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The relationship between disease severity, treatment adherence, inflammation, and neurocognitive functions in patients with obstructive sleep apnea syndrome

[1]Ömer Faruk ILDIZ, [2]Ahmet Hakan EKMEKCİ, [2]Fettah EREN, [3]Muslu Kazım KÖREZ

[1]Department of Neurology, Konya City Hospital, Konya, Turkiye; [2]Department of Neurology, Faculty of Medicine, Selçuk University, Konya, Turkiye; [3]Department of Biostatistics, Faculty of Medicine, Selçuk University, Konya, Turkiye

Abstract

Obstructive: Sleep Apnea Syndrome (OSAS) is a condition marked by recurrent interruptions in airflow during sleep, causing intermittent hypoxia and inflammation. These changes adversely affect neurocognitive functions. OSAS is linked to impairments in executive functions, memory, attention, and intellectual capacity. This study aims to evaluate the effects of OSAS on cognitive functions and inflammatory markers and the impact of Continuous Positive Airway Pressure (CPAP) treatment. *Methods:* This retrospective study included 106 OSAS patients and 49 healthy controls, classified based on their Apnea-Hypopnea Index (AHI) and CPAP treatment adherence. Patients in the treatment group used CPAP for at least 4 hours daily over 3 months. Cognitive performance was measured using the Montreal Cognitive Assessment, and inflammatory markers such as Platelet Distribution Width (PDW), Platelet-Lymphocyte Ratio (PLR), and Neutrophil-Lymphocyte Ratio (NLR) were analyzed. *Results:* MoCA scores showed significant declines in cognitive functions across all OSAS groups ($p < 0.001$), with notable reductions in executive functions, language, and abstraction. Treated patients showed higher cognitive scores, though differences were not statistically significant. PDW, PLR, and NLR levels were significantly lower in the CPAP-treated group compared to untreated patients.
*Conclusion***:** Untreated OSAS significantly affects cognitive functions, particularly executive functions, language, and abstraction. CPAP treatment provides partial cognitive improvement and reduces inflammatory markers like PLR, PDW, and NLR. These markers may be valuable in assessing treatment effects and detecting suspected OSAS. Further research with larger cohorts is needed to validate these findings and enhance clinical management.

Keywords: Obstructive sleep apnea syndrome, continuous positive airway pressure, cognitive functions

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is characterized by recurrent episodes of complete cessation or partial reduction in airflow caused by upper airway obstruction. These episodes lead to sleep fragmentation and intermittent hypoxemia.[1] Consequently, OSAS patients often experience excessive daytime sleepiness, which is one of the most commonly reported complaints, along with waking up feeling fatigued.[2] Risk factors for OSAS include age, male sex, obesity, postmenopausal status without hormone therapy, family history, craniofacial abnormalities, and smoking. Typical symptoms comprise excessive daytime sleepiness, snoring, observed apneas, non-restorative sleep, morning headaches, and fatigue.[3]

The prevalence of OSAS in adults ranges from 9% to 38%, with rates of 13% to 33% in men and 6% to 19% in women.[4] Studies have indicated that inflammation associated with OSAS may contribute to endothelial cell dysfunction, potentially impairing the structure and function of blood vessels. This endothelial damage is linked to complications in vital organs, including cardiovascular diseases, metabolic dysfunction, and neurocognitive impairment.[1]

Continuous positive airway pressure (CPAP) is the first-line treatment for OSAS. Early initiation of CPAP therapy offers the most significant functional improvement, with prolonged treatment (more than three months) and consistent adherence (at least four hours per night) shown to be more

Address correspondence to: Ömer Faruk ILDIZ, 1Department of Neurology, Konya City Hospital, Konya, Turkiye. Email: farukildiz@hotmail.com
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effective in reducing systemic inflammation.[5]

