	91.54± 3.04	90.49± 3.86	87.9± 5.98	**0.001**	**0.001**	**0.001**
Range	(57.70-98.80)	(83.00-96.80)	(66.30-96.60)	(63.70-96.50)	(57.70-98.80)			

OSAS:obstructive sleep apnea syndrome; PSG:polysomnography; M:male; F:female; WBC:white blood cell; RDW:erythrocyte distribution width; Neu:neutrophile; Lym:lymphocyte; PLT: platelet; MPV:mean platelet volume; PDW:platelet distribution width; Hb:Hemoglobin; HTC:hematocrit; MCV:mean erythrocyte volume; MCH:mean corpuscular hemoglobin; NLR:neutrophil/lymphocyte ratio; PLR:platelet/lymphocyte ratio; ODI:oxygen desaturation index; SpO2:oxygen saturation; $p<0.05$: significant

Table 2: Comparision of the severity of OSAS with comorbid diseases

Variables	Study group n=1119				p
	Total OSAS n= 921 (82.3%)				
	Control (Simple Snoring) n=198 (17.7%)	Mild OSAS n =315 (28.16%)	Moderate OSAS n=266 (23.8 %)	Severe OSAS n=340 (30.3%)	
CHF (n=143)	9(4.50)	27(8.57)	42(15.80)	65(19.11)	**0.001**
HT (n=424)	32(16.20)	95(30.3)	119(44.70)	178(52.40)	**0.001**
ASTHMA (n=254)	26(13.10)	62(19.70)	69(25.90)	97(28.50)	**0.001**
COPD (n=177)	10(5.10)	33(10.5)	55(20.70)	79(23.24)	**0.001**

p=0.001: significant; severe OSAS were significantly higher in comorbid diseases. OSAS: obstructive sleep apnea syndrome; CHF: congestive heart failure; HT: primary hypertension; COPD: chronic obstructive pulmonary disease.

NLR can be affected by many conditions. This may be due to the antihypertensive drugs used by the patients.[25] However, large-scale randomized prospective studies are needed to define these findings more clearly. Erythrocyte distribution width (RDW) is an important parameter to determine the causes of anemia and a rise in RDW is also important for platelet activation. RDW is an important indicator of prognosis in chronic patients and may play a role in predicting mortality.[8,19] Hematocrit is another marker that affects blood viscosity and platelet aggregation.[24] MPV demonstrates platelet dimension and it is the most important indicator of platelet activity.[11] In contrast, in the current study, no difference was detected between OSAS and the control in terms of these parameters (p>0.05). Another marker of platelet activation which is PDW[12,18] was found significantly higher in OSAS patients than the control group (p=0.005). However, no difference was found between OSAS severity and PDW (p>0.05). When looking to the comorbid diseases, PDW level was found higher, but not significant in HT patients. Although not significant, this finding was important because platelet activation plays a pivitol role in thrombotic events and may lead to HT related target organ damage.

Patients with congestive heart failure

Association of CHF and platelet activity

It has been reported that there was a positive correlation between AHI and platelet, while a negative correlation between AHI and PDW in CVD.[26] In addition, in another study, lower lymphocyte and higher RDW levels were found in older patients who had CVD when compared to the patients without CVD.[27] By the contrary, in the current study, no association was found between platelet, PDW, RDW and patients with and without CHF. For this comparision, we did not seperate the patients as younger or older. This may be the reason why we found different results from these studies. However, increased AHI was found more in CHF patients, showing the importance of comorbid disease in OSAS patients.

Association of CHF and NLR

Previous studies reported that, the relationship between PLR and AHI, ODI, mean and minimum O2 saturation values was meaningfull. In addition to strong correlation between PLR and OSAS severity, they also reported significant association between NLR and OSAS with CVD.[24,27] In another study, similarly, it was found that there was a positive correlation between OSAS severity and NLR. Furthermore, high NLR has been reported to be associated in OSAS with CVD.[28] Similar to that studies, in the current study also, NLR and PLR were found higher in patients with CHF. So, these inflamatuar markers may be used as biomarkers to estimate CVD in OSAS patients.