Cognitive impairments, such as deficits in attention, executive function, intellectual capacity, and memory, have been frequently observed in individuals with OSAS. While findings in this area are inconsistent, evidence suggests a potential link between cognitive decline and OSAS-related factors. Various studies have examined inflammatory markers in the hemogram, including hematocrit (HCT), lymphocyte (LYM), mean platelet volume (MPV), neutrophil-to-lymphocyte ratio (NLR), platelet distribution width (PDW), platelet-to-lymphocyte ratio (PLR), red cell distribution width (RDW), and white blood cell count (WBC). These markers have been proposed as simple, cost-effective, and practical indicators of OSAS.[6]

METHODS

Patient selection

This retrospective study reviewed all patients diagnosed with OSAS who presented to the sleep unit between January 1, 2021, and November 30, 2022. Ethical approval for the study was obtained from the local ethics committee. Inclusion criteria consisted of patients aged 18-65 years who underwent hemogram testing and cognitive assessments using the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) during evaluations at the sleep laboratory.

Patients were classified into three OSAS severity groups based on the Apnea-Hypopnea Index (AHI): mild (AHI: 5-15), moderate (AHI: 15-30), and severe (AHI > 30). Each group was further divided into treated and untreated patients. The treatment group included patients who had used CPAP for at least three months with a minimum of four hours per night. Parameters were analyzed on the day of diagnosis and at 3 months of treatment. The control group comprised individuals with no sleep-related complaints who visited the neurology outpatient clinic, matched for age and gender distribution.

The study compared neurocognitive test results and inflammatory hemogram markers (WBC, NLR, MPV, PDW, PLR, RDW, HCT, LYM) between treated and untreated OSAS patients, as well as with the control group. A total of 106 OSAS patients who met the inclusion criteria were enrolled in the study. Additionally, a control group of 49 healthy volunteers with appropriate age and gender distribution was established.

Statistical analysis

Statistical analyses were conducted using R version 4.1.2 (https://www.r-project.org). Data normality was assessed using the Shapiro-Wilk test and Q-Q plots, while variance homogeneity was evaluated using Levene's test. Numerical data were presented as mean ± standard deviation or median [interquartile range (IQR)], and categorical variables were reported as frequency (n) and percentage (%).

Comparisons of demographic, hemogram, and cognitive parameters between OSAS patients and controls were performed using Welch's F test, Kruskal-Wallis test, one-way analysis of variance, or Pearson's chi-square tests. Post-hoc analyses for significant parameters were conducted using the Games-Howell test, two-proportion Z-test, Tukey HSD test, or Bonferroni-corrected Dunn test, as appropriate.

Further analyses compared relationships between demographic, hemogram, and cognitive parameters among treated and untreated OSAS patients using independent samples t-test, Welch's t-test, Yates-corrected chi-square test, or Mann-Whitney U test. Spearman's rho correlation coefficient was employed to examine associations between AHI and hematological and memory parameters in OSAS patients. Statistical significance was defined as $p < 0.05$.

RESULTS

Clinical analysis

A total of 155 participants were included in the study, comprising 49 healthy controls and 106 OSAS patients, aged between 21 and 61 years (45.73 ± 8.67), with 109 males (70.3%) and 46 females (29.7%). AHI values were calculated for the 106 OSAS patients, and they were classified into mild (10.27 ± 2.13), moderate (21.14 ± 3.86), and severe (44.47 ± 12.45) OSAS based on their AHI values.

As the severity of OSAS increased, patients showed an increase in their Body Mass Index (BMI). The proportion of males was significantly higher in the severe OSAS group compared to the control and mild OSAS groups, whereas the proportion of females was lower (Table 1). The prevalence of diabetes mellitus was 26.4% and hypertension was 35% in the OSAS patient group.

İnflammatory and cognitive test results between groups

Concerning cognitive parameters, all OSAS

patient groups scored lower than the control group in visual executive functions, naming, language, abstraction, and overall MoCA scores but no significant difference was observed between the OSAS groups (Table 1).

Only HCT levels were significantly higher among hemogram parameters in patients with moderate and severe OSAS than in healthy controls and individuals with mild OSAS (Table 1).

Epworth Sleepiness Scale (ESS) scores were significantly higher in all patient groups with OSAS compared to the control group (Table 1).

Relations between demographic characteristics, blood parameters, and cognitive tests of OSAS patients receiving and not receiving treatment were examined.

Demographic characteristics

It was found that the average age of treated OSAS patients was higher than that of untreated patients (49.32 ± 6.35 vs. 45.00 ± 8.92, p = 0.005), and a higher prevalence of hypertension was detected in treated patients (51.2% vs. 26.2%, p = 0.016) (Table 2).

Table 1: Demographic characteristics, inflammatory and cognitive parameters of patients with OSAS and the control group

		OSAS group			
	Control group (n= 49)	**Mild OSAS (n= 31)**	**Moderate OSAS (n= 34)**	**Severe OSAS (n= 41)**	**P**
Sex (M/F)	30^{a} /19^{a}	17^{a} /14^{a}	26^{ab}/8^{ab}	36^{b}/5^{b}	0.007^{2}
Age	43.71 ± 9.25	45.00 ± 9.43	48.18 ± 8.44	46.68 ± 7.07	0.127^{1}
BMI	25.59 ± 2.10^{a}	29.15 ± 5.85^{b}	30.99 ± 3.15^{b}	31.09 ± 4.56^{b}	$< 0.001^{1}$
MoCA (Visuospatial executive)	4.55 ± 0.50^{a}	4.00 ± 0.82^{b}	3.94 ± 0.95^{b}	4.00 ± 0.81^{b}	0.001^{4}
MoCA (Naming)	3.00 ± 0.00^{a}	2.81 ± 0.40^{b}	2.88 ± 0.33	2.98 ± 0.16^{a}	0.004^{4}
MoCA (Attention)	4.84 ± 0.75^{a}	4.61 ± 1.09^{a}	5.29 ± 0.80^{b}	4.93 ± 1.01	0.023^{4}
MoCA (Language)	2.39 ± 0.49	2.13 ± 0.56	2.06 ± 0.69	2.12 ± 0.71	0.097^{4}
MoCA (Abstraction)	1.63 ± 0.49^{a}	0.84 ± 0.86^{b}	0.85 ± 0.86^{b}	1.02 ± 0.79^{b}	$< 0.001^{4}$
MoCA (Delayed recall)	3.39 ± 0.57	3.13 ± 0.67	3.21 ± 0.69	3.00 ± 0.67	0.090^{4}
MoCA (Or(Orientation)	6.00 ± 0.00	6.00 ± 0.00	6.00 ± 0.00	6.00 ± 0.00	–
MoCA-Total score	25.80 ± 1.54^{a}	23.45 ± 2.71^{b}	24.24 ± 3.17^{b}	24.02 ± 2.60^{b}	< 0.001
MMSE	27.57 ± 1.72	26.81 ± 1.94	27.00 ± 2.00	26.98 ± 1.98	0.268
WBC	7.40 ± 1.71	7.67 ± 1.62	8.04 ± 1.40	7.67 ± 1.69	0.376^{3}
MPV	9.80 ± 1.14	10.18 ± 0.97	9.52 ± 1.34	9.64 ± 1.18	0.121^{3}
PDW	12.2 [10.5 – 16.2]	12.9 [11.45 – 15.85]	12.1 [10.93 – 16.1]	12.7 [10.7 – 14.8]	0.887^{4}
RDW	13.17 ± 1.06	13.27 ± 1.09	13.42 ± 1.03	13.02 ± 1.02	0.410^{3}
HCT	43.86 ± 3.36^{a}	43.64 ± 4.04^{a}	45.45 ± 3.11^{b}	45.85 ± 3.36^{b}	0.009^{3}
PLR	128.47 ± 39.60	116.04 ± 34.90	117.39 ± 32.21	117.92 ± 31.17	0.321^{3}
NLR	1.87 [1.53 – 2.56]	1.95 [1.46 – 2.47]	1.82 [1.61 – 2.26]	1.88 [1.38 – 2.45]	0.966^{4}
Epworth Sleepiness Scale	2.04 ± 0.96^{a}	10.23 ± 1.86^{b}	11.76 ± 4.02^{b}	11.24 ± 4.76^{b}	< 0.001

1: Welch's F-test; 2: Pearson chi-square test; 3: ANOVA test; 4: Kruskal-Wallis test; Different letters in the rows indicate statistically significant differences in pairwise comparisons; M: Male; F: Female; BMI: Body Mass Index; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; HCT: hematocrit; MPV: mean platelet volume; NLR: neutrophil-to-lymphocyte ratio; PDW: platelet distribution width; PLR: platelet-to-lymphocyte ratio; RDW: red cell distribution width; WBC: white blood cell.