Table 3: Variables according to comorbid diseases

Variables	Patients with CHF	Patients with HT	Patients with asthma	Patients with COPD	Control	Control vs. CHF p	Control vs. HT p	Control vs. asthma p	Control vs. COPD p
Age (year) Mean ± SD	56.10±10.44	53.40±10.09	52.33±10.54	54.63±10.85	45.67±12.04	**0.001**	**0.001**	**0.001**	**0.001**
WBC×10^9/L Mean ± SD	8.20±2.40	8.35±2.20	8.47±2.38	8.75±2.45	8.24±2.18	>0.05	>0.05	>0.05	**0.005**
RBC count (×10^{12}/L) Mean ± SD	4.98±0.52	4.97±0.50	4.95±0.51	5.02± 0.50	5.05± 0.50	>0.05	**0.005**	**0.008**	>0.05
HGB(g/dL) Mean ± SD	14.69±1.42	14.47± 1.56	14.26± 1.60	14.69± 1.63	14.78± 1.62	>0.05	**0.001**	**0.001**	>0.05
HCT(%) Mean ± SD	43.79± 4.39	43.08± 4.68	42.79± 4.77	44.01±4.55	43.85± 4.46	>0.05	**0.045**	**0.001**	>0.05
MCV(fL) Mean ± SD	86.97± 5.88	86.56± 6.38	84.68± 5.6	86.04± 6.3	86.80± 6.15	>0.05	>0.05	**0.048**	**0.012**
MCH(pg) Mean ± SD	29.54± 2.02	29.15± 2.29	28.88± 2.20	29.38±2.32	29.36± 2.16	>0.05	>0.05	**0.002**	>0.05
RDW(%) Mean ± SD	13.79± 1.27	13.93± 1.64	13.89± 1.31	14.01±1.56	13.62± 1.67	>0.05	**0.002**	>0.05	**0.016**
Neu % Mean ± SD	57.66± 14.30	58.25± 12.69	57.86± 13.75	58.71± 13.38	58.27±10.7	>0.05	>0.05	>0.05	>0.05
Lymp % Mean ± SD	29.32± 8.74	30.36± 8.63	29.54± 8.73	29.02 ± 9.43	30.94± 8.18	**0.034**	>0.05	**0.022**	**0.006**
PLT count (×109/L) Mean ± SD	256.23± 62.32	258.17± 60.12	266.9± 62.64	262.49± 66.14	256.1± 60.4	>0.05	>0.05	**0.013**	>0.05
PDW(%) Mean ± SD	15.76± 2.14	15.92± 1.93	15.65± 2.03	15.70± 2.08	15.80± 2.13	>0.05	>0.05	>0.05	>0.05
MPV(fL) Mean ± SD	8.63± 1.25	8.66± 1.12	8.51± 1.02	8.65± 1.01	8.63± 1.06	>0.05	>0.05	>0.05	>0.05
NLR Mean ± SD	0.09± 0.08	0.08± 0.07	0.09± 0.08	0.10± 0.10	0.08± 0.07	**0.012**	>0.05	**0.014**	**0.001**
PLR Mean ± SD	9.94± 6.15	9.45± 4.96	10.29± 6.02	10.44± 6.29	9.13± 3.84	**0.001**	>0.05	**0.001**	**0.001**
ODI(events/h) Mean ± SD	38.31± 27.83	35.27± 27.29	34.39± 29.56	38.68± 30.23	22.41± 25.11	**0.001**	**0.001**	**0.001**	**0.001**
Mean SpO2 % Mean ± SD	87.83± 6.28	88.83± 5.36	88.63± 5.57	87.61± 6.28	90.74± 4.26	**0.001**	**0.001**	**0.001**	**0.001**

WBC: white blood cell; RDW: erythrocyte distribution width; Neu: neutrophile; Lym:.lymphocyte; PLT: platelet; MPV: mean platelet volume; PDW: platelet distribution width; Hb: Hemoglobin; HTC: hematocrit; MCV: mean erythrocyte volume; MCH: mean corpuscular hemoglobin; NLR: neutrophil/lymphocyte ratio; PLR: platelet/lymphocyte ratio; ODI: oxygen desaturation index; SpO2: oxygen saturation; P<0.05: significant

Patients with primary hypertension

In the current study, OSAS was found more severe in patients with HT. As seen in our study, OSAS is found more frequently at older ages. In addition, HT is seen more in older people also. Therefore, HT and OSAS may increase each other's morbidity. For this reason, in patients with severe apnea and resistant HT, OSAS should be investigated and be treated to keep blood pressure under the control.[29]

Association of HT and anemia

In one study, patients with uncontrolled HT had more normocytic anaemia than patients with well-controlled HT.[30] In current study, similarly, RBC, HB and RBC values were found to be lower and RDW was higher in OSAS patients with HT. Lower HB concentration may increase HT status and so OSAS severity.