Table 2: Demographic characteristics of patients with OSAS, comparing treated and untreated patients

	OSAS group		
	Not CPAP (n=65)	**CPAP (n=41)**	**P**
Age	45.00 ± 8.92	49.32 ± 6.35	0.005[1]
M/F	45 (69.2) /20 (30.8)	34 (82.9) /7 (17.1)	0.178[2]
Body mass index	29.90 ± 4.60	31.42 ± 4.61	0.102[3]
Diabetes mellitus	14 (21.5)	14 (34.1)	0.227[2]
Hypertension	17 (26.2)	21 (51.2)	0.016[2]

1: Welch's t-test; 2: Yates' continuity-corrected chi-square test; 3: Independent samples t-test; M: Male; F: Female.

Inflammatory and cognitive parameters

Among OSAS patients, blood parameters showed that treated individuals had significantly lower PDW, PLR, and NLR values compared to untreated patients. There was no significant difference in cognitive parameters between patients with untreated OSAS and those who received treatment (Table 3).

ESS scores were found to be significantly lower in treated OSAS patients compared to untreated patients (Table 3).

AHİ correlation analysis

The relationships between the AHI and inflammatory and cognitive parameters were examined using Spearman's rho correlation coefficient. The results showed a statistically significant positive correlation between AHI and naming ability (Spearman's rho = 0.236, p = 0.015). No statistically significant relationships were observed between AHI and other cognitive parameters or any blood parameters (Table 4).

Table 3: İnflammatory and cognitive parameters of treated and untreated patients with OSAS

	OSAS group		
	Not CPAP (n=65)	**CPAP (n=41)**	**P**
MoCA(Visuospatial executive)	4.03 ± 0.83	3.90 ± 0.89	0.488[4]
MoCA (Naming)	2.88 ± 0.33	2.93 ± 0.26	0.418[4]
MoCA (Attention)	4.89 ± 1.08	5.05 ± 0.86	0.683[4]
MoCA (Language)	2.02 ± 0.67	2.24 ± 0.62	0.087[4]
MoCA (Abstraction)	0.86 ± 0.85	1.00 ± 0.81	0.387[4]
MoCA (Delayed recall)	3.05 ± 0.69	3.20 ± 0.64	0.301[4]
MoCA (Orientation)	6.00 ± 0.00	6.00 ± 0.00	-
MoCA-Total score	23.74 ± 2.99	24.22 ± 2.52	0.394[3]
MMSE	26.88 ± 1.97	27.02 ± 1.96	0.708[3]
WBC	7.81 ± 1.51	7.75 ± 1.70	0.842[3]
MPV	9.79 ± 1.30	9.71 ± 1.05	0.730[1]
PDW	13.6 [11.4 – 16]	11.6 [10.6 – 13]	0.011[4]
RDW	13.17 ± 1.11	13.30 ± 0.94	0.538[3]
HCT	44.93 ± 3.70	45.30 ± 3.43	0.610[3]
PLR	120.34 [96.63 – 149.66]	104.71 [90.34 – 123.10]	0.045[4]
NLR	2.14 [1.62 – 2.56]	1.83 [1.33 – 2.13]	0.039[3]
Epworth Sleepiness Scale	13.37 ± 2.98	7.54 ± 1.99	< 0.001[1]

1: Welch's F-test; 2: ANOVA test; 3: Kruskal-Wallis test; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; HCT: hematocrit; MPV: mean platelet volume; NLR: neutrophil-to-lymphocyte ratio; PDW: platelet distribution width; PLR: platelet-to-lymphocyte ratio; RDW: red cell distribution width; WBC: white blood cell.

Table 4: Relationship between AHI and blood and cognitive parameters

	Apnea-Hypopnea Index	
	Sperman rho	**p**
Blood parameters		
WBC	0.009	0.927
MPV	–0.142	0.147
PDW	–0.078	0.424
RDW	–0.124	0.205
HCT	0.173	0.076
PLR	0.031	0.751
NLR	0.005	0.959
Cognitive parameters		
MoCA (Visuospatial executive)	–0.020	0.837
MoCA (Naming)	0.236	0.015
MoCA (Attention)	0.120	0.220
MoCA (Language)	0.033	0.740
MoCA (Abstraction)	0.077	0.434
MoCA (Delayed recall)	–0.062	0.530
MoCA (Orientation)	-	-
MoCA-Total score	0.050	0.611
MMSE	0.010	0.918

MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; HCT: hematocrit; MPV: mean platelet volume; NLR: neutrophil-to-lymphocyte ratio; PDW: platelet distribution width; PLR: platelet-to-lymphocyte ratio; RDW: red cell distribution width; WBC: white blood cell.

DISCUSSION

The number and diversity of studies investigating the impact of OSAS on cognitive functions are increasing. Although findings remain inconsistent, cognitive deficits have been observed in patients with OSAS. Evidence indicates impairments in intellectual functioning, memory, attention, and executive functions. An analysis of previous studies reveals contradictory findings in the literature on cognitive impairments associated with OSAS. One primary reason for these discrepancies may be the use of different tests to assess various components of cognitive domains. CPAP treatment does not reverse all identified cognitive deficits. Identifying which groups are at higher risk of cognitive impairment and understanding how and why these individuals should receive treatment are crucial goals for future research.[7]

The primary aim of this study was to investigate the presence of cognitive impairment in OSAS patients, identify the affected cognitive components, and evaluate the impact of CPAP treatment on these components. The most significant pathophysiological mechanisms underlying cognitive impairment in OSAS are intermittent hypoxemia and sleep fragmentation. Prolonged hypoxemia may lead to neurodegeneration in the hippocampus and prefrontal cortex, regions associated with executive functioning and memory deficits.[8] Sleep fragmentation, on the other hand, can result in the accumulation of toxic metabolites in the brain, triggering pathological changes similar to those seen in Alzheimer's disease.[9]

In our study, all OSAS patient groups exhibited lower total MoCA scores compared to the control group ($p < 0.001$). When subcomponents were analyzed, abstraction ($p < 0.001$), executive functions, and naming scores were significantly lower in all patient groups compared to controls. These findings align with previous research in the field.[10-18]

CPAP therapy has been hypothesized to mitigate cognitive impairment by reducing the detrimental effects of hypoxia and sleep fragmentation. However, findings regarding its efficacy remain mixed. Four studies assessing cognitive function before and after CPAP treatment using the MMSE scale reported no significant improvement in

OSAS patients[16,19-22], while other studies observed effects of varying magnitudes.[15,23-27] In our study, no significant difference in MMSE scores was identified between the control group and the OSAS patient groups (p = 0.268). Although the MMSE scores in the treated OSAS group (27.02 ± 1.96) were slightly higher than those in the untreated group (26.88 ± 1.97), this difference did not reach statistical significance (p = 0.708).

The variability in the areas and extent of cognitive improvement reported across studies can be attributed to several factors, including differences in methodologies, neuropsychological assessment tools, clinical characteristics of the participants, and levels of treatment adherence. The inconsistent findings regarding the impact of CPAP on cognitive function may stem from the heterogeneity of the data and the diverse test instruments employed. This heterogeneity could be influenced by variations in study design, differences in cognitive reserve, the specific cognitive domains examined, and other contextual factors.

In our study, the comparison of total MoCA scores between the CPAP-treated and untreated OSAS groups showed a higher mean score in the treated group (24.22 ± 2.52) compared to the untreated group (23.74 ± 2.99); however, this difference was not statistically significant (p = 0.394). Similarly, the CPAP-treated group demonstrated higher scores in specific cognitive domains, including visual executive functions, naming, attention, language, abstraction, and long-term memory. Despite these trends, none of the observed differences reached statistical significance.