Association of HT with NLR and platelet activity

We could not find a study showing the relationship between NLR and PLR in OSAS with HT. However, there are studies with conflicting results showing the relationship between HT and NLR.[29-32] It was found that there was a correlation between high NLR levels and HT risk, especially in elderly and male individuals.[31,32] Koseoglu *et al*. reported that as OSAS severity increased, PLR value decreased, but they didn't find a significant correlation between AHI and NLR values.[1] In contrast, in the current study, there was no meaningfull relation in terms of NLR and PLR between OSAS and the control, in addition to patients with HT and without HT.

Patients with asthma

Association of asthma with NLR and platelet activity

Asthma is a chronic inflammatory disease and can appear in many phenotypes.[33] It is common in OSAS and usually coexisting.[33,34] An increase in NLR is a known situation in OSAS, while Huang *et al.* showed that NLR was higher in asthma exacerbations than stable asthma patients.[34] It was reported that the PLR value was lower in OSAS than in the control.[1] In the current study, in addition to high levels of PLT, NLR and PLR, lymphopenia which is another marker for inflammation was also seen in OSAS with asthmatic patients. Furthermore, ODI level was significantly higher and minimum saturation level were lower in those with asthma. In addition to lymphopenia, high NLR, PLR, and PLT may predict OSAS severity in asthmatic patients. However, because we did not find any study about NLR and PLR in OSAS patients with asthma, these results should be confirmed by larger prospective studies.

Association of severity of asthma and OSAS

Severity of asthma increases at night and the risk of death because of asthma also increases at night or early in the morning.[33] OSAS symptoms also increase during sleep and may complicate asthma symptoms. Presence of occult OSAS in severe asthma and presence of asthma in severe OSAS should be investigated since the risk of co-occurrence is high. If OSAS is left untreated, it becomes difficult to control asthma symptoms, especially at night.

Association of asthma and anemia

It was reported that asthma patients had lower hemoglobin levels than the controls. In the current study also, results were consistent with anemia in asthmatic patients.[35] Anemia may cause an increase of OSAS findings in these patients. Further studies are needed about anemia treatment for asthma prevention.[34,35]

Patients with chronic obstructive pulmonay disease

Obstructive sleep apnea syndrome and COPD are two diseases that often co-exist within a patient. As other comorbid diseases studied in the current study, severe OSAS was seen also more common in COPD.

Association of COPD with NLR, WBC and platelet activity

Accumulated data suggests that platelet activation, such as PDW and MPV are increased in OSAS with COPD patients.[36] In the current study, there was a significant increase in RDW, as well as PLR and NLR in these patients. In another study conducted in COPD, patients presenting with an acute attack had higher WBC, RDW, NLR, PLR and lower HB, platelet, MPV, PCT, and lymphocyte than stable COPD patients.[37] In the current study, all patients with COPD were stable. NLR, PLR and also WBC levels were found to be higher and lymphocyte level was lower. As it is an inflammatory disease, high WBC, NLR, PLR and lymphopenia were expected in COPD similar to other inflamatuar diseases such as asthma. As

previously reported[1,36,37], we also suggest that an increase in these inflamatuar parameters, and an increase in AHI and ODI may indicate the presence of chronic hypoxia. So, especially in patients with increased inflammatory parameters, a very careful treatment of OSAS can protect these patients from hypoxia.

Association of COPD and anemia

Although the HB levels were normal in COPD patients, lower MCV and higher RDW levels require close follow-up of patients in terms of anemia. Because, coexistence of anemia and inflammation may increase the risk of COPD severity and so OSAS severity.

The advantage of the study was that it was accomplished by the same investigator in a single center whereas there are some limitations. In this study, OSA patients with comorbid diseases were compared according to hematological parameters. However, the condition of these patients after OSA treatment was not examined. After OSA treatment and also anemia treatment, it should be studied whether comorbid diseases of the patients are under the control or not.

In conclusion, in the current study, OSAS was found to be more severe in males and older patients. In addition, as the severity of the OSAS increased, ODI was found to be increased also. Lymphopenia, high NLR, PLR, WBC, RDW and PDW may be useful inflammatory markers for predicting the severity of OSAS in comorbid diseases. The presence of OSAS should be questioned in order to manage comorbid diseases more easily. There is a need for more comprehensive studies examining other factors affecting inflammatory markers along with comorbid diseases.

DISCLOSURE

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