The limited improvement identified in our analysis indicates the potential involvement of additional mechanisms underlying cognitive impairment in OSAS that are not alleviated by CPAP treatment. These mechanisms may include neuronal degeneration, cell death, and dysfunction of the blood-brain barrier, suggesting the need for further research to fully elucidate the complex pathways contributing to cognitive decline in OSAS patients.

Conducting randomized controlled trials to evaluate the long-term health effects of CPAP and other treatments for OSAS poses significant challenges. These include maintaining clinical equipoise, such as the ethical implications of randomizing symptomatic patients to untreated groups over extended periods, and ensuring sufficient adherence to treatment protocols. These complexities highlight the need for well-structured studies to better understand the effects of OSAS treatments on cognitive outcomes.

When all studies are evaluated, CPAP appears to have limited benefits on cognitive performance. Studies measured cognitive function and CPAP usage are limited due to study design, small sample sizes, and lack of randomization. Further research is required to investigate the impact of alternative OSAS treatments on cognitive functions.

Our results found that cognitive function is affected in OSAS patients, with more pronounced impairments in executive functions, naming, and abstraction, and that the MoCA test appears to be more sensitive than the MMSE for assessing global cognition in OSAS patients. However, although there was an increase in total cognitive score with CPAP treatment, it was not statistically significant.

The second objective of our study was to evaluate whether hematological parameters can serve as indicators of the damage caused by local and systemic inflammation in patients with OSAS and to assess the impact of CPAP treatment on these parameters.

OSAS is marked by recurrent episodes of transient hypoxemia, which is hypothesized to result in secondary polycythemia or erythrocytosis. Despite this hypothesis, systematic studies investigating this phenomenon remain limited. The most plausible mechanism underlying this process is that hypoxemia stimulates erythropoietin production, which subsequently leads to an increase in hematocrit levels. Further research is required to clarify the relationship between hypoxemia-induced hematological changes and the pathophysiology of OSAS, as well as the potential modifying effects of CPAP therapy. A retrospective study involving 1,087 male OSAS patients identified a significant correlation between HCT levels and the AHI. Multiple linear regression analysis confirmed that HCT was independently associated with AHI, highlighting the relationship between OSAS severity and increased hematocrit levels.[28] Conversely, Nguyen *et al*. reported that OSAS severity was not linked to hematocrit levels or clinically significant erythrocytosis. Instead, their findings demonstrated an inverse relationship between HCT levels and measures of oxygen saturation, such as wake oxygen saturation and mean nocturnal oxygen saturation.[29] Similarly, Choi *et al*., in a comparison between untreated OSAS patients and healthy controls, found that while OSAS severity was statistically significantly associated with minor increases in HCT levels, the condition itself did not lead to clinically significant

polycythemia.[30] These findings underscore the complexity of hematological changes in OSAS and suggest that factors beyond OSAS severity, such as hypoxemia patterns and oxygen saturation levels, may play a more prominent role in influencing hematocrit. Various hematological guidelines recommend considering OSAS as a contributing factor in the diagnostic evaluation of secondary erythrocytosis.[31] In our study, HCT levels were significantly elevated in patients with moderate to severe OSAS compared to healthy controls and patients with mild OSAS. However, no statistically significant difference in HCT levels was observed between treated and untreated OSAS patients ($p = 0.610$).

Inflammatory conditions associated with OSAS can lead to platelet activation, adhesion, and aggregation, resulting in increased platelet volume. Among the eight studies examining this phenomenon, only four reported a statistically significant association between OSAS and MPV.[32-39] The effect of CPAP therapy on MPV appears to be inconsistent across these studies. In our study, we found no significant difference in MPV values between OSAS patients and the control group ($p = 0.121$). Similarly, MPV levels did not differ significantly between treated and untreated OSAS patients ($p = 0.730$). These findings suggest that MPV may not serve as a reliable biomarker for inflammation or treatment response in OSAS, warranting further investigation to clarify its role.

PLR holds predictive value in several conditions, including cardiovascular, autoimmune, and respiratory diseases. Recent research has identified PLR as a significant marker for OSAS[40], and another study established a meaningful association between the AHI and PLR.[41] However, the findings regarding PLR in OSAS patients remain inconsistent. Two case-control studies reported no significant difference in PLR between OSAS patients and control groups[32-36,40-42], while another study noted lower PLR values in controls compared to OSAS patients.[42] Conversely, Zota *et al*. found no significant difference in PLR between OSAS patients and controls.[43] In our study, no significant difference in PLR was observed between the control group and the OSAS group ($p = 0.321$). However, when comparing treated and untreated OSAS patients, PLR was significantly lower in the treated group ($p = 0.045$). These findings suggest that PLR may have potential utility in monitoring and assessing OSAS patients, particularly in evaluating the effects of treatment. Further research is warranted to elucidate its role in clinical practice.

RDW reflects variability in red blood cell size and volume and is an inexpensive and readily available parameter that is unaffected by factors such as sex, age, or BMI. RDW has been proposed as a marker of subclinical inflammation associated with cardiovascular morbidity and mortality.[44] Recurrent hypoxia caused by OSAS accelerates erythropoiesis, which may explain the elevated RDW levels observed in individuals with OSAS.[45] Durmaz *et al*. demonstrated that RDW serves as an indicator of OSAS severity.[42] The effect of CPAP therapy on RDW levels, however, appears to be limited. Leon Subias *et al*. reported no change in RDW values after one year of CPAP therapy[44], whereas Özdemir et al. observed an increase in RDW after 3–6 months of CPAP treatment.[46] Additionally, Zota *et al*. found that RDW levels were higher in patients with severe OSAS compared to controls and suggested that an RDW value greater than 13.65 could predict moderate to severe OSAS. However, they noted no significant change in RDW levels after 8 weeks of CPAP therapy.[43] In our study, RDW values did not significantly differ between the OSAS and control groups, nor between treated and untreated OSAS patients. These findings suggest that while RDW may hold diagnostic potential in identifying OSAS severity, its utility in monitoring treatment response, particularly with CPAP, remains uncertain. Further research is required to clarify its clinical relevance in this context.

Intermittent hypoxia in OSAS stimulates the activation of nuclear factor kappa-B, which in turn activates genes responsible for granulocyte and macrophage colony-stimulating factors. This mechanism may underlie the observed association between NLR and OSAS.[47] Some studies suggest that NLR could serve as a marker of chronic hypoxic exposure in OSAS and a practical parameter for evaluating CPAP treatment efficacy.[48] Oyama *et al*. identified a significant correlation between NLR and the AHI.[49] However, Özdemir *et al*. found no significant effect of CPAP therapy on NLR values[46], and Zota *et al*. similarly reported no reduction in NLR levels after 8 weeks of CPAP treatment.[43] In our study, there was no significant difference in NLR values between the OSAS patient group and the control group ($p = 0.966$). Nevertheless, NLR values were higher in untreated OSAS patients compared to those who received treatment ($p = 0.039$). This finding suggests that NLR may have some utility in monitoring treatment response in OSAS, particularly in identifying the impact of CPAP

therapy on systemic inflammation associated with the condition.

In addition to cognitive assessments, inflammatory parameters derived from hemogram analysis were also examined. HCT levels were found to be higher in OSAS patients compared to the control group. Notably, patients who received CPAP treatment exhibited statistically significant reductions in PLR, PDW, and NLR values compared to untreated patients. These findings suggest that such parameters may offer partial utility in monitoring and prioritizing patients suspected of having OSAS. However, further large-scale studies are required to establish optimal values and clarify their role in evaluating treatment adherence and effectiveness in OSAS.

The most significant strength of our study lies in its combined evaluation of cognitive functions and inflammatory parameters that have practical applicability in the clinical management of OSAS patients. However, our study has several limitations. Its retrospective design represents a key drawback, and the single-center setting and small sample size further limit the generalizability of the findings. Future research with larger patient populations, longer follow-up periods, and prospective designs will be essential to confirm and expand upon these results.

DISCLOSURE

Ethics: This study was approval by the Selçuk Universty Ethics Committee (decision number: E-70632468-050.01.04-423025).

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